ISSN 2148-7197 • EISSN 2149-2530

Turkish Thoracic Journal

Official Journal of the Turkish Thoracic Society

ISSUE 3 JULY 2016 VOLUME 17

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Turkish Thoracic Journal

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Publishing House

bilimsel tıp yayınevi

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Official journal of the Turkish Thoracic Society

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Turkish Thoracic Journal started its publication life following the mergence of two seperate journals which are published under the titles "Turkish Respiratory Journal" and "Toraks Journal" until 2007. Archives of both journals were passed on to the Turkish Thoracic Journal.

The aim of Turkish Thoracic Journal is to publish pulmonary disease-related clinical, experimental and epidemiologic studies that are scientifically highly qualified. Additionally, reviews, editorials, letters to the editor, and case reports are also accepted. Reports presented in meetings organized by the Turkish Thoracic Society Head Office or national and international consensus reports are published as supplements. The journal is published 4 times annually, in January, April, July and October. The target-groups are chest diseases physicians, thoracic surgeons, internal medicine doctors and practitioners interested in pulmonary diseases.

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2. The aim of the journal is to convey scientific developments in thoracic diseases and surgery, and to create a dynamic discussion platform about pulmonary diseases. With this intent, the journal accepts articles from all related scientific areas that address thoracic diseases and cell biology, epidemiology, immunology, pathophysiology, thoracic imaging, pediatric chest diseases, environmental and occupational disorders, intensive care, sleep disorders and thoracic surgery. Clinical and research articles, reviews, statements of agreement or disagreement on controversial issues, national and international consensus reports, abstracts and comments of important international articles, interesting case reports, puzzling cases, writings related to clinical and practical applications, letters to the editor, and editorials are accepted.

Presentations and reports of meetings organized by Turkish Thoracic Society Head Office and its branches can be published as supplements.

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11. Simultaneously with the submission of manuscripts, the "Author Agreement Form" signed by all contributing authors should be sent to the Turkish Thoracic Journal Editorial Office via fax or e-mail. Otherwise, submitted manuscripts will not be taken into consideration.

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Research articles should include separate sections for Introduction, Material and Methods, Results, Discussion. Pharmaceutical products can be mentioned either with their generic or commercial names (generic names are preferred). Commercial names should be written with capital letters, followed by the company and its city in parenthesis. Acknowledgements, references, tables and figure legends should follow the main text. Tables should be presented at the end of the text and each on a separate page.

c. The "Acknowledgements" section should be placed at the end of the text before the references and should not exceed one paragraph.

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Supplementary
QF. Risk assessment of nickel carcinogenicity and occupational lung cancer. Environ Health Perspect 1994;102 (Suppl 1): 2755-82.

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Ennzensberger W, Fischer PA. Metronume in Parkinson's disease (Letter). Lancet 1996;347:1337.

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Congress Presentation
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Thesis
Kaplan SJ. Post-hospital home health care: the elderly's access and utilization [Thesis]. St Louis (MO): Washington Univ; 1995.

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e. Tables: Each table should be typed on a separate page and table's entries should be double-spaced. Tables should be numbered with arabic numeral(s) and cited in the order of appearance in the text. A brief title for the table should be written above the table.

f. Figures: All figures should be high-quality (at least 300 dpi resolutions) in .jpeg or .jpg format, and should be provided in black and white. If providing a better understanding of the topic, colored figures will be accepted in limited number. For each manuscript, six figures at most will be accepted. Figures should be numbered with Arabic numeral(s) in order of appearance in the text. The type of the dye that was used, magnification scales, and internal scale bar should be stated for microscopic photographs. A centimetric template should be added for pathologic specimens. Ethical values should be protected in any patient-related photograph or graphs. If the identity of the patient can be revealed by the provided photographs and graphs, a written consent should be requested from the patient. The figures should be cited in parenthesis with their respective numbers within the main text. All figure legends should be on a separate page after references and tables. A written permission is required for reproduced figures.

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h. Case reports should contain sections for English title, English running title, English abstract, keywords, Introduction, Case Presentation and Discussion. They should include new cases or imply clear messages. All submitted case reports will be first reviewed by the editorial committee and those that do not include new cases and/or do not imply clear messages could be rejected without sending it for arbitration.

i. In puzzling case reports, a short introduction should be followed by the description of the problem, presentation of clue photos and figures, definite diagnosis, and a discussion section where the diagnosis is discussed and educational messages are emphasized.

j. Disagreement/agreement articles should not exceed three pages, and clinical practice articles should not exceed three pages including text, figures, images and references.

k. The section for the "Letters to the Editor" should be formatted shortly and concisely, without any summary, and should be restricted in the number of references since it is mainly written to provide support or criticism over previously published articles.

l. Abbreviations should be written in the accepted international format and under parenthesis on the first mention and this abbreviation should be used throughout the text.

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EDITORIAL

Turk Thorac J 2016; 17

DOI: 10.5578/ttj.30512

Editorial Board Change

Metin Akgün[1,2], Oğuz Kılınç[1,3]

[1] *Chief Editor*

[2] *Department of Chest Diseases, Atatürk University Faculty of Medicine, Erzurum, Turkey*

[3] *Department of Chest Diseases, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey*

Dear Colleagues,

This June has brought a renovated editorial team to the Turkish Thoracic Journal (TTJ), which is the official journal of Turkish Thoracic Society (TTS), because past chief editors, Hasan Bayram and Öner Dikensoy, were elected for the executive board membership of TTS. We are honored to take the leader ship of the journal, which is a great challenge and a big responsibility, and thank to past editors for their great effort making the journal more visible. While Dr. Mehmet Bayram and Özge Yılmaz maintained their position as the associate editors, Dr. Ufuk Çağırıcı, Dr. Zuhal Karakurt and Dr. Zeynep Pınar Önen, became our new associate editors.

The journal has been indexed in Emerging Sources Citation Index since 2015; however, we aim to increase its impact and TTJ has been indexed in SCI-expanded in the near future. We, as the new editorial board, are very enthusiastic to strive for continual improvement in the journal. We are also aware of the challenges on this way and need to step up the gear. We would welcome and encourage physicians and researchers from worldwide to consider TTJ for submitting their manuscripts.

Yours sincerely.

Turk Thorac J 2016; 17: 89-92 DOI: 10.5578/ttj.30502

ORIGINAL INVESTIGATION

Do Meteorological Changes Have an Effect on The Occurence of Spontaneous Pneumothorax?

Menduh Oruç[1], Atalay Şahin[1], Recep Dursun[2], Mahşuk Taylan[3], Ahmet Erbey[1], Fatih Meteroğlu[1], Bülent Öztürk[1], Refik Ülkü[1]

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Abstract

OBJECTIVES: Spontaneous pneumothorax refers to the leakage of air into the space between the parietal and the visceral layers of the pleura. It occurs with or without a known lung disease. We aimed to investigate the effects of atmospheric pressure, humidity, and temperature changes on the incidence of spontaneous pneumothorax (SP).

MATERIAL AND METHODS: This study included 551 patients with spontaneous pneumothorax retrospectively screened between January 2009 and December 2013. The medical data of the patients were accessed via their medical records on the hospital automation system. The atmospheric pressure, temperature, humidity rate, amount of precipitation, and wind velocity on the day of spontaneous pneumothorax were obtained from the data provided by the general directorate of meteorology. The three consecutive days on which at least 2 cases of SP presented were collectively considered as a cluster. The study data were analyzed with the SPSS version 15 software package, using the Chi-square and the Student's t tests. A p value less than 0.05 was considered statistically significant.

RESULTS: Of the 552 patients included in the study, 89.3% had primary spontaneous pneumothorax and 10.7% had secondary spontaneous pneumothorax. Ninety-two percent of the patients were male and 8% were female. The mean age was 24 years. Clustering was observed in 71.7% of the study population. No significant differences were observed between yearly and monthly SP incidences. There were, however, differences between the days with SP and the days without SP with respect to atmospheric pressure, ambient temperature, wind velocity, and humidity rate. The differences between the atmospheric pressures were not statistically significant, although the differences between the ambient temperature and the humidity rate were statistically significant ($p \leq 0.05$).

CONCLUSION: We determined that the changes in the ambient temperature and the humidity rate affected the rate of spontaneous pneumothorax by altering the meteorological conditions.

KEYWORDS: Atmospheric pressure, temperature, pneumothorax-humidity, amount of precipitation, spontaneous

Received: *05.04.2015* ***Accepted:*** *29.12.2015*

INTRODUCTION

The term pneumothorax was first used by Itard followed by Laennec in 1803 and 1819, respectively [1]. The term spontaneous pneumothorax refers to the leakage of air of any cause into the space between the parietal and the visceral layers of the pleura [2]. It has primary and secondary types. The primary spontaneous pneumothorax (PSP) occurs without a known lung disease whereas the secondary spontaneous pneumothorax (SSP) occurs in persons with underlying lung pathology [3]. Unlike the PSP, the SSP is related to the underlying lung pathology although tuberculosis is no longer the most common underlying pathology in the developed world. The consequences of pneumothorax are more severe and generally difficult-to-treat in persons with previous lung disease [4].

The most common cause of the PSP is the tearing of the apical subpleural blebs. The affected patients are typically young, tall, and thin males. Some authors have linked the high rate of incidence of the PSP in those patients to a higher apical pleural negative pressure. The SSP variety, on the other hand, usually occurs due to an underlying lung disorder, such as obstructive lung disease, tuberculosis, immune deficiency syndromes, sarcoidosis, pneumonia, or cystic fibrosis [5]. Some authors have hypothesized that there is a prominent link between the SP rate and low humidity in that the bronchoconstriction occurring during humidification of dry air inside the airways may play a role in the

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physiopathology of pneumothorax and thus atmospheric pressure changes as well as humidity and increased temperature may increase SP rate [6-9].

We investigated the effects of the meteorological changes including atmospheric pressure, humidity, and temperature changes on the incidence of spontaneous pneumothorax (SP) in a continental climate.

MATERIAL AND METHOD

After obtaining the approval of our university's local ethics committee, we retrospectively studied the patients who presented to the departments of emergency medicine and chest surgery and were diagnosed with SP between January 2009 and December 2013. The patients in whom a tube thoracostomy procedure was not performed (those with minimal pneumothorax) were excluded. Minimal pneumothorax cases, which are radio occult on chest X-Rays, were treated with oxygen support and did not undergo any surgical intervention including needle aspiration. The 551 patients included in the study were analyzed through hospital records with regard to exposure to cigarette smoke, clinical properties, and comorbidities. The clinical properties of the patients who underwent tube thoracostomy or, after tube thoracostomy failure, video-assisted thoracoscopic surgery or axillary thoracotomy were studied. Treatment options in pneumothoraces were not compared in this study.

The general directorate of Meteorology provided the meteorological variables including the daily atmospheric pressures (hPa), temperature levels, humidity rate, amount of precipitation, and wind velocity on the days of patient presentations. As of the date of the study, there were 14 reading stations in our geographical region. According to the information provided by the local authorities, all meteorological data were analyzed under similar conditions and in similar stations. The data in question included temperature readings in centigrade (C°) degrees, daily average pressure (hPa) in millibars, daily average humidity in percentage (%), the amount of precipitation in millimeters, daily maximum wind velocity in m/sec and wind direction in direction name. In addition, the minimum values of the atmospheric pressure, temperature, and humidity rate were substracted from the maximum values of the same parameters to calculate the maximum-minimum difference. Then, based on the day of hospital presentation of 551 patients, we compared the daily atmospheric pressure, temperature readings, humidity rates, the amount of precipitation, and the wind velocities of that day. The three consecutive days on which at least 2 cases of SP presented were collectively considered as a cluster and the meteorological events at the clustering days were recorded.

Statistical Analysis

The meteorological data were analyzed with the SPSS version 15 software package (SPSS Inc. Chicago, Illinois, USA), using the Chi-Square and the Student's t tests. The demographic variables of the patients were analyzed using the Chi-Square and the Student's t tests. A p value less than 0.05 was considered statistically significant. Logistic regression analysis was conducted to investigate the association between the occurrence of pneumothorax and meteorological variables.

RESULTS

The mean age of the study population was 23.96 ± 9.28 years and 92% were male (Figure 1). PSP was present in 89.3% of the patients and SSP in the rest. The disease predominantly affected males (92%). PSP was most commonly seen in the second decade while SSP was more common in those aged over 40 years. Males had SP at earlier ages than their female counterparts. Among the PSP group, pneumothorax was right-sided in 252 (45.65%) patients and left-sided in 240 (43.47%) patients; the difference between the number of right- and left-sided pneumothoraces in PSP and SSP was not statistically significant (p= 0.95); and the proportion of smokers (n= 492, 89.3%) were much more in number than non-smokers (n= 59, 10.7%), and the difference between the two groups was not significant (p= 0.07) (Figure 1).

There were no significant differences between the monthly and yearly distribution of the pneumothorax cases during the years 2009-2013. The cases were the least common in winter (n= 130) and fall (n= 131) and the most common in summer (n= 147) and spring (n= 140). Sorted by month of incidence, the highest number of cases occurred in September (n= 55), followed by May and July (n= 54 for each), while the least number of cases occurred in January (n= 38) and November (n= 39). Other months had very similar number of cases (Figure 2). Significant differences were found between the patients with respect to age and gender (p< 0.001). As the patients were retrospectively assessed, the day of SP incidence was accepted as the day of hospital presentation. Clustering was observed in 71.7% of the patients. A cluster contained 2.82 patients on average. Clusters occurred during or after decreasing in humidity. There was an association between days with pneumothorax and days on which ambient temperature rised.

The days with SP incidents had significantly different atmospheric pressure, ambient temperature, wind velocity, and humidity rate when compared to the days without SP (p< 0.05). The amount of precipitation and the difference between the maximum and minimum atmospheric pressure were not significantly different at the days with SP incidents

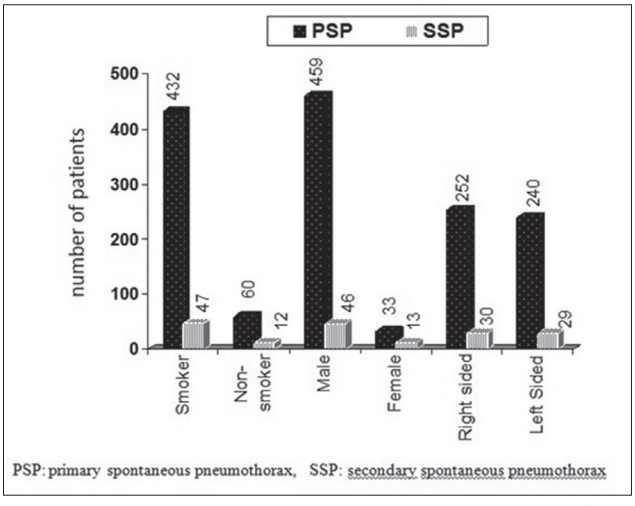

Figure 1. The demographic and clinical characteristics of the pneumothorax cases.

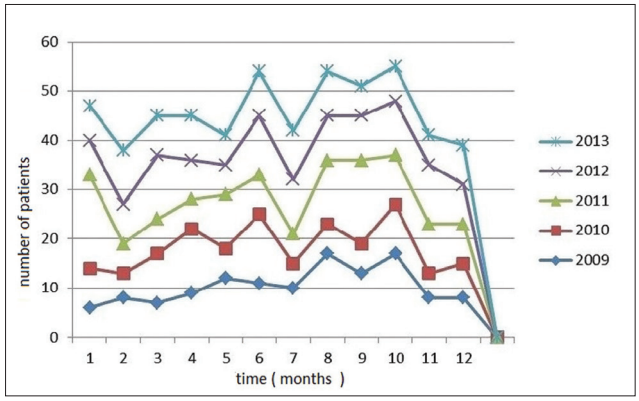

Figure 2. Number of pneumothorax cases by month during the years 2009 to 20013.

(p≥ 0.05). The minimum and maximum temperatures were significantly different (p< 0.05). The mean temperature rise and the humidity rate were significantly different between the groups (p< 0.05). The meteorological conditions of the day before the day of SP incidence were also not significantly different (Table 1). Table 2 shows factors associated with pneumothorax occurrence. R2 value was 0.276 and statistically significant (p< 0.001).

DISCUSSION

Incidence of pneumothorax is around 18-28/100.000 in men and 2-6/100.000 among women [3,7]. In our study, 92% of the patients were male and the rest were female. Unlike PSP, SSP is related to the underlying lung pathology; however, tuberculosis has lost its top place among the causative conditions in developed world. The clinical outcomes are graver and the treatment poses more challenges in patients with previous lung disorders [4]. In our study the PSP patients had no underlying lung pathology but most of those with SSP had chronic obstructive pulmonary disease or tuberculosis. Smoking was considered as the most common etiological agent. While the smoking habit was related to a pneumothorax risk of 12% in healthy men, it was 0.1% in non-smokers [10]. In our study 492 males were smokers. The rate of smoking was high among both smokers and non-smokers, albeit statistically non-significant.

Spontaneous pneumothorax develops secondary to some factors that induce rupture of bullae and blebs in persons with no known disease. There is, however, no consensus as to the causes that precipitate SP incidence and increase the number of SP cases. Transpulmonary pressure gradient leads to air entrapment and development of SP. A sudden change in pressure may cause SP during flight or diving. Many former studies have investigated the impact of meteorological variables (atmospheric pressure, ambient temperature, amount of precipitation, humidity rate, and wind velocity) on the incidence of SP [7,11]. A clustering pattern of the hospital presentations of the SP cases have led to scrutinization of the climate and weather conditions. It has been suggested that the undulation of the weather conditions cause weakening of the walls of small air cysts in lungs. However, we obtained results similar to some other trials that have reported no relationship between SP incidence and seasons, months [7]. SP occurs in episodes and clusters [11,12]. More than 2 cases in 3 consecutive days are considered a cluster of cases [7,12]. We found a clustering rate of 71.7% in our study. Some previous studies have found a relation between the atmospheric pressure changes, windy days and SP incidence [12]. Meteorological changes not only cause SP but also certain other respiratory problems. Having born as a result of this interaction, cough plays a triggering role. Unlike literature data, our results suggested no effect of daily drops in atmospheric pressures on SP occurrence. Some studies have reported that temperature changes exert significant effect on SP incidence and our results were compatible with those observations [8,9]. This phenomenon may be explained by the effect of temperature on pressure [13,14]. Temperature and humidity readings that were found in significant relationship with SP occurrence in our study may be observed in stormy days with higher wind velocities [15,16]. Changes in air composition such as higher concentrations of ground ozone levels in addition to heat waves and extreme

Table 1. The meteorological variables on the days with versus without SP occurrence

Parameters	Days with SP Mean ± SD	Days without SP Mean ± SD	p
Minimum temperature ºC (min.)	10 ± 8.7	9.06 ± 8.6	0.037
Maximum temperature ºC (max.)	24.3 ± 11.5	22.9 ± 11.4	0.037
Temperature difference ºC (max-min)	14.2 ± 4.9	13.9 ± 5	0.231
Minimum atmospheric pressure (mbar)	932.8 ± 5.9	933.29 ± 5.97	0.182
Maximum atmospheric pressure (mbar)	936.34 ± 5.98	936.76 ± 5.87	0.205
Atmospheric pressure difference (mbar)	3.49 ± 1.62	3.46 ± 1.76	0.769
Total amount of precipitation (mm)	4.32 ± 6.12	4.95 ± 7.69	0.452
Wind velocity (m/s)	1.46 ± 0.69	1.4 ± 0.67	0.112
Mean atmospheric pressure (mbar)	934 ± 5.89	935 ± 5.83	0.195
Mean temperature ºC	17.28 ± 10.3	16 ± 10.2	0.034
Humidity (%)	49.9 ± 25.5	52.8 ± 25.4	0.044

SP: Spontaneous pneumothorax.

Table 2. Factors associated with accurence of pneumothorax in the logictic regression model

Factors	Sig. P	OR	95% C.I.
Min C°	0.185	1.038	0.98-1.09
Max P	0.580	1.017	0.95-1.07
Rainfall	0.464	0.987	0.95-1.02
Wind	0.700	1.079	0.73-1.59
Humidity	0.845	1.002	0.98-1.02

Variable(s) entered on equation: Min C^0: Minimum temperature, Max P: Maximum pressure, rainfall, wind, humidity.

meteorological events may fluctuate and cause respiratory diseases. High levels of ozone were found to be a precipitating factor in the damage of lung tissue elasticity and also be a factor in the rupture of blebs or bullae in occurrence of SP during spring season [17].

Bertolaccini et al. found that SP incidence was significantly affected by smoking and viral infection in addition to higher concentrations of environmental pollution and constant exposure to allergens [14]. For this purpose they evaluated meteorological variables and variables of the environmental pollution altogether. In that analysis, the daily mean maximum ozone and the daily minimum nitrogen dioxide (NO_2) were significantly related to SP occurrence. The mean amount of the particles causing daily environmental pollution and the daily minimum and maximum nitrogen dioxide (NO_2) were less important [14]. Although SP clustering due to environmental pollution is common, as stated by some publications, we did not evaluate the relationship between the industry-related environmental pollution and SP clustering since no such pollution was evident in our study. Many of changes in climate are reported to have negative effects on respiratory health and the frequency and severity of respiratory diseases. The effects of meteorological changes on respiratory diseases are still not well defined, and more studies addressing this topic are needed [18].

In conclusion, in this study we determined that the changes in the temperature readings and the humidity rates alter weather conditions, affecting SP incidence. Although we found some relationship between some meteorological variables and SP incidence, there is still a need for more comprehensive multicentric and prospective studies.

The authors declare that we did not have any financial relations/support concerning the study. We also state that we scientifically contributed to and took responsibility in the study and declare that there is no conflict of interest.

Author Contributions: Concept - M.O., A.S.; Design - M.O., B.O.; Supervision - A.Ş., F.M.; Funding - M.O., A.E.; Materials - M.O., R.D., F.M.; Data Collection and/or Processing - M.O., A.Ş.; Analysis and/or Interpretation - A.Ş., M.O., R.Ü; Literature Review - B.Ö., A.E.; Writer - A.Ş., R.D.; Critical Review - M.O., R.Ü

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial supports.

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Turk Thorac J 2016; 17: 93-99 DOI: 10.5578/ttj.30503

ORIGINAL INVESTIGATION

Arterial Blood Gas Analysis in Chronic Obstructive Pulmonary Disease Patients Undergoing Coronary Artery Bypass Surgery

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Abstract

OBJECTIVES: We aimed to investigate the impact of arterial blood gas (ABG) on morbidity and mortality in chronic obstructive pulmonary disease (COPD) patients undergoing CABG surgery.

MATERIAL AND METHODS: The records for 75 COPD patients who underwent elective CABG surgery our institution clinic between November 2008 to 2011 and had a forced expiratory volume in 1 second (FEV_1) /forced vital capacity (FVC) ≤ 70% value in the pulmonary function tests (PFT) performed prior to the surgery were evaluated retrospectively. COPD patients were divided into two groups; Group 1; FEV_1 ≥ 60% and Group 2; FEV_1 ≤ 59%. Groups were compared for mortality and adverse events after identification of other preoperative and postoperative factors that could affect mortality and adverse events. An ABG was obtained immediately before and 3 to 6 hours after surgery to study the predictive value of ABG in seperate COPD groups.

RESULTS: There were no significant differences in patients with high partial pressure carbondioxide ($PaCO_2$) preoperative values compared to patients with normal values. Also there were no significant differences in patients with lower partial pressure of oxygen (PaO_2) preoperative values compared to patients with normal values in terms of mortality. Postoperative myocardial infarction (MI) was significantly higher in patients with low PaO_2 values ($p< 0.05$).

CONCLUSION: In conclusion, in our study, there could not be found a relation between the degree of preoperative obstruction and mortality for COPD patients who underwent CABG surgery. ABG was not found useful for predicting mortality in COPD patients undergoing CABG surgery, but could be useful to predict postoperative MI in patients with COPD.

KEYWORDS: Coronary artery bypass graft surgery, chronic obstructive pulmonary disease, arterial blood gas analysis

Received: *18.09.2015* ***Accepted:*** *20.01.2016*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a partially reversible disease characterized with the limitation of airflow, which develops as a result of the inflammation of the respiratory tract. COPD is a substantial problem affecting pre and post-operative success in patients on whom adult coronary artery bypass grafting (CABG) is performed. It was first expressed in 1963 that COPD is a relative contraindication in terms of coronary artery surgery [1]. It has been known till then that the association of CABG (coronary artery bypass grafting) and COPD is a dangerous one. Mortality reaching up to 50% was found in studies carried out in the past years and the presence of COPD created unrest [2]. However, in recent years, preoperative intense therapies, use of more efficient medication and showing more sensitivity to patients with COPD have decreased mortality and morbidity [3].

Arterial blood gas (ABG) is a frequently used test before anesthesia induction in cardiovascular surgery and in the evaluation of postoperative patients. Therefore, ABG analysis may have the significance of predicting mortality and postoperative events in COPD patients undergoing CABG. Consequently, this study aimed to investigate the effects of ABG on postoperative morbidity and mortality after CABG in patients with COPD.

MATERIALS AND METHODS

Seventy-five COPD patients, on whom elective CABG was performed and whose respiratory function test (RFT) values were as force expiratory volume (FEV_1) / force vital capacity (FVC) ≤ 70%, were retrospectively included into the study. Patients with missing data or the ones that underwent additional procedures (heart valve surgery or aneurysmectomy)

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were excluded from the study. Moreover, patients operated on for valvular diseases, patients with asthma, sleep-apnea syndrome and the ones with restrictive and combined respiratory function disorder were also excluded from the study. All clinical and demographic data of the patients present in the files and their postoperative mortality and complication data were recorded. Respiratory function tests were routinely carried out before surgery while the patient was seated by using a computer system (Jaeger, Master Screen, MS Pneumo; Erich Jaeger GmbH; Hoechberg, Germany). The best one out of the three test done consecutively is accepted for analysis. FEV_1 and FVC values of the pulmonary test results were measured as liters and the percentages of the expected values were obtained. COPD groups were divided into two as Group 1: $FEV_1 \geq$ %60 and Group 2: $FEV_1 \leq$ %59 (Table 1). Below-mentioned preoperative variables that could affect the result of the surgery were recorded in both groups. Both groups were compared in terms of both mortality and morbidity-affecting events and with respect to the effect of arterial blood gas results on mortality and morbidity in these groups. In the blood samples obtained from the radial artery for arterial blood gas analysis, parameters of PH, partial oxygen pressure (PaO_2) and partial carbondioxide pressure ($PaCO_2$) were recorded. In addition, in the postoperative period, the same parameters were recorded from the blood gases routinely taken 3 and 6 hours after post-extubation and during 3 L/min oxygen intake. Medica Easystat (Medica Corp. Bedford, MA, USA) is used for blood gas analyses. In preoperative blood gas analysis, $PaCO_2$ 44 mmHg and higher was considered high; PaO_2 70 mmHg and lower was considered low.

Preoperative Variables

Patient characteristics and comorbid diseases having an effect on the operation including age, gender, body mass index (BMI), history of smoking, creatinine, blood urea nitrogen (BUN), diabetes mellitus (DM), history of COPD, re-done CABG, previous myocardial infarction (MI), cerebrovascular disease (CVO), arterial hypertension (HT), and ejection fraction (EF) in COPD groups were compared with regard to Euroscore, and a statistically significant difference was not found except for history of COPD (Table 2).

Definitions

History and physical examination records, chest radiography records, blood gas analyses and spirometric measurements of all the patients included into the study were retrospectively reviewed, and COPD diagnosis was confirmed by a chest diseases specialist in line with these records. Having FEV1/FVC ≤ 70% on spirometer and SFT were accepted as airway obstruction. Hospitalization duration of eight and more than eight days was considered prolonged hospitalization. Intubation of more than 24 hours was considered prolonged intubation. On PA chest radiography, closure in costophrenic sinus and homogenous density images whose gap faced upwards following obscured diaphragmatic contour were evaluated as pleural effusion. Respiratory distress was accepted present in patients with dyspnea, discomfort, tachycardia, tachypnea (respiratory rate more than 20), and elevated wheezing on postoperative records. For the diagnosis of pneumonia, in addition to the occurrence of new and progressive infiltrations on chest radiography, at least two of the criteria of elevated body temperature (> 38°C), purulent tracheobronchial secretion and leukocytosis should have been present. Renal failure was defined as a creatinine level over 2 mg/dL postoperatively or as the need for hemodialysis, stroke was defined as regional neurologic dysfunction that could ameliorate without sequela, and mortality was defined as death due to any reason before discharge.

Operative Technique

Following median sternotomy, moderate (28°C) systemic hypothermia was established with venous cannulation from the ascending aorta and right atrium. Myocardium protection was provided by intermittent cold K+ blood cardioplegia. Left internal mammary artery and saphena were used as bypass graft. Principally, distal anastomoses were made. Proximal anastomoses were made to the aorta under lateral clamp. When it was necessary, mechanical and pharmacological support were given to disconnect from cardiopulmonary bypass (CPB). All patients were taken to the intensive care unit in the postoperative period.

Statistical Analysis

Descriptive values for the obtained data were given as mean ± standard deviation (SD) and number (percentage) frequencies in charts. Preoperative categorical measurements between the groups and morbidity and mortality parameters were analyzed with $\chi 2$ test. For continuous variables, normal

Table 1. COPD groups

	Group 1 (n= 37)	Group 2 (n= 38)	p
FVC (L)	3.21 ± 0.64	2.38 ± 0.64	0.0001
FVC%	81.56 ± 11.17	61.73 ± 12.60	0.0001
FEV_1 (L)	2.17 ± 0.44	1.49 ± 0.37	0.0001
FEV_1%	71.34 ± 9.32	48.18 ± 9.26	0.0001
FEV_1/FVC	66.90 ± 2.80	62.70 ± 5.81	0.005
PEF (%)	61.95 ± 12.79	45.77 ± 12.75	0.0001
FEF 25-75	45.55 ± 8.69	29.43 ± 7.62	0.0001

COPD: Chronic Obstructive Pulmonary Disease, FEF 25-75: Force expiratory flow in 25-75% of the expiration phase, FEV_1: First second force expiratory volume, FEV_1 %: The percentage of first second force expiratory volume, FVC: Force vital capacity, FVC %: The percentage of force vital capacity, FEV_1/FVC: The rate of first second force expiratory volume to force vital capacity, PEF: Force expiration peak flow rate.

Table 2. Preoperative data of COPD groups

	Group 1 (n= 37)	Group 2 (n= 38)	p
Age	61.91 ± 8.71	59.81 ± 7.32	0.261
Gender (M/F)	35/2 (94.6%/5.4%)	37/1 (97.4%/2.6%)	0.537
BMI kg/m^2	25.38 ± 4.29	26.82 ± 3.11	0.103
Cigarette (package/year)	37 (100)	34 (89.5)	0.017
Creatinine (mg/dL)	0.93 ± 0.18	1.00 ± 0.21	0.107
BUN (mg/dL)	18.62 ± 4.86	18.94 ± 5.07	0.777
DM (existent/non-existent)	10/27	13/15	0.499
COPD history (existent/non-existent)	6/31	22/16	0.001
Redo ACBG done/not done)	2/35	3/35	0.665
MI (postoperative) (existent/nonexistent)	16/21	23/15	0.133
CVO (existent/non-existent)	1/36	0/0	0.232
HT history (existent/non-existent)	18/19	26/11	0.082
EF (%)	53.18 ± 10.97	49.15 ± 11.55	0.126
Euroscore	3.72 ± 2.20	3.73 ± 2.12	0.989
Euroscore %	4.15 ± 3.97	3.93 ± 2.74	0.781

BMI: Body mass index, BUN: Blood urea nitrogen, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, Redo ACBG; MI: Myocardium infarction, CVO: Cerebrovascular disease, HT: Hypertension, EF: Ejection fraction.

distribution and assumptions of equality of the variances were respectively evaluated with Kolmogorogv-Smirnov and Levene tests. Inter-group differences for continuous variables were analyzed by Student's t test. SPPS for Windows (version 18) was used for calculations and $p< 0.05$ was considered statistically significant.

The ethics committee and human research committee of the center where the study was conducted gave approval before the commencement of the study.

RESULTS

Data belonging to the COPD groups are given in Table 1. Demographic characteristics except for smoking and COPD history and the distribution of comorbid diseases were equal. Preoperative data of the COPD groups are given in Table 2.

Perioperative Results

When the operative data, including cardiopulmonary bypass time, cross clamp time, rate of patients on whom LIMA was used, intubation duration, intensive care unit stay, and hospitalization duration of the COPD groups were compared between each other, no statistically significant difference was found (Table 3). Moreover, coronary artery bypass grafting on beating heart was performed in three patients each in both groups.

The Effect of COPD Groups on Morbidity and Mortality

Mortality was found significantly high in Group 1 ($p< 0.037$). When the effect of COPD groups on morbidity was compared, arrhythmia was found significantly high in Group 1 ($p= 0.024$). Regression analysis could not be done since the number of mortality was low. When cause of death of the three patients who died were explored, each patient was extubated on time after the operation. One of the patients died due to arrhythmia non-responsive to treatment, the other died due to having undergone revision surgery for bleeding twice and having developed pneumonia afterwards, and the third one died because of pneumonia (Table 4).

Table 3. Operative data of the COPD groups

	Group 1 (n= 37)	Group 2 (n= 38)	p
CPB (d)	102.97 ± 34.82 (n= 34)	115.31 ± 59.63 (n= 35)	0.299
CC (d)	69.97 ± 28.82 (n= 34)	73.05 ± 40.86 (n= 35)	0.719
Lima	29 (80.6)	32 (86.5)	0.494
Intubation (s)	18.13 ± 17.90	16.23 ± 10.06	0.572
Intensive care (g)	1.40 ± 0.76	1.78 ± 2.00	0.278
Hospitalization (g)	7.54 ± 4.03	7.02 ± 2.62	0.514

CPB: Cardiopulmonary bypass, CC: Cross clamp time.

Table 4. Comparison of the effect of COPD groups on morbidity and mortality

	Group 1 (n= 37)	Group 2 (n= 38)	p
Mortality	3 (8.1)	0 (0)	0.037
Prolonged hospitalization	6 (16.2)	7 (18.4)	0.801
Prolonged intubation	5 (13.5)	2 (5.3)	0.213
Pneumothorax	0 (0)	2 (5.3)	0.09
Pleural effusion	6 (16.2)	2 (5.3)	0.117
Pneumonia	2 (5.4)	1 (2.6)	0.537
Respiratory distress	7 (18.9)	5 (13.2)	0.496
Arrhythmia	13 (35.1)	5 (13.2)	0.024
Postoperative MI	0 (0)	1 (2.6)	0.241
Re-intubation	2 (5.4)	0 (0)	0.09
Revision	4 (10.8)	1 (2.6)	0.143
Hypotensive shock	1 (2.7)	0 (0)	0.232
Frenic nerve paralysis	2 (5.4)	0 (0)	0.09
Stroke	2 (5.4)	0 (0)	0.09
Acute renal failure	0 (0)	1 (2.6)	0.143

The effect of the values of arterial blood gas analysis on morbidity and mortality

When patients with high preoperative $PaCO_2$ (n: 10) were compared with the ones with normal $PaCO_2$ (n: 65) in terms of mortality and morbidity parameters, a statistically significant difference was not found ($p> 0.05$). When patients with low preoperative (n: 13) PaO_2 were compared with the ones with normal PaO_2 in terms of morbidity and mortality parameters, prolonged hospitalization and arrhythmia rates were found high in patients with normal preoperative PaO_2 ($p< 0.05$). Postoperative MI was found high in patients with low preoperative PaO_2 ($p= 0.05$) (Table 5).

The effect of COPD groups on arterial blood gas analysis

When the parameters of preoperative, post-extubation and 3-6 h after extubation arterial blood gas analysis were compared, no significant difference was found. Interestingly, the number of patients with high preoperative $PaCO_2$ was higher in Group 1 than in Group 2. The number of patients with low preoperative PaO_2 was close to each other between the groups (Table 6).

DISCUSSION

Cardiopulmonary bypass (CPB) deteriorates alveolar stability by triggering complement cascade and changing neutrophil sequestration in the pulmonary microvascular bed, the formation of free oxygen radicals and the structure of alveolar surfactant. CPB is known to negatively affect respiratory functions. In patients undergoing CABG, the effect of COPD becomes a substantial problem due to the additional influence of CPB and sternotomy [4]. COPD has been defined as the most important preoperative risk factor for morbidity and mortality in patients on whom coronary artery surgery is performed [5,6]. Unwanted events of the respiratory system, such as respiratory failure and pneumonia, can cause postoperative complication in COPD patients on whom CABG is performed [7]. There are studies showing that as the stages of COPD increase so does morbidity and mortality in COPD patients on whom coronary artery surgery is performed [8,9]. It has been reported in many studies that postoperative complications are most frequently seen in the COPD patient group when compared to the control group [6-9].

It has been found in a study by Samuel et al. [6], where they have evaluated 191 patients undergoing CABG surgery, that intra-hospital mortality rates in patients with mild to moderate COPD were similar with the patients without COPD. Futer et al. [8] have evaluated mortality and morbidity according to obstruction severity in COPD patients and mortality has been found to be associated with the degree of obstruction. The patients whose FEV_1 value was under 60% was found to be specifically higher than those whose mortality was over 60% (24.6% vs. 1.4%) ($p< 0.001$). With the impact of this last study, the detection of moderate or advanced COPD in preoperative evaluation was accepted a risk for mortality. However, in recent years, it has been found in a study by Mangenes et al. that CABG surgery can be performed without increased mortality risk when severe COPD patients were compared with mild-to-moderate COPD patients and the ones with normal respiratory functions [3]. When postoperative results of severe COPD patients (FEV_1 less than 50% and FEV_1/ FVC less than 0.7) were compared with that of the mild-to-moderate COPD patients (FEV_1 50% and over, FEV_1/FVC less than 0.7) and the ones with normal pulmonary functions, it was found that apart from increased pulmonary infection risk, inclination to postoperative atrial fibrillation and a bit increased hospitalization duration, the results were similar. Similar to the study of Mangenes et al., our study also established that moderate-advanced COPD did not carry a risk in terms of mortality and in fact, mortality was seen to be

Table 5. Comparison of the effect of COPD groups on morbidity and mortality

	Preop $PaCO_2$ Normal (n= 65)	Preop $PaCO_2$ High (n= 10)	p	Preop PaO_2 Normal (n= 62)	Preop PaO_2 Low (n= 13)	p
Mortality	3 (4.6)	0 (0)	0.349	3 (4.8)	0 (0)	0.280
Prolonged hospitalization	12 (18.5)	1 (10)	0.485	13 (21)	0 (0)	0.019
Prolonged intubation	6 (9.2)	1 (10)	0.938	5 (8.1)	2 (15.4)	0.438
Pneumonia	3 (4.6)	0 (0)	0.349	3 (4.8)	0 (0)	0.280
Pneumothorax	2 (3.1)	0 (0)	0.446	1 (1.6)	1 (7.7)	0.283
Pleural effusion	6 (9.2)	2 (20)	0.344	6 (9.7)	2 (15.4)	0.562
Respiratory distress	9 (13.8)	3 (30)	0.228	9 (14.5)	3 (23.1)	0.462
Re-intubation	2 (3.1)	0 (0)	0.446	2 (3.2)	0 (0)	0.379
Arrhythmia	16 (24.6)	1 (10)	0.668	18 (29)	0 (0)	0.005
Postoperative MI	1 (1.5)	0 (0)	0.591	0 (0)	1 (7.7)	0.05
Hypotensive shock	1 (1.5)	0 (0)	0.591	1 (1.6)	0 (0)	0.536
Revision	4 (6.2)	1 (10)	0.668	4 (6.5)	1 (7.7)	0.873
Frenic nerve damage	1 (1.5)	1 (10)	0.205	1 (1.6)	1 (7.7)	0.283
Stroke	2 (3.1)	0 (0)	0.446	2 (3.2)	0 (0)	0.379
Acute renal failure	1 (1.5)	0 (0)	0.591	1 (1.6)	0 (0)	0.536

PaO_2 : Partial Oxygen Pressure, $PaCO_2$: Partial carbondioxide pressure.

Table 6. Investigating the effect of COPD groups on arterial blood gas

	Group 1 (n= 37)	Group 2 (n= 38)	p
Preop Ph	7.41 ± 0.02	7.41 ± 0.02	0.723
Post-Ext. Ph	7.38 ± 0.05	7.38 ± 0.03	0.756
Ext. 3 h Ph	7.38 ± 0.03	7.39 ± 0.03	0.367
Preop $PaCO_2$	39.87 ± 4.78	38.59 ± 4.79	0.249
Post-Ext. $PaCO_2$	38.42 ± 6.09	39.37 ± 5.10	0.462
Ext. 3 h $PaCO_2$	39.61 ± 4.99	39.50 ± 4.82	0.928
Preop PaO_2	82.17 ± 15.36	81.00 ± 11.11	0.705
Post-Ext. PaO_2	114.96 ± 38.96	110.61 ± 34.64	0.611
Ext. 3 h PaO_2	117.91 ± 40.08	104.43 ± 23.97	0.080
Preop O_2 sat	95.16 ± 6.50	96.36 ± 0.29	0.269
Post-Ext O_2 sat	97.47 ± 2.18	97.31 ± 2.82	0.788
Ext. 3 h O_2 sat	97.39 ± 2.05	97.55 ± 1.74	0.739
Preop $PaCO_2$	7* (%18.9)	3* (%7.9)	0.156
Preop PaO_2	6** (%16.2)	7** (%18.4)	0.801
Ext. 3 h $PaCO_2$	5 (%13.5)	4 (%10.5)	0.690

PaO_2 : Partial Oxygen Pressure, $PaCO_2$: Partial carbondioxide pressure.
* The number of patients with high $PaCO_2$.
** The number of patients with low PaO_2.

higher in the in mild-moderate COPD (Group 1) when compared with the moderate-advanced COPD (Group 2) [3]. These findings and results make us think that there are other factors affecting mortality independent of COPD stages in COPD patients on whom coronary artery surgery is performed. However, it is not possible to make a definite judgement due to total mortality count, limited size of the study sample and the retrospective nature of the study.

There are two studies involving the analysis of extra-thoracic arterial blood gas analysis, defending two different views. Fuso et al. have indicated that the presence of preoperative hypoxemia with moderate and advanced obstruction plays an important role in the development of postoperative respiratory complication [10]. On the other hand, it has been expressed in another study that preoperative PaO_2 and $PaCO_2$ values are not beneficial in designating postoperative

respiratory complication [11]. Changes in ABG after CABG surgery may be related to circulatory failure, pulmonary disease or mechanic ventilation change [12]. In our study, the effect of PaO_2 and $PaCO_2$ on mortality was not detected among COPD stages. The effect of preoperative PaO_2 values on morbidity was found varying. While postoperative MI was found significantly high in patients with low PaO_2, prolonged hospitalization and arrhythmia rate were found significantly high in patients with normal PaO_2. When myocardial ischemia is considered to be related to the imbalance between oxygen transport and necessity, it can be thought that elevated myocardial oxygen need caused by surgical stress in patients with low preoperative PaO_2 values increases postoperative MI rate by deteriorating this balance. As a result, sustaining normal preoperative PaO_2 limits to decrease postoperative MI in COPD patients is vital. In patients that have normal values of PaO_2, it is not clear to what prolonged hospitalization or elevated arrhythmia rate is related and most probably, they are related to other factors.

In a study involving patients on whom coronary artery surgery is performed, postoperative atrial fibrillation (AF) has developed in 1503 patients (32.3%), and it has been emphasized that many factors including chronic pulmonary diseases play a role in the development of AF [11]. Supraventricular arrhythmia has been observed to be the most frequently encountered reason of morbidity after CABG in patients with COPD when compared to the control group [13]. In our study, arrhythmia rate was observed to be significantly higher in Group 1. Moreover, in the comparison of the group with normal preoperative arterial blood gas analysis and the one with low preoperative arterial blood gas analysis, arrhythmia was found significantly higher in the group with normal PO_2 value. This situation makes us think that the effect of the degree of obstruction in COPD patients and the presence of preoperative hypoxemia on the development of postoperative arrhythmia is limited.

Although some authors object the implementation of SFT in the preoperative period, some studies also make us think that it can be important in confirming and designating the degree of COPD diagnosis and deciding on surgical risk [14,15-18]. Spirometric evaluation carried out before the surgery can reform surgical results in high-risk patients. Quitting smoking, bronchodilator treatment and steroid treatments, which are postoperative morbidity-decreasing strategies in patients with confirmed COPD diagnosis, have been indicated to provide success in the postoperative period [6]. We are of the opinion that respiratory function tests be routinely performed in patients undergoing major cardiac surgery due to the fact that a part of the COPD patients are not aware of the disease and that it may help designating postoperative COPD attack. It has been reported in a study by Öz et al. that postoperative parameters of moderate COPD patients on whom they administered treatment in the preoperative period were better when compared to the ones that did not receive any treatment [19].

In our results, a statistical change was not detected in postoperative $PaCO_2$ values in cases with mild and advanced COPD.

Limitations to the Study

The most important limitations to the study are as follows: it is a single-center, retrospective study with a limited number of patients and the number of patients in whom mortality was seen is low. As the number of patients that died in the postoperative period (n= 3) is low, it is not possible to definitely specify the predictor values of ABG parameters on mortality or if the severity of COPD has an effect on mortality. Regression analysis could not be performed in this study because of the same reason, and therefore, it is not possible to designate factors affecting mortality with the data of this study. These questions will be clarified with a prospective study with a larger cohort.

In conclusion, an association was not found between the degree of preoperative obstruction and mortality in COPD patients on whom CABG is planned. ABG parameters taken from COPD patients in the preoperative period do not have any mortality-prediction value in COPD patients and COPD subgroups (mild or moderate-advanced). However, preoperative low PaO_2 levels may be predictive of postoperative MI. Yet, since the number of patients included into the study and who died is low, we are of the opinion that this study should be repeated with larger patient groups.

Written consent was not obtained from the patients since this is a retrospective study.

Author Contributions: Concept - S.A., S.Ö., R.G.; Design - S.A., R.G.; Supervision - S.A., R.G., S.Ö., T.S.G.; Funding - R.G., N.Y.; Materials - R.G., S.İ.; Data Collection and/or Processing - S.İ., S.Ö., T.S.G., N.Y.; Analysis and/or Interpretation - S.İ., S.Ö., N.Y.; Literature Search - T.S.G., S.Ö.; Writer - S.Ö., S.İ.; Critical Review - S.Ö., N.Y., T.S.G., S.İ.; Other - R.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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Turk Thorac J 2016; 17: 100-104 DOI: 10.5578/ttj.30504

ORIGINAL INVESTIGATION

The Effect of Flexible Bronchoscopy on Anxiety in Children

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Abstract

OBJECTIVES: Flexible bronchoscopy (FB) is a semi-invasive diagnostic tool that allows direct visualization of the airways. The use for diagnostic and therapeutic purposes in children is incrasing with the developments in modern anesthesia. Irrespective of the type of the invasive diagnostic procedure, these interventions are known to cause anxiety in patients. The aim of our study was to evaluate the anxiety and depression status in children hospitalized for bronchoscopy and to investigate the effects of FB.

MATERIAL AND METHODS: Thirty children hospitalized for FB and 30 controls, aged 7 to16 years, were enrolled in this study. Anxiety was evaluated with the "Hospital anxiety and depression scale" (HADS)" besides other parameters recorded.

RESULTS: The mean HADS anxiety scores in the patient and control groups were respectively 10.1 (3.5) and 2.7 (1.3) (p= 0.001). The mean HADS depression scores were respectively 8.8 (3.7) and 2.2 (1.1) (p= 0.001). Among the patients, 50% had anxiety and 53.3% had findings while none in the control group showed signs of anxiety and depression. A positive correlation was found between the age and, anxiety and depression scores in patients' groups (respectively r_1= 0.257; p= 0.05 and r_2= 0.288; p= 0.02).

CONCLUSION: Anxiety was demonstrated in nearly half of the children hospitalized for bronchoscopy. It has been observed that behavioral and physical problems may be encountered in approximately 40-60% of children who feel generalized anxiety before anesthesia, during the preoperative, postoperative period, and subsequent periods. These results suggest that the detection of children with increased anxiety and indicate the individual requirements can be assisted pharmacological and psychological supports.

KEYWORDS: Flexible bronchoscopy, children, anxiety

Received: *11.11.2015* ***Accepted:*** *12.02.2015*

INTRODUCTION

Pediatric flexible bronchoscopy (PFB) is a diagnostic tool enabling direct visualization of the nose, pharynx, larynx, and the tracheobronchial tree [1]. From 1978, when Wood et al. first used PFB, onwards, its indications, application methods, diagnostic use, and the safety of the procedure have been defined, and flexible bronchoscopy (FB) became a popular tool in evaluating the airways of pediatric patients. FB is performed under general anesthesia in the operating room with a team made up of a bronchoscopy specialist, an assistant physician, a bronchoscopy nurse and an anesthesiologist for diagnostic or therapeutic purposes or in order to obtain secretion or cells from the lungs. With the improvement in modern anesthesiology techniques, younger and sicker children are evaluated more safely when compared to the past [1,2].

Whatever the type of interventional diagnostic methods is, it is known that the decision of an interventional procedure creates anxiety on the individual [3]. Due to the fact that children have limited cognitive development, limited understanding of their diseases, and poor strategies to deal with the diseases, they are fragile against hospitalization [4]. The first step to be taken in competing with anxiety is to detect it with valid and clinically-evaluable instruments. It will be easier to help the patient and his/her relatives once these factors are detected [4]. Hospital Anxiety and Depression (HAD) scale is a scale designed to determine the levels of anxiety of the patients and to make the patient discover how he/she feels about him/herself [5].

The aim of this study was to evaluate the anxiety and depression levels of pediatric patients admitted to hospital for bronchoscopy by carrying out the HAD scale and assess the effects of FB on the level of anxiety. Children with elevated levels of anxiety would be detected, and pharmacologic and psychologic support systems oriented at their individual needs would be recognized.

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MATERIALS AND METHODS

Thirty pediatric patients between the ages of 7 and 16, who were admitted to hospital for bronchoscopy, were included into this case control study. The control group comprised thirty healthy pediatric patients who applied to the pediatric polyclinic and did not have any acute or chronic diseases and on whom no interventional procedure was performed.

Study Design

The children on whom bronchoscopy was to be performed were admitted to hospital one day prior to the operation for preoperative preparations. The sociodemographic characteristics, height and weight of the patients were recorded. After having obtained family consent, the HAD scale was filled out by the children themselves without having being informed about the FB procedure since it affects the scoring of the HAD scale. The diagnoses of the patients prior to bronchoscopy were recorded. Afterwards, the children on whom FB was to be performed and their parents were informed about the reason of the procedure, how the procedure would be performed, and the reliability and possible complications of the procedure verbally or by drawing pictures to the extent of their cognitive levels, and then, informed consent forms were taken from the families. After having recorded the sociodemographic characteristics, height and weight of the patients in the control group and having received informed consent forms from their families, the HAD scale was filled out by these children themselves.

With the purpose of premedication, the children on whom flexible bronchoscopy was to be performed were given 2% lidocaine solution using an age appropriate mask by means of nebulisator and 0.5 mg/kg/dose midazolam intranasally for sedation one hour prior to the procedure in order to obtain local anesthesia. The time between premedication and the start of the FB procedure was recorded. FB procedure was performed under general anesthesia given through a mask. Pediatric flexible bronchoscope (Olympus BF3C20, Japan) with an outer diameter of 3.6 to 4.9 mm and an operation channel diameter of 1.2 to 2.2 mm was used in the FB procedure. Respiratory frequency, PaO_2, $EtCO_2$, and heart rate were recorded at the start and at the fifth, tenth, fifteenth, thirtieth, and forty-fifth minutes of the FB procedure. Specimens were taken with bronchoalveolar lavage from all cases for cytological analysis. Direct microscopic evaluation, Lowenstein-Jensen culture and polymerase chain reaction analyses were performed on the specimens taken for microbiologic evaluation for tuberculosis bacillus. The time between intra-FB and the post-bronchoscopic period until children regain consciousness in the recovery room and the complications that arose were recorded. The diagnoses made as a result of the data obtained pre and post-bronchoscopy were also recorded.

Hospital Anxiety and Depression Scale

Hospital anxiety and depression scale was developed by Zigmond and Snaith to determine the risk of anxiety and depression in patients and to measure its level and change in severity. It was designed to scan mood disorders in a medically diseased population. It is a scale used frequently in hospital settings, which scans the signs of anxiety and depression and which is filled out by the patient himself. In order to differentiate between psychiatric and physical signs, the scale emphasizes subjective destruction rather than physical signs. Depression subscale considers anhedonia instead of sadness as the basic symptom [6]. The scale is comprised of a total of fourteen questions, and seven (odd numbers) measure anxiety and the other seven (even numbers) measure depression. The cut points of the Turkish version of the HAD scale was found 10 for the anxiety subscale and 7 for the depression subscale. 7-item depression subscale is scored between 0 to 21 and a cut point of 0-7= Normal, a cut point of 8-10= Mild, a cut point of 11-14= Medium, and a cut point of 15-21= Severe mood disorder.

Ethics Committee

This is a case control study which was evaluated and approved by the Ethics Committee of Celal Bayar University.

Statistical Analysis

Statistical analysis of the study was performed using SPSS 15.0 (Chicago IL) computer program, and $p< 0.05$ was considered a s statistically significant. Student's t-test was used to compare the age, height, weight, and anxiety and depression scores between the patient and the control groups. Gender distribution between the groups was assessed by Pearson's Chi-square test. Pearson's correlation test was used in the correlation of the anxiety and depression scores with age.

RESULTS

The study included thirty patients on whom bronchoscopy was performed and thirty controls. The patient group included 12 (40%) male and 18 (60%) female patients while the control group included 14 (46.7%) male and 16 (53.3%) patients (p= 0.79) (Table 1). Mean age of the sick children was 10.9 (3.3) years and mean age of the control group was 10.2 (2.3) years (p= 0.38) (Table 1).

HAD scale anxiety scores were found respectively as 10.1 (3.5) and 2.7 (1.3) in the patient and control groups (Figure 1). HAD scale depression scores were found respectively as 8.8 (3.7) and 2.2 (1.1) in the patient and control groups (Figure 1). While anxiety signs were detected in 50% and

Table 1. Sociodemographic characteristics of the children included into the study

	Bronchoscopy group (n= 30)	Control group (n= 30)
Age	10.9 (3.3)	10.2 (2.3)
Height (cm)	134.2 (23.9)	132.2 (15.9)
Weight (kg)	32.4 (13.6)	31.8 (11.2)
Gender		
Male	12 (40.0)	14 (46.7)
Female	18 (60.0)	16 (53.3)

* Student's t-test.
$ Pearson's Chi-Square [% (n)].

Table 2. Anxiety and depression states of the children included into the study

	Bronchoscopy group (n= 30)	Control group (n= 30)	p*
Anxiety score	10.1 (3.5)	2.7 (1.3)	0.001
Depression score	8.8 (3.7)	2.2 (1.1)	0.001

* Student's t-test.

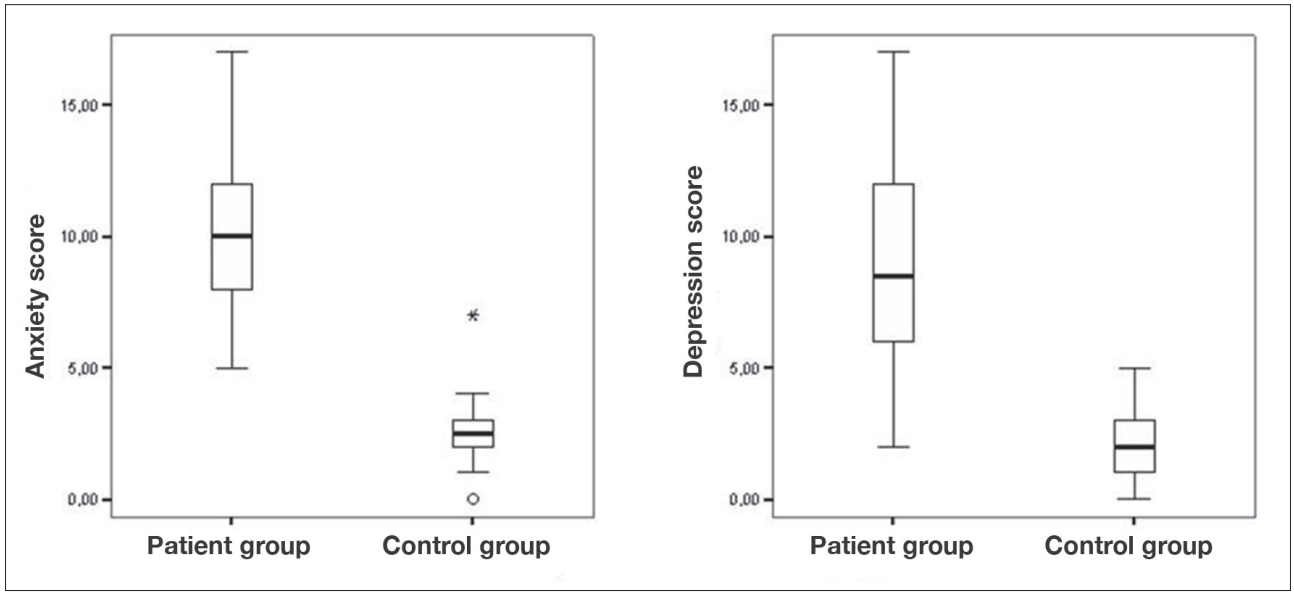

Figure 1. Anxiety and depression scores of the bronchoscopy and control groups.

depression signs in 53.37% of the patients in the patient group, no signs of anxiety and depression were detected in the control group. HAD scale determined a positive correlation between anxiety and depression scores and age (r_1= 0.257; p= 0.05 and r_2= 0.288; p= 0.02, respectively).

Figure 2 shows the diagnoses of the patients before and after bronchoscopy. The most frequent bronchoscopy indications were tuberculosis, exploration due to hemoptysis, bronchiectasis, and asthma. In patients on whom bronchoscopy was performed, mean premedication time was 52.9 ± 9.4 min, mean bronchoscopy procedure duration was 14.9 ± 10.5 min and mean anesthesia period was 27.2 ± 13.2 min.

As a complication, bronchospasm was seen in three patients in the reanimation period after bronchoscopy and in one patient during anesthesia prior to bronchoscopy.

While bronchiectasis was the most encountered disease in bronchoscopy, it was followed by tuberculosis, outer pressure to the airway and re-fistula diagnoses that developed after operated tracheoesophageal fistula.

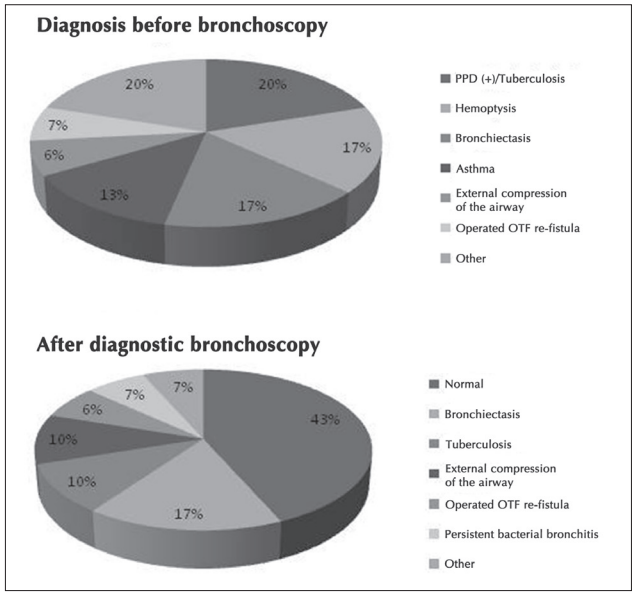

Figure 2. Preliminary diagnoses and post-flexible bronchoscopy diagnoses of the patients.

DISCUSSION

As a result of this study, it was shown with the HAD scale that anxiety and depression rates were higher in children admitted to hospital for bronchoscopy than the healthy controls.

Bronchoscopy is the procedure with which the upper and lower airways are visualized endoscopically. The pioneers of this procedure were rigid bronchoscopes, which were then followed and advanced by flexible bronchoscopes that have been in use for the last twenty years. Flexible bronchoscopes (FB) are increasingly preferred thanks to their ease of use and scarcity in side effects. If the benefit provided by FB is much more when compared to the risk of the procedure, FB is indicated [2]. While deciding on FB in children, patient history, findings of physical examination and the results of

previous diagnostic tests should be taken into consideration. FB takes an important place in the diagnosis and treatment of pediatric respiratory tract diseases. FB is performed in children in cases like long-lasting chronic cough, recurrent pneumonia, suspicion of foreign object aspiration, and accumulated secretions in the tracheobronchial tree. Whether or not there is a history of foreign object aspiration, diagnostic and therapeutic bronchoscopy should not be avoided in suspected cases [7].

Disease and hospitalization cause anxiety in children [4,8]. In our study, anxiety was detected in 50% of the patients. Anxiety is a normal, intuitive reaction which is developed against a threat or lack of an object and is accompanied by various unpleasant bodily senses [9]. Anxiety progresses with symptoms like edginess, concern, tachycardia, trouble in breathing, zonesthesia, trimmer in hands and feet, and excessive sweating [10]. Anxiety in hospitalized children can develop due to diverse reasons, such as being harmed physically, being operated on, fear of not waking up after anesthesia or dying, loss of control, pain, being isolated, having to leave loved ones, and distancing from social life [3,8,11,12].

The unfamiliarity of the hospital setting, the staff, the necessity to communicate with strangers, the use of medical terms by the healthcare team, the materials used and procedures to be performed are full of obscurities for children of all ages, and it should be noted that these factors have an effect on the children's level of anxiety. The fact that an intervention is to be employed in addition to hospitalization makes the child to get more stressed and affects the child psychologically and physiologically [4,11,13]. FB procedure in children is performed under general anesthesia in the operating room in our department.

It would be wise to be aware of the changing behavioral characteristics of children in different age periods and a connection should be made as regards their perception and comprehension of events. Children at the age of 7 to 11 start to comprehend the reasons of diseases with the help of cognitive maturity [14]. They show their reactions to the physicians and nurses by crying, yelling and even by acting resented. On the other hand, they sometimes withdraw, do not make any contact with the environment and show an excessive calmness. Unless the children are provided with all necessary information regarding the procedure in this period, isolation and feeling of loneliness, which increase preoperative anxiety, are induced [3]. Therefore, explaining the procedure verbally or with pictures to these children in this age group reduces anxiety [15]. The children in the adolescent period (13-18 ages) have the cognitive capability to understand related explanations about bronchoscopy [15]. The adolescent period is when the children accept who they are and are sensitive to the changes in their body images. The sick children in this age group are afraid of losing control and being separated from their peers [13]. In a study carried out on adolescent patients, it has been put forward that the concepts of disease and hospital create major stress, and trouble related to hospitalization in pediatric or adult clinics is encountered. It has been shown that informing these adolescent patients one week prior to the procedure reduces anxiety [11].

When the literature was reviewed, it was seen that there is no study on bronchoscopy procedure and its effects on anxiety in children. The majority of the studies comprise the ones related to anesthesia and surgical interventions. It has been determined that more than 40-60% of the children undergo anxiety and fear in the preoperative period, especially during anesthesia induction [14,16,17]. Wollins et al. have shown that hospital setting causes anxiety in approximately 38% of the children between the ages of 5-12 undergoing elective surgery and again that a high degree of anxiety is observed in the preoperative period in 53% of these children [18,19]. Similarly, anxiety was observed in 50% of the patients in our study. In a study carried out in adolescents between the ages of 11-18, preoperative anxiety has been detected in more than 80% of these adolescents [20]. The higher rate of anxiety level in this study when compared to the rate found in ours can be explained by the fact that anxiety increases in parallel with age and that the age of this study group is higher than ours [20].

Kain et al. have established in a study carried out in children on whom minor surgery was to be performed that with increasing age, the rate of anxiety also increases in the preoperative period [21]. Similarly, anxiety and depression rates that increase with age were also observed in our study. However, Vagnoli et al. have not observed anxiety and depression rates that increase with age in their study [12]. The reason could originate from the method used or the fact that the study group was small in size.

A series of prevention strategies have been developed to reduce preoperative anxiety incidence in children. Both pharmacologic (like sedatives) and non-pharmacologic (presence of family, behavioral preparation programs, music, acupuncture, and etc) approaches have been proven to be useful [17]. Özen at al. have shown in their study that patient approach and information given before the intervention are effective in reducing anxiety [22]. In a study by Kain et al., it has been shown in children over the age of six that therapeutic games performed 5-7 days prior to surgery and surgery preparation programs involving behavioral methods like the introduction of the hospital and the operating room are effective in reducing anxiety levels in children [23].

Similarly, Cuzzocrea et al. have demonstrated that anxiety is low in children on whom preoperative physiological program is applied in the pediatric surgery clinic [8]. In our study, illuminating explanations regarding FB procedure were given after HAD scale was filled out so as not to affect the results of the HAD scale.

In conclusion, being sick and admitted to hospital affect the lives of children in many ways and increase their concerns and worries. Especially cases, where surgical intervention is needed for the diagnosis or treatment of a disease, bring out psychological problems like the development of high level of anxiety in children. It was shown in our study by the HAD

scale that anxiety was developed in half of the children that would undergo bronchoscopy. Since behavioral and physical problems such as enuresis, nutrition disorders, apathy and sleeping disorders are observed to be seen in more than half of the children that frequently go through anxiety in the period before anesthesia, it would be wise to detect these children with anxiety and provide them with necessary pharmacologic and psychologic support aimed at individual needs.

The limitations of our study could be the fact that psychiatric interviews were not carried out with the patients and that the effect of medical disease severity on anxiety was not looked into.

Author Contributions: Concept - H.Y., Ö.Y., A.T., İ.T.; Design - H.Y., Ö.Y., A.T.; Supervision - H.Y., Ö.Y., A.T., İ.T.; Data Collection and/or Processing - H.Y., Ö.Y., A.T., İ.T.; Analysis and/or Interpretation - Ö.Y., A.T.; Literature Search - A.T., Ö.Y.; Writer - A.T., Ö.Y., H.Y.; Critical Review - H.Y., Ö.Y., A.T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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Turk Thorac J 2016; 17: 105-108 DOI: 10.5578/ttj.30505

ORIGINAL INVESTIGATION

Analysis of Patients with Spontaneous Pneumomediastinum

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Abstract

OBJECTIVES: Spontaneous pneumomediastinum is characterized by the presence of air in the mediastinum without any reason. The objective of this study is to report our experience in the diagnosis and treatment of this clinical condition.

MATERIAL AND METHODS: 21 patients with spontaneous pneumomediastinum who were referred to our clinic between January 2010 and May 2015 were evaluated retrospectively. The presence of radiological pneumomediastinum and the absence a traumatic cause were taken as the basic criterion.

RESULTS: The mean age of the patients was 24.78 ± 4.37 years. Thirteen patients were male, eight patients were female. The main complaints of the patients were chest pain, dyspnea, neck pain, sore throat and cough. Thirteen patients were smokers. Seven patients had a prior history of asthma, five patient had chronic bronchitis and one patient had cronic obstructive lung diseases. No precipitating factor was identified in 9 patients. While initial complaints was associated with physical effort in 7 patients, three patients cough and two patients had a history of severe crying. Pneumomediastinum was diagnosed by chest radiography in 8 patients, and with chest CT in 13 patients. All the patients were performed bronchoscopy and radiograph of esophagus. Electrocardiogram was taken for all patients. Arrhythmia was detected in 4 of the patients. Treatment included analgesia, rest and oxygen therapy. Mortalitiy and morbidity were not seen. The mean length of hospital stay was 4.4 ± 2.17 days.

CONCLUSION: Spontaneous pneumomediastinum is a benign process. Despite its low incidence, it should be considered in the differential diagnosis of acute chest pain.

KEYWORDS: Spontaneous pneumomediastinum, mediastinal emphysema, dyspnea, subcutaneous emphysema

Received: *28.08.2015* ***Accepted:*** *19.11.2015*

INTRODUCTION

Pneumomediastinum is the presence of free air in the mediastinum due to traumatic or spontaneous reasons. Spontaneous pneumomediastinum is a subgroup of mediastinum, which does not cause any substantial complications or life-threatening symptoms and occur without an apparent cause and ameliorate on its own [1]. Its incidence is low. It has been reported that most of the patients are young males and that it is encountered approximately at the age of 20 [2].

The pressure between pulmonary interstitium and alveoli play an important role in the pathophysiology of spontaneous pneumomediastinum. The increase in pressure difference causes the alveoli to rupture and the air in the pulmonary interstitium accumulate by spreading to the hilus and mediastinum [2-4]. Asthma exacerbation, infections (pneumonia, small air way infections) and cough are among the most common reasons [1,5]. The most common clinical findings are chest pain, dyspnea and subcutaneous emphysema [6].

This study aimed to discuss the findings and results of the patients whose follow-up and treatment was carried out by our clinic due to spontaneous pneumomediastinum in light of the literature.

MATERIALS AND METHODS

Twenty-one patients treated for spontaneous pneumomediastinum between January 2010 and May 2015 were retrospectively evaluated. Patient charts were reviewed. Age, gender, radiologic findings, laboratory results, predisposing factors, precipitating causes, patient habits, treatments, hospitalization duration, mortality, and morbidity were studied.

1st International and Intercontinental Critical Care and Emergency Medicine Congress. 06-08 November 2013, Turkey.

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Inclusion criteria to the study were the presence of pneumomediastinum radiologically and non-existence of a traumatic cause (tracheobronchial tree or esophagus perforation, thoracic or cardiac surgeries, chest wall injuries, infections, and neck or abdominal surgeries).

Approval was obtained from the Ethics Committee of Dicle University, Medical Faculty (approval no/date: 314/02.09.2014).

Statistical Analysis

Continuous variables, mean ± standard deviation and categorical variable were all expressed as number-rate in statistical analysis.

RESULTS

Mean age was 24.78 ± 4.37 years. Thirteen patients were males (62%) and 8 were females (38%). Two of the male patients were children at the ages of 6 and 9. The mother of one of the children had received inpatient treatment in our clinic due to spontaneous pneumomediastinum twice. Blood samples belonging to the mother and the child were taken under genetic analysis. No chromosomal anomalies were detected.

The most common symptom among the patients was centrally located chest pain (n: 19 patients, 90%). Seventeen patients (81%) had dyspnea, 15 (71%) had cough, 11 (52%) had neck pain, 5 (24%) had aphonia, 4 (19%) had subcutaneous emphysema located in the neck, and 4 (19%) had difficulty in swallowing (Table 1).

Predisposing factors of the disease were smoking in thirteen patients (62%), asthma in 7 (33%), chronic bronchitis in 5 (24%), and chronic obstructive pulmonary disease in 1 (5%) (Table 1).

While precipitating factors of the disease were physical effort in seven patients (33%), cough in 3 (14%) and severe crying in 2 (10%) (pediatric patients), there were no distinct precipitating factors in nine patients (43%) (Table 1).

The duration between the diagnosis of the disease and setting of the complaints was between 1 hour and 3 days. Most complaints of the patients were nonspecific except for subcutaneous emphysema (n: 4). Hamman's sign, which is accepted pathognomic for pneumomediastinum, was present in 4 patients (19%).

All patients underwent chest radiography and 13 had additional computed thoracic tomography, and it was realized that diagnosis was made with chest radiography in 8 (38%) and computed thoracic tomography in 13 patients (62%). Main findings on chest radiography were subcutaneous emphysema and air column in the mediastinum, and on computed tomography, it was extensive air image in the mediastinum (Figures 1,2).

There was no abnormal finding in laboratory tests (complete blood count, routine biochemistry, coagulation tests, arterial blood gases) apart from eosinophil and leucocyte elevation. Arrtyhtmia was detected on the electrocardiography of four (19%) patients.

It was seen that oral intake of the patients diagnosed with spontaneous pneumomediastinum was stopped until having eliminated esophagus injuries and thatbronchoscopy was performed and esophagus passage graphy was taken to exclude trachea or esophagus rupture.

Primary treatment of the patients included analgesia, bed rest and oxygen therapy. It was established that reponse to

Table 1. Distribution of symptoms, predisposing and precipitating factors in patients with spontaneous pneumomediastinum

	Number of patients (n)	Percentage (%)
Symptoms		
Chest pain	19	90
Dyspnea	17	81
Cough	15	71
Neck pain	11	52
Aphonia	5	24
Subcutaneous emphysema	4	19
Difficulty in swallowing	4	19
Predisposing factors		
Smoking	13	62
Asthma	7	33
Chronic bronchitis	5	24
Chronic obstructive pulmonary disease	1	5
Precipitating factors		
None	9	43
Physical effort	7	33
Cough	3	14
Severe crying	2	10

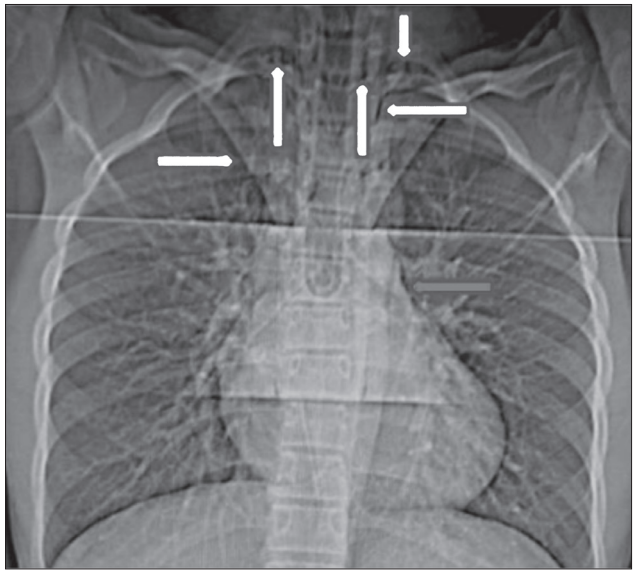

Figure 1. Chest radiography of a patient with pneumomediastinum.

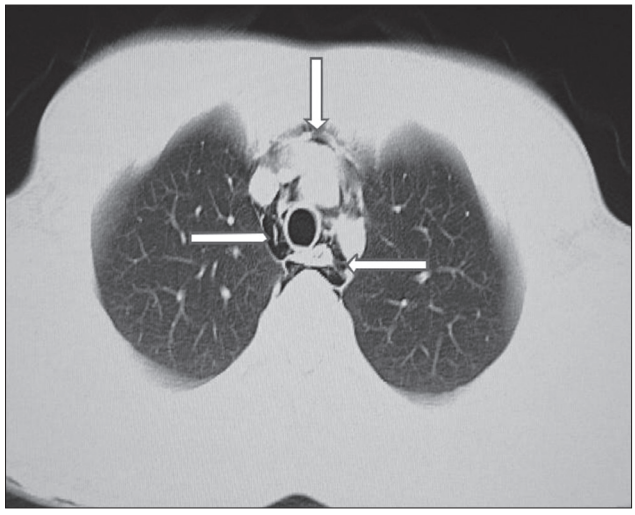

Figure 2. Computed thoracic tomography of a patient with pneumomediastinum.

treatment was achieved from the 2-3 L/15-20 min of oxygen therapy and in 3-4 days with additional treatments with bronchodilator, antbiotics and antitussive.

There were no complications apart from a temperature of 38-39°C in 4 patients (%19). L was determined that relapse (5%), which responded to conservative treatment, developed in a female patient three months later and no mortality occurred. Mean hospitalization duration of the patients was 4.4 ± 2.17 days.

DISCUSSION

Even though the incidence of spontaneous pneumomediastinum is low, it is not accurately known. Newcomb et al. [2] have reported this rate as 1 in 29.670 and Maravelli et al. [7] have reported it between 1/7.000-1/32.000. The disease primarily affects young males and is seen around the age of 20[2]. The number of males was 1.62 times more than females and mean age was 24.78±4.37 in our study.

Spontaneous pneumomediastinum may occur with three mechanisms: 1) gas production and air accumulation due to mediastinal infections; 2) air accumulation in the mediastinum owing to the rupture in the cutaneous or mucosal membranes; 3) pressure difference between pulmonary interstitium and alveoli. Rupture occurs in the alveoli due to pressure difference and the air accumulated in the interstititum spreadsthrough the hilus and to the mediastinum, which has lower pressure, from the lung periphery (Macklin effect). As the air pressure in the mediastinum increases, air leak to the cervical region, within soft tissues and to the retroperitoneal space is seen. These three mechanisms make up the basic pathophysiology of spontaneous pneumomediastinum [1,8].

Both predisposing and precipitating factors have been reported in spontaneous pneumomediastinum. Asthma is the most common predisposing factor [9]. Narcotic drug use has also been reported among predisposing factors. Primary precipitating factors are cough, sneeze, defecation, childbirth and vomiting [1,2,10]. The most common predisposing factors in our study were smoking with a rate of 62% and asthma with a rate of 33%. Precipitating factors were physical effort with a rate of 33% and cough with a rate of 14%. However, there were no precipitating factors in 43% of the patients. The most common symptoms in spontaneous pneumomediastinum are chest pain, dyspnea, neck pain, and discomfort. The most commonly reported symptom is chest pain. Other symptoms include painful swallowing, cough, dysphonia (difficulty in speaking), back pain, and stomachache. The most commonly reported sign on physical examination is subcutaneous emphysema located in the neck with a rate of 10%-100% [1,2,6,10,11}. The prevalence of Hamman's sign, which is described as a crunching, rasping sound, synchronous with the heartbeat, during oscultation of the anterior chest area, has been reported in various rates, changing between 0%-100%. In recent studies, this rate has been reported lower [12]. Hamman's sign was present in four patients in our study. The most common symptom, which was centrally located chest pain, was followed by dyspnea, cough, neck pain and saphonia.

Diagnosis is usually made with posteroanterior chest radiography and lateral radiography. Sakai et al [13]. have recommended the evaluation of the mediastinum with tomography since chest radiography isgenerally normal in patients with spontaneous pneumomediastinum. Computed thoracic tomography is among the gold standard of imaging techniques in patients that have a low amount of pneumomediastinum. In our study, eight patients were diagnosed with chest radiography and thirteen with tomography.

Main approach in the treatment of spontaneous pneumomediastinum is bed rest, oxygen therapy and analgesia. Patients respond well to this treatment. Similarly in many studies, treatment duration has been reported between 2 to 5 days [1,2,3,12]. Mean hospitalization duration in our study was 4.4 ± 2.17 days.

Complication development that could cause life-threatening situations is very rare in spontaneous pneumomediastinum. Gerazounis et al [14]. have reported relapse occurring in late periods. In our study, one female patient suffered a relapse that developed in the late period. Spontaneous pneumomediastinum also developed in the child of the same

patient. Pathology was not detected in the genetic analysis performed on both the mother and the child.

In conclusion, primary spontaneous pneumomediastinum is an uncommon pathology of thoracic surgery, which does not have adverse results. Despite encountered in low numbers, differential diagnosis should be considered in patients with acute chest pain since it has a very different treatment protocol when compared to other clinically similar diseases.

Consent could not be obtained from the patients since this was a retrospective study (5-yearfile scanning).

Conflict of Interest: Concept - M.Ç.; Design - M.Ç.; Supervision - M.Y.; Resources - M.Ç., M.N.K., M.Y.; Materials - M.Ç., M.N.K., M.Y.; Data Collection and/or Processing - M.Ç.; Analysis and/or Interpretation - M.Ç., M.N.K.; Literature Search - M.Ç., M.N.K., M.Y.; Writing - M.Ç.; Critical Review - M.Ç., M.N.K., M.Y.; Other - M.Ç., M.N.K., M.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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Turk Thorac J 2016; 17: 109-113 DOI: 10.5578/ttj.30506

ORIGINAL INVESTIGATION

Depressive Symptoms in Patients with Obstructive Sleep Apnea

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Abstract

OBJECTIVES: Different studies have investigate depressive symptom degree within sleep disordered patients with obstructive sleep apnea (OSA). However, little is known and unclear about OSA in patients with depression symptom in the literature. The purpose of this study was to investigate patients with OSA would have a higher prevalence of depression symptom relative to control patients.

MATERIAL AND METHODS: 72 patients with OSA (AHI ≥ 5) and 24 control subjects (AHI < 5) were assessed for depression symptom using the Beck Depression Inventory. Participants were underwent an overnight polysomnography assessment. An apnea-hypopnea index ≥ 5 events per hour was used as diagnosis for OSA. The associations between each total score on the Beck Depressive Inventory (BDI) and polysomnographic parameters were examined by correlation analysis.

RESULTS: We demonstrated that BDI scores has statistically significant correlation with the OSA in our present study according to similar previous studies (p= 0.008). Oxygen Desaturation Index (ODI) has correlated with BDI (r= 0.31).

CONCLUSION: These findings show that the frequency depression symptom is higher among individuals with OSA. Patients with OSA should be screened cautiously for depressive disorders.

KEYWORDS: Obstructive sleep apnea, depressive symptoms, beck depression index

Received: *10.07.2015* ***Accepted:*** *25.11.2015*

INTRODUCTION

Obstructive sleep apnea (OSA) is a common form of sleep-disordered breathing defined by repetitive upper airway obstruction during sleep and concurrent hypoxemia, causing excessive daytime sleepiness (EDS) and sleep fragmentation. Apart from EDS, other symptoms may also compromise quality of life, cause neuropsychological changes, affect day time activities, trigger cognitive dysfunction, and lead to psychological changes, including depression [1-3]. Depressive symptoms overlap those of many medical conditions, including OSA [4,5]. Again, OSA is common and adversely affects psychological well-being. Consequently, OSA symptoms may simulate those of depressive conditions.

Moreover, overlapping symptoms, such as a reduction in or loss of facial expression, deficitsin task initiation, and slower (passive) psychomotor functioning, may develop in those with either depression or OSA (reflecting diurnal sleepiness in the latter patients). Some patients may have intermediate conditions [6]. Although the association between OSA and depression remains unclear, OSA is associated with the presence of depressive symptoms. Clinically, the disturbed sleep of depressed individuals is abnormal in structure and cannot halt the progression of depressive symptoms.

Assessment of depressive symptoms is a substantial task. Several scales have been developedand confirmed as measures of the severity of depressive symptoms; these include the popular Beck Depressive Inventory (BDI), which is moderately specific and sensitive when used toidentify depressive disorders in both otherwise healthy individuals and those with comorbid medical conditions [7,8]. OSA patients have scored higher than controls on the BDI [9].

The existence of a relationship between depression and OSA remains speculative. Some authors have suggested that sleep fragmentation and the oxygen desaturation associated with OSA trigger depression [10,11]. However, others found no relationship between depressive symptoms and OSA [12]. However, it is reasonable to state that OSA is associated with the presence of depressive symptoms.

The aim of the present study was to measure the frequency of depressive symptoms in OSA patients, to describe these symptoms, and to determine patient characteristics according to the severity of OSA. In addition, we examined which

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OSA variables (the apnea-hypopnea index [AHI], the arousal index, the minimal oxygen saturation level, and/or the oxygen desaturation index) most accurately predicted the presence of depressive symptoms?

MATERIAL AND METHODS

Clinical Characteristics of Patients

We managed this research at the sleep laboratory of Mevlana University, from Jun 2014 to January 2015. All patients who provided the standard indications for polysomnographic evaluation for the suspected diagnosis of OSA were appropriate for registration into the research. Incomplete and unhealthy events were removed from the research; for this reason, the knowledge were collected from 96 patients who were evaluated to diagnose for OSA in respect of ICSD-3. Before information collection, informed consent was obtained from each participant. The information about gender, age, height, weight, and medical history of the patients was obtained and analyzed, and unnecessary information were eliminated.

Criteria for inclusion in the research were: A clinical history of severely snoring and witnessed apnea, No patients had chronic lung disease, and none were receiving bronchodilator treatment. No other psychiatric disorders, including personality disorders or substance dependence, anxiety disorder, no serious medical disorders, such as cerebral vascular disease, cardiac disease, neurological disease or; renal dysfunction, no other sleep disorders, such as periodic limb movements or hypersomnia.

Patients were interviewed and evaluate dusing three tools.

1. The ESS (Epworth Sleepiness Scale) questions the personal to rate the subjective sleepiness in eight different particular conditions, on a 0-3 scale, with 0 meaning no possibility at all of falling asleep, and 3 showing a high possibility of falling asleep. Hence, outcoming in a final score of 0 (least sleepy) to 24 (most sleepy). There is a fixed scoring recommendation of 10 as a probably excessive daytime sleepiness.

2. Depressive Symptoms

The Beck Depression index is a 21-item questionnaire used to assess self-reported depressive symptoms [13]. Though the BDI is not enough to diagnose depressive disorders, the BDI has been commonly utilized on to assess depressive symptoms and has been established to be sensitive and moderately specific in describing depressive disorders, both in otherwise healthy personals and in patients with comorbid medical diseases [14]. The Beck scores categorized the severity depression into four groups in successive attitude. BDI categories are normal (0-9), mild (10-15), moderate (16-23), and severe (24-63).

3. Polysomnography

Afterwards, whole individuals get through two nights of standard polysomnography System (Philips Respironics, Murrayville, PA) with Alice Sleepware Software. This polysomnogram is for diagnosing OSA containing four electroencephalograms (C3-A2, C4-A1, O1-A2, O2- A1) right and left electroculograms and electromyograms of anterior tibialis muscles and chin, oral and nasal flow with a thermistor, abdominal and thoracic respiratory movements with a tightness measure, and arterial oxygen saturation with a finger oximeter.

Sleep stages were scored in 30 s epochs in respect of the criteria and respiratory incidents were scored using standard criteria by a physician blind to the purpose of the research and the subject's identity. Apnea was described as a total interruption of airflow continues at least 10 s. Hypopnea was described as 50% or greater decrease in airflow continues at least 10 s and related with arousal from sleep [15]. The apnea-hypopnea index (AHI) was described as the score of apneas + hypopneas per hour of sleep. Apnea severity indices contained AHI and mean arterial oxygen saturation.

In the current research, the AHI criteria for OSA were based upon the ICSD-3, requiring an AHI ≥ 5 as a cutoff number for OSA. Hence, the sample was separated into two groups: those with an AHI ≥ 5, referred to as the OSA group, and those with an AHI < 5, referred to as the control group [16].

To assess obesity, we determined the BMI, which is figured out as body weight in kilograms divided by the square of the height in meters. Obesity was defined by a body mass index 30 kg/m^2 figured out from self-reported weight and height. The Mevlana University Medical Faculty ethics committee approved the study and patients who agreed to participate in the research gave informed consent.

Statistical Analysis

Means with standard deviations or percentages were used to describe the sample. OSA group and control group differences were evaluated with unpaired t-tests. Comparison forcategorical variables was done using the chi-square test or Fisher's exact test, where appropriate was used to compare these proportions in different groups. We analyzed the correlations among improvement rates in BDI scores, AHI, ODI, mean arterial oxygen saturation, and alterations in various sleep structures using the Pearson correlation. A p value < 0.05 was took into consideration statistically significant. Data analyses were conducted using Statistical SPSS 15 (California states, US).

RESULTS

The baseline characteristics of patients and normal control subjects are shown in Table 1. The mean total BDI score (± SD) was 13.5 ± 9.1, and females did not score significantly higher than males (10.5 ± 8.7) (p= 0.09) in this regard. The OSA group had a mean BDI score of 12.9 ± 9.8, and the control grouphad a mean score of 8.8 ± 4.7 (p= 0.008) (Table 1).

Patient distribution by BDI category is shown in Table 2. More than half of all OSA patients (59.7%) had depressive symptoms; about 34.7% had scores suggesting at least mild depression, and about 25% had scores suggesting moderate-to-severe depression.

Table 1. The baseline characteristics of the patients and normal control subjects are shown in Table 1

Characteristics	GRUP I (AHI > 5)	GRUP II (AHI < 5)	p value
Participants	72	24	
Male/female	42/30	10/14	0.36
Age, yr.	51.4 ± 13	45.6 ± 11.1	0.14
BMI	33.8 ± 6.5	30.8 ± 6.4	0.2
ESS score	9.0 ± 6.8	8.0 ± 5.3	0.43
AHI, per h	31.8 ± 22.7	1.8 ± 1.5	< 0.0001
Mean SaO_2, %	92.6 ± 2.6	94.5 ± 1.5	< 0.0001
Lowest SaO_2, %	76.2 ± 11.8	88.8 ± 2.3	< 0.0001
ODI	37.0 ± 27.9	4.3 ± 5.1	< 0.0001
Arousal index	19.5 ± 13.2	9.8 ± 4.4	< 0.0001
BDI	12.9 ± 9.8	8.8 ± 4.7	0.008

Data are presented as mean ± SD unless otherwise indicated. NS: Not significant, AHI: Apnea-hypopnea index, BDI: Beck depression index, BMI: Body-max index, ESS score: Epworth sleeiness scale, Lowest SaO_2: Lowest saturation oxygen, Mean SaO_2: Mean saturation oxygen, ODI: Oxygen desaturation index.

Table 2. Information about prevalence distribution of patients according to the BDI categories

BDI groups	OSA (+)	Control	p value
Normal	29 (%40.3)	11 (%45.8)	
Mild depression symptom score	25 (%34.7)	11 (%45.8)	
Moderate depression symptom score	9 (%12.5)	2 (%8.3)	
Severe depression symptom score	9 (%12.5)	none	
Total	72 (%100)	24 (%100)	0.509

BDI: Beck depression Index, OSA: Obstructive sleep apnea, P value was determinated by fisher test.

Correlations were found between higher BDI scores and ODI (r= 0.31, p= 0.002). Other OSA severity variable (AHI, AI, mean SaO_2, Lowest SaO_2) was not correlated with BDI scores (Table 3).

We were compared categorical variables. Neither the BMI northe gender distribution differed between the OSA and control groups. Thus, between-group sex differences were evaluated and any statistical difference was not obtained (p> 0.05). ESS (Epworth sleepiness scale) not influence BDI scores.

DISCUSSION

We sought to identify the depressive symptoms associated with OSA and the correlations between various parameters of sleep apnea and depression. We found that the presence of depressive symptoms increased the risk of OSA, which is in agreement with earlier findings indicating that OSA was closely linked to depression. According to the BDI, 41 (59.7%) and 29 (40.3%) of OSA patients exhibited or lacked depressive symptoms, respectively. The control group included 11 (45.8%) asymptomatic subjects. More than half the OSA patients (59.7%) reported depressive symptoms. A previous study found that the overall prevalence of such symptoms among those with sleep disorders was high, as 41% of OSA patients had significant levels of depression, and a meta-analysis showed that 7-63% of OSA patients were depressed [17,18]. The wide range is attributable to variations among populations.

Females exhibited a some what higher frequency of depressive symptoms, although this difference did not reach statistical significance. The frequencies of depressive symptoms were independent of the analytical tool employed.

We also used the oxygen desaturation index (ODI) to determine if ODI values were correlated with BDI scores. It is possible that severe oxygen desaturation during sleep plays a significant role in the development of neuropsychological disturbances, increasing BDI scores. The ODI clearly affected

Table 3. Pearson correlation scroe between BDI and OSA severity index parameters

Variables	BMI	AHI	Mean SaO_2	ODI	Lowest SaO_2	Arousal Index	ESS
BDI	0.13	0.24	-0.20	0.31*	-0.20	0.15	0.02
p value	0.20	0.019	0.048	0.002	0.06	0.12	0.85

AHI: Apnea-hypopnea index, BDI: Beck depression index, BMI: Body-max index, ESS score: Epworth sleeiness scale, Lowest SaO_2: Lowest saturation oxygen, Mean SaO_2: Mean saturation oxygen, ODI: Oxygen desaturation index. * There was positivie correlation beetwen BDI score and ODI.

the frequency of depressive symptoms, as we found that ODI values were positively associated with BDI scores, supporting the hypothesis that OSA and depression may be associated. Nocturnal hypoxemia is associated with periodic reductions in oxygen saturation caused by disturbed respiration [19]. A strong correlation was evident between BDI scores and the ODI (which is a measureof OSA severity), which is consistent with the study conducted by Deldin et al., who explored whether individuals with depression had ventilatory and/or hypoxic abnormalities [20]. In contrast to controls, depressive individuals had more flow limitations/h, an increased proportion of such limitations associated with desaturation, and more desaturation events. The effect of OSA on the severity of depression was not explored [20]. In the context of hypoxemia, Engleman et al. showed that the extent of cognitive impairment in OSA patients was closely associated with the intensity of hypoxia [21]. Thus, the hypoxemia associated with OSA may also influence mood.

We found thatthe extent of respiratory distress (the AHI score) did not correlate with the BDI score. Likewise, the large study conducted by Pillar and Lavie with 2.271 clinical referrals (with RDI (respiratory desaturation index) scores < 10 to > 30) found no relationship in males between depressive symptoms and RDI scores obtained using the Symptom Checklist 90 [22]. The Hospital Anxiety and Depression-Depression Scale (HAD-D) scores of 44 Swiss OSA patients and 16 snorers were not correlated with their AHI scores [23]. However, most studies on OSA patients have found positive relationships between AHI scores and the severity of depressive symptoms. Andrews et al. considered that factors other than hypopnea and apnea, shared by depressive and OSA patients, explained the connection between OSA and depressive symptoms evident in many clinical studies [24]. Such variations infindings may be attributable to the use of different methodologies, especially the tools employed to identify depressive symptoms. Additionally, cut off scores varied and different factors were assessed. The development of depressive symptoms is complex and multifactorial. Further research is needed to determine the relationship between depressive symptoms and AHI scores.

The principal feature of OSA that may trigger sleep fragmentation is recurrent arousal associated with hypopnea and apnea. Sleep fragmentation explains the EDS of OSA patients. The EDS evaluated using the ESS was correlated with the extent of depression on the HAD-Din 44 patients with OSA [23]. However, wefound no correlation between the arousal index and BDI scores, probably because we measured depression differently.

In adults, OSA and depression have been shown to be related. We found no correlation between BDI scores and age or sex; 65.9% of female and 78.8% of male OAS patients had depressive symptoms. This is in contrast with the finding of a previous study in which the prevalence of depressive symptoms was greater in females [25].

We examined associations between BMI and the severity of sleep apnea. Subjects classified as “overweight” or “obese” were more prone to OSA compared with those who were “underweight” or within the “normal” weight range. As shown in several previous studies, wefound that high AHI scores (reflecting anincreasing severity of OSA) were associated with high BMIs (p= 0.028) [24]. However, we found no relationship between BMI and depressive symptoms.

Several limitations of our research should be mentioned. First, the number of subjects was limited. The cross-sectional design rendersthe interpretation of associations questionable. Patients were recruited from those who visited the sleep laboratory, which compromises the generalizability of our findings. The control group also had some OSA symptoms and were thus not representative of the general population. This may have caused us to underestimate the association between OSA and depressive symptoms. The numbers of females and males in the two groups differed. In addition, data were gathered using self-report questionnaires, and some subjects may thus have overstated their perceived problems.

However, systematic evaluation of depressive symptoms in OSA patientsusing standardized clinical questionnaires is routine in many sleep disorder laboratories. However, the questionnaires were not designed to evaluate depression in OSA patients in particular and may be inappropriate foruse in such patients, as it remains uncertain whether OSA and depression are true comorbidities or if they simply share symptoms [24,26]. For example, 31% of patients who snored only during the night had some form of depression. Consequently, some of our OSA patients complained chiefly of symptoms other than sleepiness and snoring, such as depression.

In conclusion, our results contribute to the emerging literature on the association between depressive symptoms and OSA and are thus of clinical significance. Depression was widespread in patients with OSA. Systematic assessment of depressive symptoms in OSA patients using clinical questionnaires is routine in sleep disorder centers. Collectively, the evidence suggests that individuals with depressive symptoms should be screened for OSA.

Disclosure

The authors have no conflicts of interest to declare in relation to this work.

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/30At7d

Author Contributions: Concept - H.K.; - Supervision - H.K.; Analysis and/or Interpretation - F.K.; Litarature Review - H.K.; Writer - H.K.; Critical Review - R.A.

Conflict of Interest: No conflict of interest was declared by the author.

Financial Disclosure: The authors declared that this study has received no financial support.

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Turk Thorac J 2016; 17: 114-117 DOI: 10.5578/ttj.30507

REVIEW

How to Conduct a Pleural Research: Master's Advice

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Received: *28.06.2016* ***Accepted:*** *08.07.2016*

I have been doing medical research for nearly 50 years and most of it has dealth with pleural disease. While doing research during these years, I have also mentored many young researchers. This article summarizes what I have learned during this time.

Why Do Research? There are several reasons that one might want to do research and the reason will vary from person to person. First, one might do research to get **rich**, but the great majority of researchers do not get rich. Second, on might do research to get **famous**, but only a rare researcher gets famous. Third, one might do research to earn a **free trip**. Certainly, if you perform research and your abstract is accepted for presentation, you might get a free trip to an interesting place. Fourth, one might do research to get a **good professional position**. It is unequivocal that the more publications one has, the more opportunities there are professionally. Fifth, one might want to **answer a question** about the diagnosis or treatment of a disease. This is a very rationale reason to perform research. Lastly, on might want to **discover something that is unknown**. The last two reasons are the reasons that I have done most of my research.

What is necessary to perform research? There are many things that some think are necessary to perform research including a genius level of IQ, a lot of money, an inquisitive mind, dedication, persistence and organization. In my opinion, the most important element is **persistence**. I have worked with many individuals who start a project but never complete it. They most commonly stop after the research is completed, but before the paper is written. They may also stop while they are writing the protocol, doing the research or writing the paper. To be a successful researcher, one must be persistent. The second most important element is **organization**. By organization, I mean arranging one's life so time is not wasted. Do not waste time complaining about things. I keep a list of things that I need to do on my computer. When I have a number of minutes free I look at the list and see what I can accomplish in that number of minutes. If one is organized, one will not spend an hour looking for a paper. If one has their life organized, then they will have time for those things outside of research that gives them enjoyment. The third most important element is **dedication**. If you watch sporting events or go to movies rather than work on your research, you will be less likely to be successful. The fourth most important element is to have adequate **money**. Obviously, your research will fail if you do not have adequate funding. However, it should be noted that much research is completed with no funding. When I wrote the paper on Light's criteria, I had no funding for the project. The fifth most important element is to have an **inquisitive mind**. This element is important to aid the researcher in formulation the research and analyzing the data. The least important of the elements is a **genius level of IQ**. It certainly helps to be smarter than the average person, but a genius level of IQ is not necessary.

What are the different types of research? The types of research include case reports, reviews of the literature, retrospective reviews of case series, prospective reviews of case series, evaluation of new diagnostic tests, evaluation of new therapies, evaluation of new medical devices, and papers on basic science. **Case reports** are frequently the type of research than one starts with. However it is difficult to get case reports published in first rate journals because the publication of case reports decreases the impact factor of that journal. However, there are several pulmonary journals that are on Medline that now publish only case reports. **Reviews of the literature** are worthwhile but again are hard to

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get published unless one is invited to write the review. **Retrospective reviews of case series** are certainly useful and generally do not cost any money. However, with retrospective reviews, often some of the data points are missing. **Prospective reviews of case series** again do not cost any money and if they are organized, missing data should not be a problem. However, it may take years to accumulate the appropriate number of patients. **Evaluation of new diagnostic tests** is very important in advancing the practice of medicine. When a new diagnostic test is evaluated, it is important to compare the results with the new test with a test that has previously been used as the gold standard. **Evaluation of new therapies** is one of the most commonly performed types of research. Ideally evaluation of new therapies should be done with randomized double-blind controlled studies. If the study is not blinded, the researcher probably believes in his new therapy and will be biased in evaluating the results. **Evaluation of new medical devices** is also important in advancing medicalscience. Again it is best to do randomized controlled studies but frequently with medical device studies it is difficult to design the study so that it is blind. Lastly, a large percentage of medical research has to do with **basic science**. I did no basic science or animal studies until after I had been doing research for 20 years. I rapidly discovered that animals were much easier to recruit than patients. However, basic science research requires more resources than do many types of human research.

How do you get started to do research? The first thing you need to do is to **develop an idea**. How do you develop the idea? It can be a question raised when taking care of a patient. It can be a question raised by an associate, an attending or a subordinate. It can be a question raised while attending a lecture or while reading the medical literature. It can also be a question raised while dreaming or even while drinking.

Once you have the idea, then you need to **develop a hypothesis**. For example, this treatment is better than that treatment. Once you have you question and your hypothesis, you should review the literature. PubMed is a good place to start. You should narrow your search as far as is practical. One should obtain a copy or down load to your computer all pertinent reference papers. Do not rely on review papaers. Do not use Wikipedia.

It is important to organize the pertinent references. I recommend transferring all abstracts to your computer. Keep them organized by putting them in alphabetical order by the first author's last name. Make notes on the abstracts as pertinent. Make an outline of what you have found in your review.

Once you have your idea formulated and have the literature reviewed, then discuss the proposal with your associates. Carefully consider their comments, but you do not have to accept them all. At this time you should also evaluate the resources necessary to complete your project. How many patients will be needed to answer your question? How much money will it take to conduct the study? Take into account personnel, Elisa kits, animals, pharmaceuticals, pipettes, etc. What space is necessary including office space, freezer space, and laboratory space? Estimate how long it will take to complete the study. In general it is a good idea to multiply your estimate by at least a factor of two.

Is the research ethical? It is important to make certain that the research is ethical. For human subjects, the question I ask myself is as follows: Would I volunteer for this project if I qualified to participate. If the answer to this question is no, then the research should not be performed.

Writing the protocol. Before the research can be conducted, a research protocol needs to be written. You should start with the specific objectives and hypothesis. Then you should set the stage for your protocol by wring the background information which is essentially a review of the literature in the context of your research. Then describe the actual research protocol. Make this very detailed. Do not leave anything open to question. Include the statistical method of analysis in the protocol and perform a power analysis. Include references in the protocol.

Necessary Approvals Before Research Can Begin. If the project involves humans, approval must be obtained from the Institutional Review Board (IRB) before the study can be started. IRB approval is necessary even if you are doing a chart review but this does not require a written informed consent. IRB approval is also necessary if blood or tissue is obtained for use in present or future studies. Most journals will not accept a paper for publication if the project has not been approved by an IRB. If animals are being studied, the animal studies committee must approve the project. If radioisotopes are used in the study, the radioisotope committee must approve the project. If biohazards are involved, e.g. Staph.aureusor asbestos, the biohazard committee must approve the project. If you are studying a new drug or an old drug for a new indication, your proposal must be submitted to the National Health Service (NIH in the United States).

Eliciting Cooperation of Collaborators. One needs to create a WIN WIN situation in order to elicit the cooperation of collaborators. By this I mean that you need to create a situation in which you win (your project gets done) but the collaborator also needs to benefit. This at times can be troublesome. This can be in the form of a co-authorship on the manuscript, saving the collaborator work, a dinner, a book or money. It is important to avoid the following. It is unethical to provide direct payment of patient referral. Also avoid competition for patients that the collaborator wants to study, do not make extra work for the collaborator where he/she gets nothing in return.

Performing the Research. It is important to have everything organized before you actually start the research. Effort is

wasted if everything is not done on the first patients. It is best to develop forms for all the data which will be collected. The forms should be such that the data is easily transferred to a computer. The responsibilities of all co-investigators and collaborators should be well defined. Once the research is started, one should be patient, persistent and compulsive. If the research is going poorly and the chances for success appear minimal, the research project should be stopped.

Reasons for Failure of Research Projects.The most common causes for failure of a research project are a lack of organization or a lack of persistence. Other reasons for failure include the following: Inadequate literature review – after the research has been started it becomes apparent that the study has already been done or that the hypothesis is completely different from what is accepted in the medical literature. It is also possible that someone completes an identical project before you project is completed, but this is uncommon. Inadequate numbers of patients can lead to failure of a project as can lack of the required cooperation. In some instances, there is just not enough time to complete the project. This is particularly likely to happen when residents, fellows or visiting researchers are primarily responsible for the project. And lastly and most importantly, the research is done but the paper never gets written. This has happened to me numerous times in my career.

Analyzing the Data. After the research is completed, it is time to analyze the data. Many individuals are frightened by statistics. However, data analysis is easy if the data is organized. The actual statistical analysis will depend upon the design of the project. In general one desires to discover whether the results in two groups differ significantly. Basic terms in statistics are the mean (the average value), the median (the value with an equal number of results above and below) and the variance which is a measure of the variability of the results in one group.

Minimize the Variance. The formula for the variance is shown in the following equation

$$\text{Variance} = \text{Sum}(x_i - x_{mean})^2/(n-1)$$

Where x_i is the value of the ith observation, x_{mean} is the average of all the obervations and n is the total number of observations in the group. The standard deviation (SD) is the square root of the variance. The standard error of the mean (SEM) is the SD divided by the square root of n. In order for two means to be different with a probability (p) value less than 0.05, the two means need to be separated by at least 2 SEMs. From the above discussion, it is apparent that if the variance is minimized, the two means are more likely to differ significantly. In performing research, it is important to make every effort to minimize the variance. This can be achieved by paying careful attention to the details to decrease the randomness of the results.

Writing the Manuscript. The main sections of the manuscript are the abstract (summary), the introduction (why?), the materials and methods (how?), the results (what you found) and the discussion (so what). When I write a manuscript, I write the sections in the following order. First I write the material and methods section. This section is the easiest to write - just cut and paste from the protocol (remember to change tenses from future to past). I then write the results with the liberal use of tables and graphs. I then write the introduction again relying heavily on the protocol. I do not write the introduction initially because the results of the study may alter the introduction somewhat. I then write the discussion. Lastly I write the abstract. I write the abstract last so that is will be consistent with the remainder of the paper.

Writing the discussion. The discussion without a doubt is the most difficult part of the paper to write. Before I start writing the discussion, I always make an outline of what I want to include in the discussion. In the outline, the first entry is a brief summary of the results of the study and the last entry is the conclusion of the study. The other entries in the discussion should compare the results of the present study with those reported previously, the clinical implications of the study, and the limitations of the study.

Tips on Writing. Write in a simple manner. Keep the sentences short. The first sentence in each paragraph should say what that paragraph is going to say. This makes it easy for the reader to speed read the paper. If the reader agrees with and knows about what is said in the first sentence, he/she can skip the rest of the paragraph. If you have difficulty writing on paragraph, go to a different paragraph. Writing the manuscript is a big task. Count your successes as paragraphs, not entire papers. If you write one paragraph per day, you will have at least 12 manuscipts a year.

Submitting the Paper. Before you submit the manuscript, have someone whose first language is English (if you are submitting to an English journal) review the manuscript an edit it. The more people you have review the manuscript before submission the better. Next you need to choose the journal for submission of your paper. One should look at previous editions of the journal to see if they have accepted similar papers on similar subjects. It is best to select a journal with a high impact factor. After the journal is selected, read the instruction to the authors carefully and follow the instructions. If the instruction state that the upper limit of words is 3000, do not submit a manuscript with 4000 words. If you do not follow the directions, the reviewers will think that you are not a careful researcher.

When the Paper is Accepted Provided Revisions Are Done. Rarely is a paper accepted without some revisions being requested. The goal of revising the paper is to get it accepted for publication. A rebuttal letter should be written where the critiques of each of the reviewers is addressed. List each criticism by a reviewer and then formulate a response. It is best to use different fonts when listing criticisms and making responses. When the reviewer requests an explanation of

something, he wants it explained in the manuscript-not only in the rebuttal letter. Make simple requested changes without argument. Remember the reviewer is trying to make the paper better. Thank the reviewers for their constructive criticisms whether or not you like them.

When the Paper is Rejected. If the paper is rejected, do not give up but rather plan on resubmitting. Remember that submitting a paper is a little like playing the lottery – sometimes you get favorable reviewers and sometimes you get unfavorable reviewers. Remember the reviewers frequently do not agree-maybe you were just unlucky or alternatively maybe the paper is really bad. There are many medical journals and some have higher standards than others. Before you submit to another journal, look carefully at the criticisms and answer as many as possible. You may get the same reviewer again and nothing irritates a reviewer more than seeing the same paper again without any changes.

Conclusions. The most important factors for successful research are persistence and organization. Before the research is started, review the literature and writ a detailed protocol. Create win win situations to elicit the cooperation of collaborators. Write the paper one paragraph at a time. Respond to reviewers and chane the paper as suggested.

Turk Thorac J 2016; 17: 118-121 DOI: 10.5578/ttj.30508

CASE REPORT

Response of Complex Undefined Hypereosinophilic Syndrome to Treatment with Imatinib

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Abstract

Hypereosinophilic syndomes (HESs) include potentially lethal multisystem disorders characterized by eosinophilic infiltration of a variable spectrum of target organs, predominantly the skin, heart, lungs, gastrointestinal tract, and nervous system. Based on recent advances in molecular and genetic diagnostic techniques and increasing experience with differences in clinical features and prognosis, subtypes have been defined, including "myeloproliferative-HES ", "lymphocytic-HES", "familial eosinophilia", "overlap HES", "undefined HES" ("complex undefined HES", "simple undefined HES", "episodic undefined HES") and "eosinophil associated diseases" (such as Churg-Strauss syndrome). HES should be kept in mind in the differential diagnosis of eosinophilic lung diseases especially in patients with peripheral eosinophilia and pulmonary infiltrates. Corticosteroids represent an effective firstline approach to decreasing eosinophil counts in the majority of cases. Imatinib might be used for corticosteroid nonresponders. We herein report a patient with "complex undefined HES" who had disease resistant to corticosteroids, but who had a significant response after treatment with imatinib.

KEYWORDS: Hypereosinophilic sydrome, Churg-Strauss syndrome, complex undefined hypereosinophilic syndrome, imatinib

Received/Geliş Tarihi: *18.02.2015* ***Accepted/Kabul Tarihi:*** *02.07.2015*

INTRODUCTION

After excluding secondary factors that can cause hypereosiniphilia, hypereosiniphilia is evaluated under hypereosiniphilic syndorme (HES). The criteria for hypereosiniphilic syndrome are as follows: 1) eosinophile over 1500/mm^3; 2) persistent eosinophilia (does not have to last more than 6 months) or organ damage/dysfunction; 3) exclusion of secondary reasons of eosinophilia [1]. HESs are examined under six separate headings including "myeloproliferative –HES (M-HES)", "lymphocytic-HES" (L-HES), "familial eosinophilia", "overlap eosinophilic HES", "undefined HES", and "eosinophil associated diseases" [2]. Undefined HES is also examined under three separate headings including "complex undefined HES", which is symptomatic organ infiltration associated with eosinophilia; "simple undefined HES", where the disease progresses with only eosiphilia elevation without organ involvement; and "episodic HES' where the disease progresses with cyclic angioedema and esosiniphilia. Recently Churg-Strauss Syndorme (CSS) also named as "Eosinophilic granulomatosis polyangiitis" has been examined under the sub-group of esoniphilia related HES diseases and is a necrotizing systemic vasculitis that affect small-medium diameter blood vessels [3,4].

Complex undefined HES is an ecarttaion diagnosis, which can progress with multiple organ involvement and mimic many diseases. Therefore, a very extensive differential diagnosis needs to be made. CSS, one of the eosinophilic lung diseases, must be considered in differential diagnosis since treatment and prognosis can be different. This study presents a case that was referred to our clinic with CSS diagnosis but received "complex undefined HES" diagnosis.

CASE PRESENTATION

A 40-year-old male patient was given inhaler as a result of asthma diagnosis in different clinics to which he applied with complaints like cough and dyspnea; however, these treatments were not beneficial at all. Due to the detection of peripheral eosinophilia, asthma-like symptoms, pulmonary nodules on thoracic computed tomography (CT), and eosinophilia in transbronchial biopsy, the patient received CSS diagnosis and was started on methylprednisolone 40 mg/day which was gradually decreased. Owing to the fact that there was no ameliorartion in his symptoms,

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methotrexate 15 mg/day was added to the patient's treatment one year later. The patient had been using methylprednisolone (24 mg/day) and methotrexate (10 mg/day) before he applied to our clinic. The patient who had not had regression in his complaints and had developed corticosteroid side effects (myopathy, cushingoid appearance) applied to our clinic. The patient who described dyspnea with mild effort had a cough that hit during daytime and increased with exercise. Patient history did not include allergic asthma, rhinitis, nasal polyposis, and atopic dermatitis. The patient did not describe any bruxing, itching in the anal region, consuming raw food, and suspicious travel. The patient did not have drugs, food, bee allergies, did not smoke, and had not undergone surgeries. There was no characteristic to be detected in the patient's and family history. Blood pressure at the time of admission was 130/80 mmHg, respiratory rate was 20/min; pulse was 90/min; and saturation at room temperature was 95%. Respiratory and other system examinations were normal. Blood eosinophilia ratio of the patient with mild leukocytosis was found as 37% (4280/mm^3). Anemia and thrombocytopenia were not detected. Bilateral bronchovascular shadows became evident on the posteroanterior lung graphy.

Since symptoms of cough and dyspnea continued in our case and due to eosinophilia, examinations were conducted towards the etiology of hypereosinophilia. Microscopic investigations of the faeces were negative. Prick tests carried out with food (mutton, chicken, apple, orange, banana, strawberry, peanut, hazelnut, tomato, walnut, lemon, potato, kiwi, rye flour, wheat flour, cow milk, cocoa, egg white, egg yolk, shrimp, fish) and aeroallergens (*Dermatophagoides pteronyssinus, Dermatophagoides farinae, Betulacees, Salicacees,* field pollen, compositae, tree pollen, grain pollen, *Penicillum*, *Aspergillus*, *Cladosporium*, Alterneria, cockroach, cat, dog, horse) (Stallergenes, France) were detected negative. Mild restrictive pattern was present in pulmonary function tests and there was no reversibility. Routine laboratory tests were also normal. C-reactive protein, rheumatoid factor, anti-cyclic citrullinated peptide, sedimentation, aaspergillus-specific IgE, anti-nuclear anticore, anti-neutrophil cytoplasmic anticore, anti-dsDNA, creatine kinase, Troponin T, immunoglobulins weredetected normal. Anti-HIV, hepatitis marker, cyst hydatid IHA/IFAT, amoebiosis IFA were negative. Only vitamin B12 was high (1291 pg/mL).

Milimetric nodular appearances with ground glass densities in upper lobes were determined on thoracic CT (Figure 1a). Pathological findings were not detected on paranasl CT and upper and lower abdomen CT. Echocardiography was normal. Eosinophilia-rich inflammatory cells were detected in transbronchial lung biopsy. Numerous eosinophilic granulocytes were present in bone marrow biopsy. Increase in blast and malignant infiltration were not detected (Figure 2). JAK-2 mutation and Philadelphia chromosome were negative. Lymphoreticular malignancies were excluded. Solid organ malignancy was not considered in the patient in whom no primary malignancies were detected. Due to the fact that Vitamin B12 value was high, advanced molecular tests were asked for HES variant sub group analysis. FIP1-like1 (FIP1L1) and platelet-derived growth factor receptor (PDGFR)α mutation were found negative.

Our case received a diagnosis of complex undefined HES since eosinophilia-rich cellularity compatible with HES was detected in bone marrow biopsy, necrosis and eosinophilic infiltration where granulomatosis reaction was not present was detected in lung biopsy, and other diagnoses that could cause eosinophilia were eliminated. Our case did not respond to corticosteroid treatment and imatinib mesylate 400 mg/day was started. Clinical response was achieved in the first two weeks of treatment. As all complaints disappeared and eosinophil levels returned to normal in the first month, the dosage was decreased to 100 mg/day. Radiologic improvement was present on thoracic CT (Figure 1b). The patient still receives imatinib 100 mg/day in the first year of treatment. No side effects related to imatinib has been observed. Our case was presented with a review of the literature after receiving his consent.

DISCUSSION

Hypereosiniphilia has a wide range of evaluation areas from parasitic diseases to drugs, leymphoreticular malignancies,

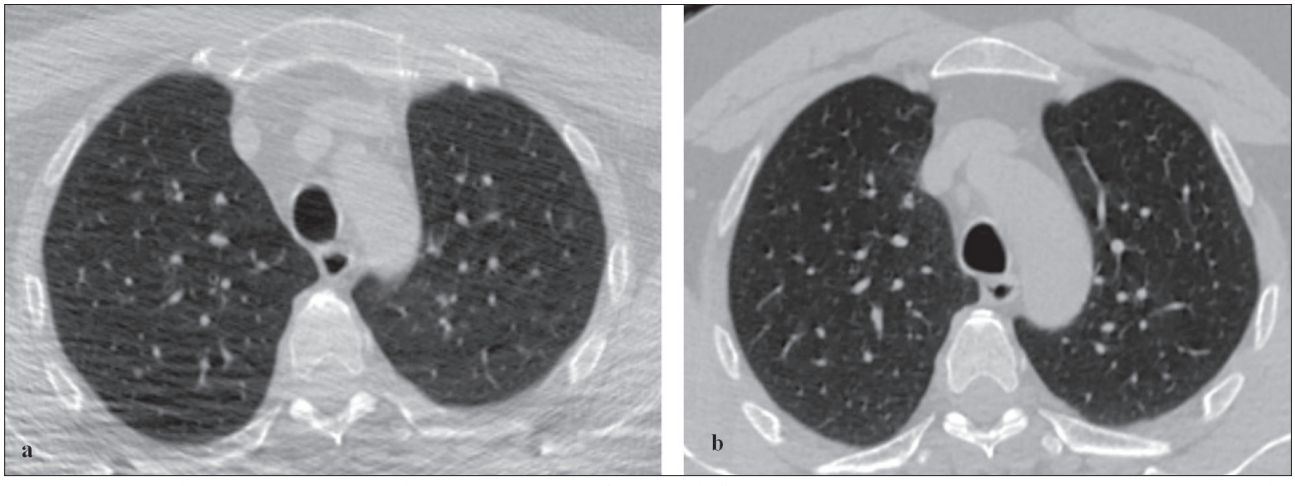

Figure 1. (a) Centrilobular ground glass nodules in upper lobes of the lung before imatinib treatment, **(b)** Regression is seen in centrilobular ground glass nodules 1 year after imatinib treatment.

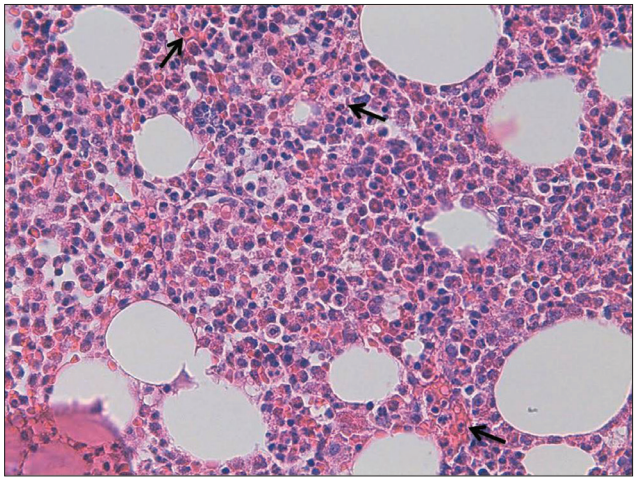

Figure 2. Bone marrow biopsy is cellular and dominance attracts attention in myeloid elements mostly eosinophilic series (x400, HE)

solid organ malignancies, CSS, and ABPA [5]. Practical approach consists primarily the inquiry of history of drug use that could cause esosinophilia and the history of parasitic infection. If there is history of drug use, it should be stopped. If these conditions do not exist, other secondary reasons for hyperesoniphilia should be looked into [5]. Microscopic investigations of the faeces were carried out six times on separate days and serologic tests were asked for parasitic infections. The test results were negative. Furthermore, parasite or history of drug use that could cause Löffler syndrome was not present.

Patients with asthma should be evaluated for CSS and ABPA in case of very apparent eosinophil [6,7]. Six criteria have been established by ACR for the diagnosis of CSS syndrome, including 1) Asthma; 2) Eosinophilia > 10%; 3) Mononeuropathy or polyneuropathy; 4) Pilmonary infiltrates on radiologic imaging; 5) Paranasal sinus pathologies; and 6) Pathologic ampling where extravascular eosinophilic infiltrations are shown [8]. Carrying four or more of these critera enable CSS diagnosis in patients who have already been proven to have vasculitis histapathologically [9]. Our case carried three of the ACC criteria (sosinophilia > 10%, eosinophilic tissue infiltration and ground glass nodules on thoracic CT) and did not have a histopathological diagnosis compatible with vasculitis. Moreover, CSS prodromal period findings were not present. Hence, CSS was not considered in our case. The diagnosis of ABPA, one of the causes of hyperesoniphilia, was excluded due to the normal value of T. IgE, having not detected aspergillus sensitivity on skin prick test, and negative value of aspergillus-specific IgE. A probable solid organ malignancy that could cause hyperesophilia was not considered in our case who did not have any complaints regarding weight loss and loss of appetite, on whose radiologic examinations, a primary malignancy was not detected, and whose sedimentation and tumor markers were normal. Blood eosinophilia can accompany organ-specific eosinophilic diseases, such as chronic eosinophilic pneumonia (CEP), eosinophilic gastroenteritis, and some dermatological disorders [5]. Dermatological and gastrointestinal involvement was not present in our case. Having not detected radiological findings compatible with CEP and having had no corticosteroid response had us move off from CEP diagnosis. "Familial HES" was not considered since there was no family history of HES. Myeloproliferative and lymphoproliferative malignancies were ruled out as a result of peripheral smear, bone marrow biopsy, flow immuncytometry, and cytogenetic investigations.

If the underlying reason of eosinophilia is not detected, advanced diagnostic tests should be asked for to detect HES variants [5]. In most M-HES patients, due to the interstitial deletion on the 4q12 chromosome, FIP1-like1 (FIP1L1) and platelet-derived growth factor receptor (PDGFR)α genes are caused to fusion, which results in the activation of tyrosine kinase [10]. FIP1L1-PDGFRα mutation was detected negative in our case. However, carrying four or more of the following eight characteristics in FIP1L1-PDGFRα negative HES cases is evaluated under: 1) the presence of dysplastic eosinophils on peripheral smear; 2) having serum vitamin B12 level over 1000 pg/mL; 3) having serum tryptase level over 12 ng/mL; 4) anemia, thrombocytopenia or the association of both; 5) hepatosplenomegaly; 6) over 80% cellularity in bone marrow biopsy; 7) the presence of dysplastic ast cells in bone marrow (being 25% more than spindle-shaped mast cells); 8) Myelofibrosis (having antireticuline anticore staining in bone marrow biopsy) [2]. M-HES diagnosis was not considered for our case since he did not carry the criteria apart from Vitamin B12 elevation.

L-HES is characterized with nonmalignant expansion of T cell population that can produce eosinophilopoetic cytokine. IgE, IgM and IgG are generally detected high in L-HES cases [11]. Other frequently seen characteristics include 1) skin involvement; 2) frequent presenceof history of atopy; 3) glucocorticosteroid response is generally very good [12]. L-HES variant diagnosis was also not considered in our case as atopy was not detected, immunoglobulins were normal, and particularly there was no corticosteroid reponse in our case. After having excluded all secondary reasons that could cause hypereosinophilia and other diseases ranking among the sub-groups of HES, our case was diagnosed with complex undefined HES.

Although all organs theoretically have the potential to infiltrate with eosinophils, cardiovascular, pulmonary, skin, nervous, and gastrointestinal sytems are the most frequently affected and pulmonary involvement is seen around 50% [13]. Only pulmonary involvement was present in our case.

In FIP1/PDGFRα negative HES cases, first choice of treatment is corticosteroids. In cases that do not respond to corticosteroid treatment and those who cannot use this drug due to its side effects, many cytotoxic drugs have been used instead. Hydroxyurea is the most studied among all. However, its use as monotherapy shows limited benefit. Moreover, therapeutic effectiveness of effective immunomodulator treatments on Th2 type cytokines (IL5, IL-4) and treatments like cyclosporine and alemtuzumab on IFN-α have been shown in selected cases [2,11,14]. Imatinib mesilate is a tyrosine kinase inhibitor. It is used in the treatment of PDGFRα-related HES

that causes the activation of tyrosine kinase by generating the fusion of FIP1/PDGFRα genes. Its use on PDGFRα negative HES cases is limited [4]. However, imatinib can be considered second choice treatment in cases with no response to corticosteroid [5,15].

In FIP1/PDGFRα positive HES cases, response to imatinib is very quick. Eosinophil generally regresses to normal values within 1 week, and symptoms and findings improve in 1 month. The dosage of imatinib is decreased to 100 mg/day when eosinophilia and its symptoms are under control. In FIP1/PDGFRα negative HES cases, a higher initial dose of 400 mg/day can be needed [2]. Despite corticosteroid treatment, clinical response could not be received and eosinophil levels did not regress in our case, which led us to start imatinib treatment. After this treatment, an apparent clinical response was achieved in one week and eosinophils regressed to normal values.

In conclusion, complex undefined HES is an ecartation diagnosis. Its differential diagnosis should be made with eosinophilic lung diseases which are pulmonary disease groups that progress with particularly peripheral eosinophilia or tissue infiltration. Imatinib should be definitely kept in mind in the treatment of these patients that do not respond to corticosteroid treatment.

Author Contributions: Concept - İ.Y. L.K; Desing - Ç.P., N.T.; Supervision - İ.Y., L.K.; Funding - İ.Y., L.K., N.T., Ö.C., Ç.P., H.B., İ.G.; Materials – İ.Y., L.K., N.T., Ö.C., Ç.P., H.B., İ.G.; Data Collection and/or Proccessing - İ.Y., L.K., N.T., Ö.C., Ç.P., H.B., İ.G., A.Y.; Analysis and/or Interpretation - İ.Y., L.K., N.T., Ö.C., Ç.P., H.B., İ.G., A.Y.; Litarature Review - İ.Y., L.K., N.T., Ö.C., Ç.P., H.B., İ.G., Writer - İ.Y., L.K., N.T., Ö.C., Ç.P., H.B., İ.G., A.Y.; Critical Review - İ.Y., L.K., N.T., İ.G., Ç.P., .H.B., Ö.C., A.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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Turk Thorac J 2016; 17: 122-124 DOI: 10.5578/ttj.30509

CASE REPORT

A Pulmonary Tuberculosis Case Presented with Tonsillar Involvement*

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Abstract

Tonsillar tuberculosis is a rare form of extra pulmonary tuberculosis. We reported a case with tonsillar tuberculosis secondary to pulmonary tuberculosis in this paper. A 26 year old, unimmunocompromised man admitted to head and neck surgery clinic with complaints of fever, throatache and difficulty swallowing. The patient was consulted by infectious diseases clinic because of examination findings and his history. Asid fast basili was determined in tonsillar lesion smear, sputum and the patient was diagnosed as tonsillar and pulmonary tuberculosis. Antituberculous agents were started. Complaints of the patient were decreased and any adverse effect was developed. Treatment was completed in 9 months. In patients with long-term difficulty swallowing and fever, countries in which tuberculosis is prevalent, tonsillar tuberculosis should be considered, even if the patients were unimmunocompromised.

KEYWORDS: Tuberculosis, tonsillitis, pulmonary tuberculosis

Received: *05.10.2015* ***Accepted:*** *16.12.2015*

INTRODUCTION

Tuberculosis (TB) is a widely encountered infectious disease that may affect all organs and tissues. After vaccination applications and anti-TB treatments, a dramatic decrease has occurred in the incidence of the tuberculosis infection [1]. Upper respiratory tract infection is seen in approximately 2% of the cases with active tuberculosis [2]. Despite the decrease in incidence with the pasteurization of milk, it is not surprising to encounter tonsillar TB since tonsils are lymphoid tissues and they frequently come into contact with positive sputum due to localization in cases with active tuberculosis [3].

This study aimed to report a case presented with difficulty in swallowing and sore throat and diagnosed with tonsillar TB secondary to pulmonary tuberculosis.

CASE PRESENTATION

A 26-year-old male patient with no previously known illnesses had applied to head and neck surgery polyclinic with fever, sore throat, and difficulty in swallowing and speaking complaints ongoing for five weeks. On examination, both tonsils were detected hypertrophic oropharynx and white plaques were seen on the tonsils (Figure 1). The patient, whose posteroanterior chest radiography was taken, was referred to infectious diseases polyclinic due to opacity increase in the left upper zone and the presence of suspected cavitation on radiography (Figure 2).

The patient was observed to be fatigued during his first examination. The patient who looked thin was found out to have lost approximately 9 kg in one month. Patient history revealed that TB was present in his father and older brother. Upon admission, patient's temperature was 38.7°C and respiratory rate was 25/min. Extensive rale was heard in

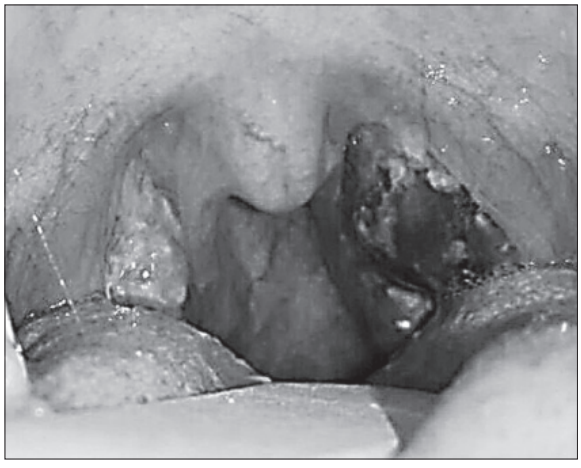

Figure 1. Bilateral tonsils in the oropharengeal examination of the patient.

** The 7th Eurasia Congress of Infectious Diseases (EACID) 2015, Tbilisi, Georgia*

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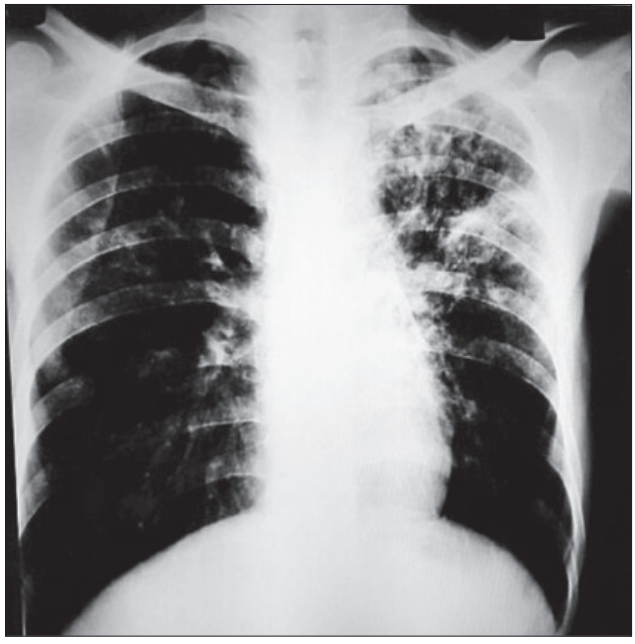

Figure 2. Cavitary lesions in the posteroanterior chest radiograpghy of the patient.

both lungs. Lymphadenopathy, approximately 1 x 1.5 cm and 1 x 2 in size, was detected on both anterior cervical chains. Throat culture was taken For microbial examination. When patient history was probed into, it was found out that the patient had applied to an infectious diseases polyclinic with the same complaints there weeks prior and oral antibiotics were prescribed with a diagnosis of bacterial tonsillitis but no culture was taken.

Laboratory results upon admission were as follows: white blood cell count 4200/mm^3, hemoglobin 8.9 mg/dL, hematocrit % 37.5, erythrocyte sedimentation rate 45 mm/sa, C-reactive protein 2.5 mg/dL, serum alanine aminotransferase 41 IU/L, and serum aspartate aminotransferase 38 IU/L. Human immunodeficiency virus (HIV) of the patient was detected negative with enzyme linked immunosorbent assay (ELISA).

In the smear of the plaques and sputum of the patient, acid-resistant bacilli (ARB) were detected positive (Figure 3).

The patient was started on anti-tuberculosis treatment (300 mg/day isoniaside, 600 mg/day rifampicin, 1200 mg/day ethambutol, 1500 mg/day streptomycin) with a diagnosis of tonsillar tuberculosis secondary to pulmonary tuberculosis. No side effects related to treatment developed. In the meantime, microbacteria growth was established in the sputum culture. Examination findings of the patient regressed in the first month of the treatment and the plaques on the tonsils disappeared. The treatment of the patient was completed in nine months. The patient gave consent to the presentation of this case that was diagnosed late.

DISCUSSION

Extrapulmonary localization of tuberculosis is seen very rarely and tonsillar lesions are even rarer [1,4]. Upper respiratory tract is protected thanks to the inhibitor effect of the sputum

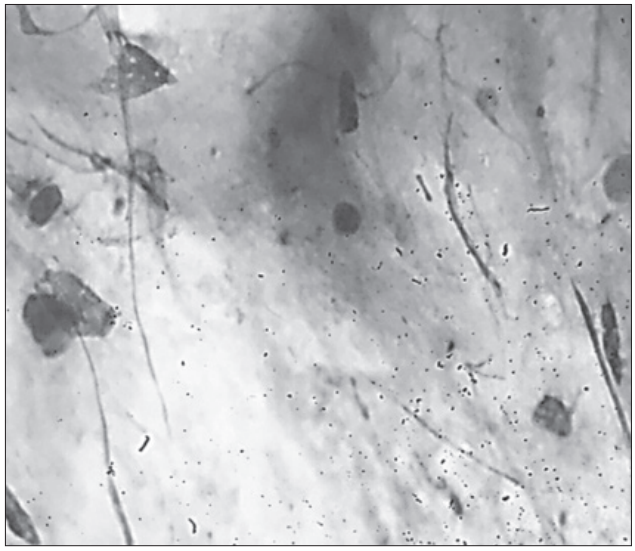

Figure 3. Acid-resistant bacilli in the sputum sample.

on TB bacillus. The presence of saprophytes, the fact that striated muscles antagonize bacterial invasion and the protective epithelium of the oropharyngeal mucosa create an inhibitor effect on bacillus [1,5]. However, oral TB may develop as a result of drinking contaminated milk and the agent is frequently *M. bovis*. Oral TB in adults develops secondary to pulmonary TB [6]. It is our belief that since our patient had ARB (+) pulmonary tuberculosis, the reason was positive sputum exposure.

Extrapulmonary tuberculosis can be seen as a result of decreased host response related to chronic alcoholism, long-term steroid use, chronic obstructive pulmonary disease (COPD), diabetes, chronic renal failure, pregnancy, and HIV infection [7,8]. Patient history did not include any use of immunosuppressant agents and when the patient was evaluated for HIV, anti-HIV negativity was established. However, TB history was present in the patient's family.

Oral tuberculosis lesions can be seen in forms of ulcer, nodule and plaque [9]. The most frequently encountered form of tonsil TB is the ulcer form and the patient had bilateral white plaques. Due to the similarity of the symptoms and abnormal tonsil findings, tonsil TB shows resemblance to malignant tumors and differentiation of the two can be difficult. Traumatic ulcerations, actinomyces, syphilitic ulcers and Wegener granulomatosis are other diseases that should be considered in differential diagnosis [4,5].

Radiological evaluation of the lungs, serologic tests, bacterial and fungal cultures and direct ARB evaluation of the lesion and the sputum are adjuvant methods in diagnosis. Dental practitioners and head and neck surgery specialists should be attentive to oral TB in patients who are in close contact with people with low socio-economic level, history of smoking and who are known to have TB, especially in countries where TB prevalence is high. In the present case study, the patient was referred to infectious diseases polyclinic with a preliminary diagnosis of tonsil TB after having applied to the head and neck surgery polyclinic.

In conclusion, TB is a serious and life-threatening disease, which should be kept in mind in differential diagnosis in the presence of an infectious case in countries where TB is endemic. In the presence of bilateral but non-proportional tonsil hypertrophy accompanied by cervical lymphadenopathy, TB should be considered in differential diagnosis even if the patient's immune system is strong.

There is no conflict of interest among authors in this case report and no financial support has been received.

Author Contributions: Concept - C.K.; Design - E.K.K.; Supervision - E.K.K.; Resources - E.K.K.; Materials - C.K; Data Collection and/or Processing - E.K.K.; Analysis and/or Interpretation - E.K.K.; Literature Search - E.K.K.; Writing Manuscript - E.K.K.; Critical Review - C.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial supports.

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Turk Thorac J 2016; 17: 125-127 DOI: 10.5578/ttj.30510

CASE REPORT

Squamous Cell Cancer of The Lung with Synchronous Renal Cell Carcinoma

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Abstract

Coexistence of two or more primary cancers is a relatively rare case. Not with standing that the coexistence of multiple primary cancers is often discussed in the literature, there is a small number of publications concerning the coexistence of squamous cell lung carcinoma and renal cancer. In this case report, detection of both squamous cell lung carcinoma and primary renal cancer in one male patient is going to be discussed.

KEYWORDS: Lung cancer, multiple primary cancers, synchronous tumor, renal cancer

Received: *18.09.2015* ***Accepted:*** *15.12.2015*

INTRODUCTION

Cancers grown at more than one focuses are multiple primary cancers (MPC). MPC was documented for the first time in 1889 by Billroth et al. Warren used MPC definition, afterwards [1,2]. MPC can be classified as synchronous and metachronous. If primary tumors were diagnosed at the same time or within six months, they are called as synchronous cancer; if second primary tumor is diagnosed after six months of diagnosis of the primary tumor, it is called as metachronous cancer [3]. Many MPC's were reported in the literature. Although primary squamous lung cell carcinomas or renal cancer cases are very frequent, synchronous presentation of the squamous cell histologic subtypes of these cancers is very rare. In this case report, primary squamous lung cell carcinoma and synchronous renal cancer will be reported.

CASE PRESENTATION

A 55-year-old male patient with respiratory disorder and haemoptysis symptoms admitted to the clinic. In the chest radiograph an approximately 6 x 7 cm mass adjacent to the left hilum was detected and patient was directed to us (Figure 1). In the patient's history, there wasn't any known chronic illness and drug use but the patient was smoking 40 packs in a year. In family history, there was no malignancy. On physical examination; patient's fever was taken as 36.3°C, pulsation 105/min, blood pressure 100/60 mmHg and respiratory rate as 16/min. During lung auscultation; bilateral diffuse rhonchus and a decrease in the lung sounds at lingula were detected. In the laboratory tests: white blood cell 13.38 x 10^3/µL, hemoglobin: 12.5 mg/dL, platelet: 519 x 10^3/µL, total calcium: 12.7 mg/dL, erythrocyte sedimentation rate: 17 mm/h and C-reactive protein: 13 mg/L were found. In thoracic computed tomography (CT), central soft tissue densities that show nodularity in patches at the left hilar level and cavitary lesions with irregular inner contour, with 6.5 x 8 cm of axial extent, forming pleural retraction that abutting fissure at the upper lobe segments were identified (Figure 2a). Also an approximately 9 cm lesion was detected in the lower $^1/_2$ part of the right kidney within the upper abdominal organ section (Figure 2b). Through the positron emission tomography (PET-CT) an approximately 80 x 70 x 78 sized mm mass (SUV max: 17) that its boundaries cannot be well-defined from the left pulmonary artery which encircles the main left bronchus and its branches extend from the hilus of the left lung to the lateral costal pleura. In the lower $^1/_2$ segment of the right kidney, a 9 cm sized mass (SUV max: 19) was detected. According to these symptoms bronchoscopic biopsy was conducted on the lower end of the left main bronchus in another hospital via fiberoptic bronchoscopy. A sample was taken via tru-cut biopsy conducted on the lesion in the right kidney. With reference to the lung and kidney biopsy results, non-small cell lung carcinoma (favoured with squamous cell carcinoma) and renal cell carcinoma were determined, respectively (Figure 3a,b).

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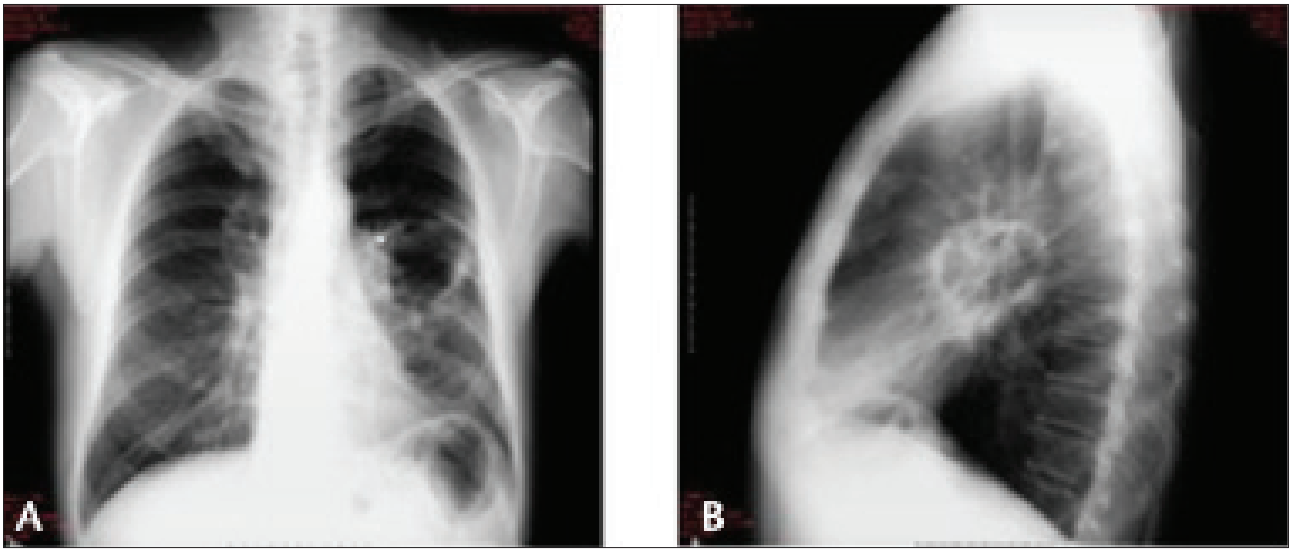

Figure 1. Posterior-anterior and lateral chest radiograph.

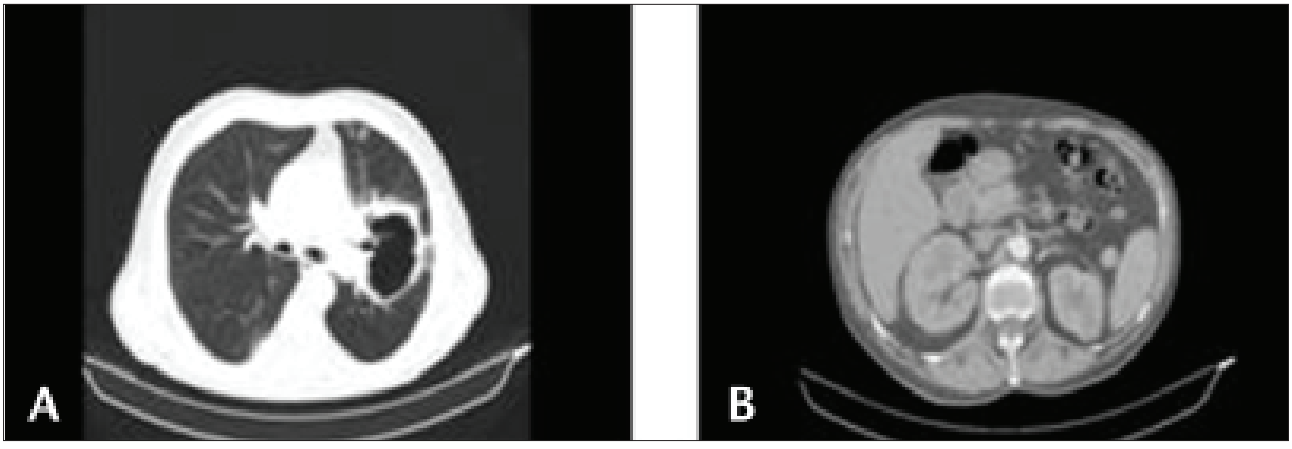

Figure 2. Computed tomography image, **(A)** renal mass, **(B)** lung mass.

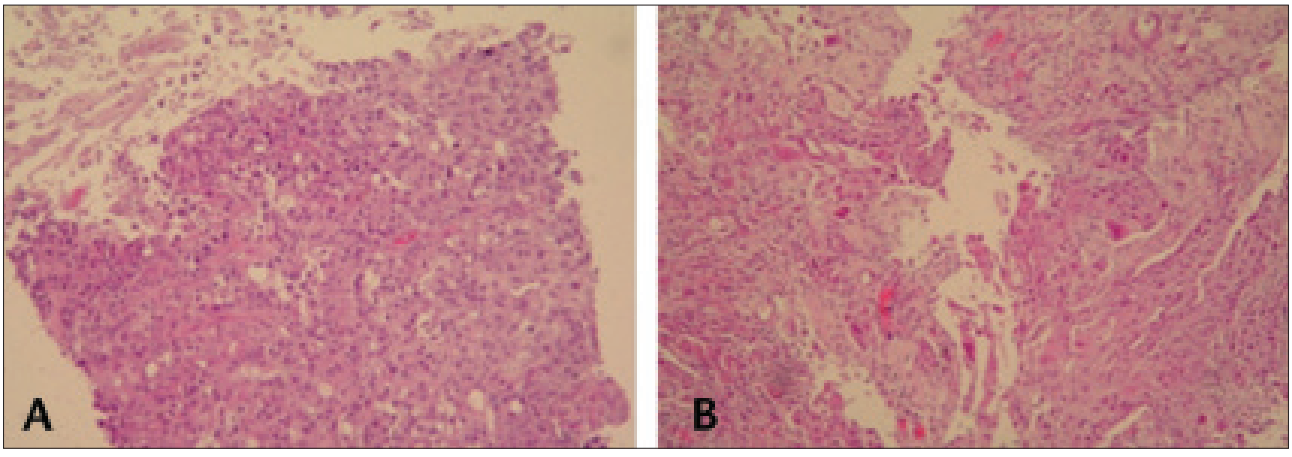

Figure 3. Pathology images, **(A)** renal cell carcinoma pathology images, **(B)** squamous cell carcinoma.

As regard to synchronous squamous lung cell carcinoma and renal cell carcinoma, gemcitabine-cisplatin-interferon treatment was started. Upon the suggestion of radiation oncology department, radiotherapy was planned due to massive hemoptysis.

DISCUSSION

Although MPC's are rarely seen, its incidence has steadily increased with the advancing imaging techniques. Incidence rate was indicated as 0.73-11.7% in the recent publications[4]. MPC cases are mostly seen in lung, genitourinary, hepatobiliary

and gastrointestinal tracts [4-6]. The most common primary tumor regions that synchronize with lung cancer are lung (31%), head and neck (20%) and uroepithelial (11%) tissues [7]. In the literature, coexistence of lung cancer with primary renal tumors is less common than other uroepithelial tumors. There may be an agent involved in the aetiology that causes both these primary cancers. In our case, this agent was smoking which is carcinogen for both lung and kidney. We come across four cases and a population-based study about this coexistence in the literature. In the community-based study, patients who were diagnosed with primary renal cancer were studied for 12 years to observe secondary primary cancer development. Synchronous tumors were observed in 53 out of 1425 patients. Primary lung cancer was observed in 8 of them (15.09%) [8].

Synchronous lung and renal cancer were detected in patients whose chest X-Rays were taken due to another reason in the case study presented by Libby et al. In the case study presented by Otsuki et al., patient with lesions on the kidney and adrenal gland were investigated; renal clear cell carcinoma and metastatic adenocarcinoma in the adrenal gland were detected [9]. Along with further investigation, a mass lesion was detected in the lung and they were identified as primary lung adenocarcinoma [10]. Similarly, in Farrero and Ferrigno D. 's cases, synchronous lung and renal cancers have been diagnosed [11,12].

We presented this case due to synchronous primary renal cancer to primary lung cancer is a rare condition as it's understood from the researches available in the literature. Our case was presented with dyspnoea and haemoptysis. Further investigations were made based on the lesion diagnosed in neighbourhood of the left lung hilum via chest X-Ray. In the imaging of the lung, lesion in the right kidney was observed in cross sections. At first sight, lung cancer metastasis was considered. Via bronchoscopic and tru-cut biopsies, primary squamous lung cell cancer and primary renal cell cancer were diagnosed. Gemcitabine-cisplatin-interferon combination therapy was given to the patient and radiotherapy was planned for massive hemoptysis.

Not with standing that the coexistence of primary renal cancer and primary lung cancer have a narrow coverage in MPC's, metastasis to each other is significant. Due to the fact that metastasis and primary cancer treatments differ from each other, the possibility of primary cancer should be considered when a lesion is detected on any of them.

Author Contributions: Concept - İ.A., O.Y., H.A.; Desing - İ.A., O.Y., H.A.; Supervision - İ.A., O.Y., H.A., D.Y., A.N.Ö., Y.A., N.Z.; Funding - İ.A., O.Y., H.A., D.Y., A.N.Ö., Y.A., N.Z.; Materials - İ.A., O.Y., H.A. D.Y., A.N.Ö., Y.A., N.Z.; Data Collection and/or Proccessing - İ.A., O.Y., H.A., D.Y., A.N.Ö., Y.A., N.Z.; Analysis and/or Interpretation - İ.A., O.Y., H.A., D.Y., A.N.Ö., Y.A., N.Z.; Litarature Review - İ.A., O.Y., H.A., D.Y., A.N.Ö., Y.A., N.Z.; Writer - İ.A., O.Y., H.A.; Critical Review - İ.A., O.Y., H.A., D.Y., A.N.Ö., Y.A., N.Z.

Conflict of Interest: The authors declare that they have no conflict of interest. All subjects were provided informed written consent prior to participation in the report.

Financial Disclosure: The authors declared that this study has received no financial supports.

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Turk Thorac J 2016; 17: 128-131 DOI: 10.5578/ttj.30511

CASE REPORT

The Right Inferior Pulmonary Vein Related Inflammatory Myofibroblastic Tumor in an Adult Case*

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Abstract

Inflammatory myofibroblastic tumor (IMT) is a rare neoplasm, which is derived of mesenchymal origin. Here we present an adult case with IMT, the origin of which was considered to be right inferior pulmonary vein. A male patient who was 52 years old, admitted to our outpatient clinic with the complaint of shortness of breath. He had cigarette smoking history for 30 years. On direct posterior - anterior X-Ray of the chest, a well-circumscribed mass with calcification in right hilum of the lung was observed. There was a mass which was extending to the inferior inferior pulmonary vein from right hilum of the lung, was measured 70 x 60 mm on computed tomography of the chest. Hamartoma, teratoma and Castleman Disease were among the possible diagnoses. On diagnostic bronchoscopy, signs of pressure from outside to the bronchi of the right middle and lower lobe was observed. Surgical excision is decided and the mass was totally excised through a muscle-sparing thoracotomy. The mass thought to arise from the inferior pulmonary vein on intraoperative inspection and right inferior lobe excision is undertaken by intrapericardial approach. No postoperative complication is encountered. Histological examination of the mass indicated inflammatory myofibroblastic tumor. Main treatment of IMT is surgical excision with negative surgical margin. Here in we present an IMT which is encountered at an unexpected location is excised completely with right lower lobe excision by an intrapericardial approach.

KEYWORDS: Inflammatory myofibroblastic tumor, rare lung neoplasm, benign lung neoplasm

Received: *06.07.2015* ***Accepted:*** *14.10.2015*

INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is a rare neoplasm of mesenchymal origin. As well as being locatedgenerally in the lungs of children and adolescents, it can be seen nearly everywhere in the body. Tumors of pulmonary and, more rarely, cardiac origin are seen in the adult period. Locally invasive and noninvasive forms have been defined for the ones located in the lungs[1].

This study aimed to present a case with IMT completely resected by thoracotomy, which was perhaps directly rooted from right inferior pulmonary vein (RIPV) and invaded the RIPV macroscopically, and to discuss diagnosis and treatment options in cases with IMT located in the thorax.

CASE PRESENTATION

A 52-year-old male patient presented to the chest disease clinic with a complaint of dyspnea. The patient had been smoking for thirty years. There was no previous disease in patient's history. Coarse rales were heard in the right lower zone on auscultation.

A smoothly-marginated lesion showing calcification in the right hilar region was seen on chest radiography (Figure 1A, B). A hypodense, smoothly-marginated mass, 70 x 60 mm in size, involving calcification and stretching out to the inferior pulmonary vein was seen on computed tomography (Figure 2). Findings of external pressure on mid-right and lower-right lobe were detected on bronchoscopy performed for probable diagnoses of hamartoma, teratoma and Castleman disease.

Biochemical evaluation was as follows: C-Reactive Protein: 7.67 mg/dL, WBC: 10950/mm^3, 1 hour erythrocyte sedimentation rate: 49, and hemoglobin: 14.2 g/dL. First second force expiration volume (FEV_1) of the patient was 1540 mL (49%), force vital capacity (FVC) was 2510 mL (65%), FEV_1/FVC was 61, residual volume was 3280 mL (158%), and total lung volume was 6470 mL (106%) in the best respiratory function test of the patient while using a bronchodilator.

Surgical resection of the tumor was planned and was completely excised with muscle-protecting thoracotomy. It was observed during intraoperative evaluation that the tumor was well-marginated; however, while it could be dissected

* Toraks 18th National Congress, 1-5 April 2015, Belek, Antalya

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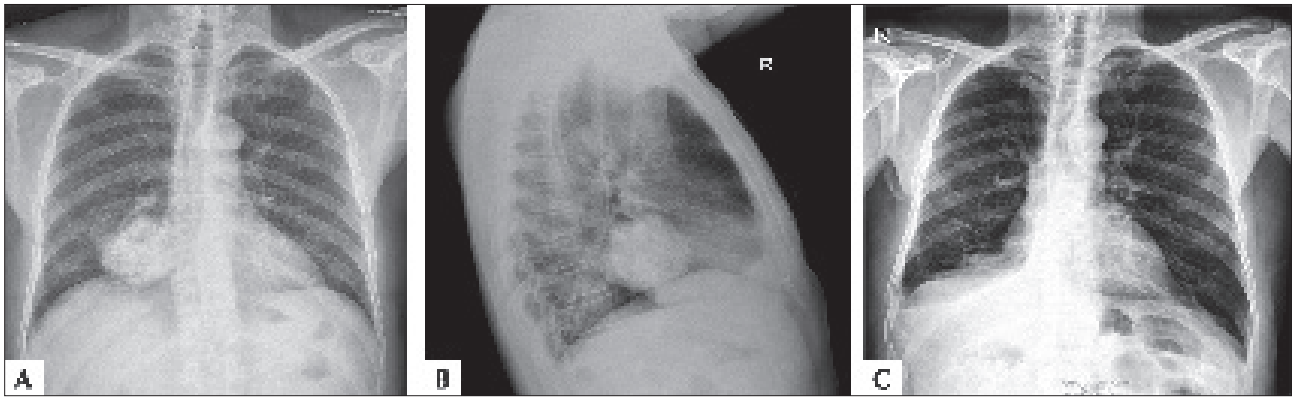

Figure 1. (A) Pre-operative PA chest radiography of the patient, **(B)** Pre-operative lateral chest graphy of the patient, **(C)** Post-operative PA chest radiography of the patient.

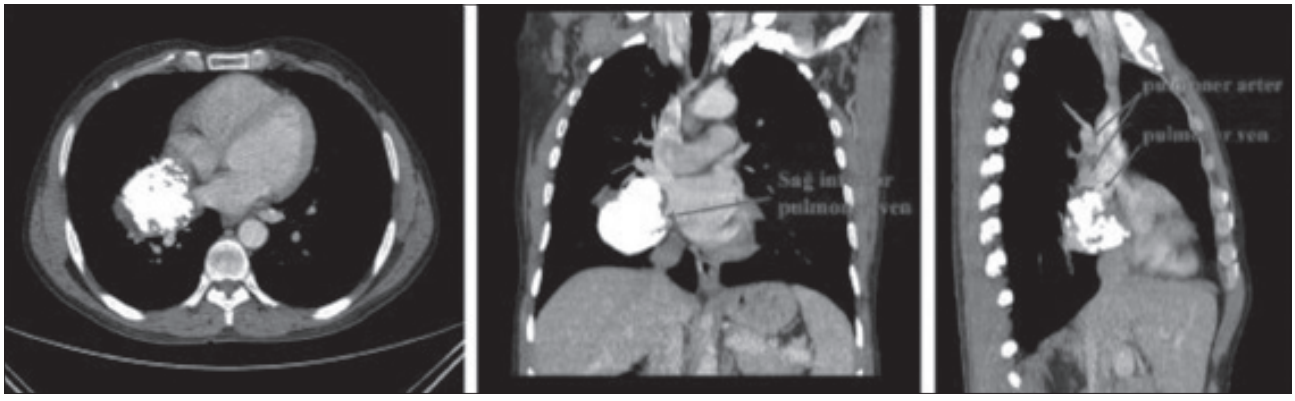

Figure 2. Thoracic CT sections of the patient.

from the lung parenchyma with a good margin, it did not allow for a dissection in the inferior pulmonary vein region (Figure 3A). Hence, intrapericardial right-lower lobectomy was performed. There were no postoperative complications.

Pathologically, a nodular, solid, calcified, brown mass leaning against the pulmonary vein, approximately 6.5 x 5 x 5 cm in size, was seen in the lung on macroscopic examination (Figure 3B). On the external surface of the material, nodular protrusions in the visceral pleura covering the lesion drew attention. Lung parenchyma was normal in regions without the lesion. On the myxoid collagenous bed, a tumoral proliferation, with a fusiform nucleus, generated by cells showing minimal pleomorphism, which created random bundles in some regions, was seen. Plasma cells and lymphocytes generating lymphoid follicles in some regions were observed on the tumor bed (Figure 4). The number of mitoses per 50 high-power fields were two in the microscopic examination. While actin was found positive on immunohistochemical examination, desmine, p53, HHV-8, CD117 and ALK were found negative. CD34 was detected positive around vascular regions and in Bcl-2 lymphocytes. Ki-67 proliferation index was found as 3%. IMT diagnosis was made with these findings.

There are no recurrent findings in the patient who is in his ninth month after resection (Figure 1C).

DISCUSSION

Among the primary pulmonary regions of the adult period, IMT is a rarely encountered tumor with a rate of less than 1%. 44% to 78% of the cases of pulmonary origin are symptomatic [1,2,3]. Cough, fever and dyspnea are frequently seen signs [1,2,3]. IMT of cardiac origin is mostly in the form

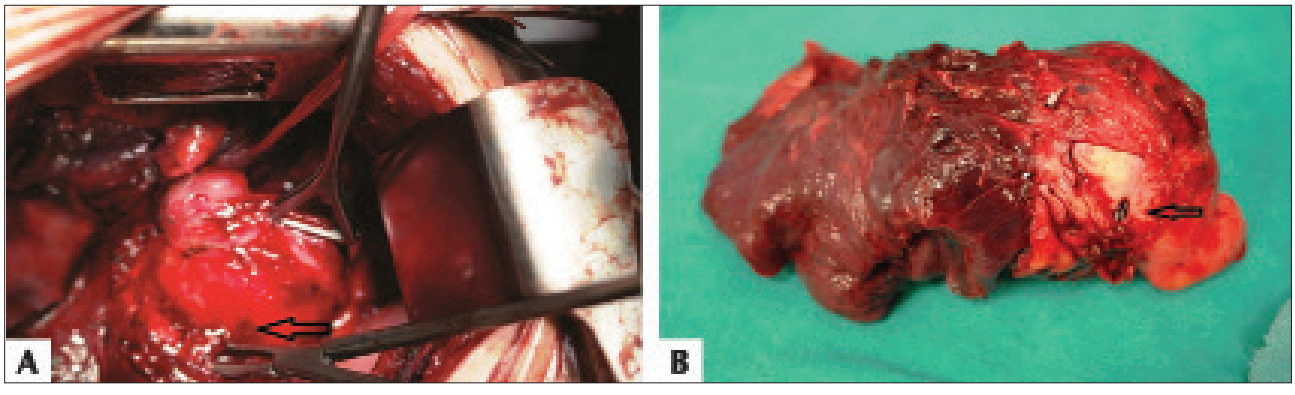

Figure 3. (A) Pulmonary vein branch continuing to the lung parenchyma from within the mass, **(B)** Vein branch progressing into the mass.

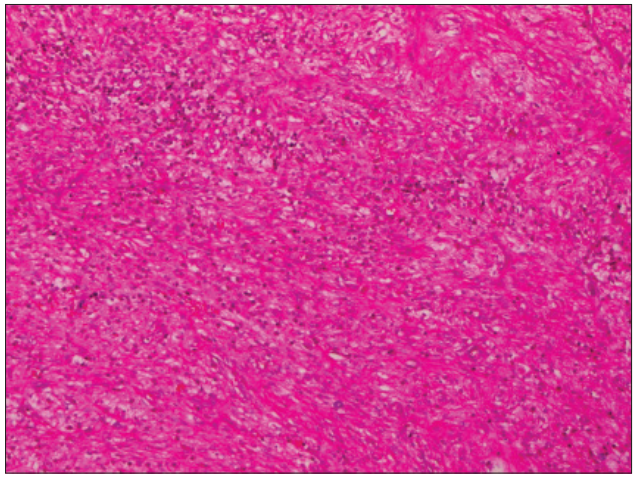

Figure 4. Fusiform cell proliferation infiltrated with lymphocyte and plasma cells X10, H&E.

of polypoid lesion with small myocardial infiltrations [4]. There is no specific symptom and it can show signs according to the location site [5]. IMT associated withheart valves and coronary arteries can progress fatally [4].

Radiologic findings also vary just as the symptoms. According to Argons et al., IMT is generally seen in the lower lobes as a solitary, peripheral mass with sharp margins, and invasion, mediastinum involvement and invasion of the hilar structures are extraordinary symptoms [6]. Melloni et al. [3] have specified that lesions are 3 cm and under in 61% of the cases and that radiologically, lesions with pneumonic infiltrations in the lower lobes are seen in 28% of the cases. Yet, in a series of Cerfolio et al. [1], mean tumor diameter of the cases is 4 cm (between 1 and 15 cm) and lesions of 48% of the cases are masses. Since a high rate of the patients was symptomatic in the series of Cerfolio et al. [1], it makes us think that symptoms may be associated with not only the location of the lesion but also with its size. Radiologic findings show differences in invasive and noninvasive forms of the lesion, which also asserts mortality suspicion. Hirai et al. [7] have detected irregularly-marginated lesions in 36%, spicule contour lesions in 18% and lesions showing pleural notch in 18% of the patients, and emphasized that it is difficult to differentiate IMTs from primary pulmonary cancers. FDG-PET may be helpful in malignity differentiation; however, it should not be forgotten that its specifity is low in cases with acute, active inflammation [7]. Calcification is not generally seen in small lesions. Fabre et al. [2] have reported calcification in 6 of the 7 patients with lesions larger than 4 cm. The tumor was 6.5 cm in our case and showed intense calcification, and thus, FDG-PET was not performed. Pulmonary lesions that may cause calcification (like hamartoma, teratoma and Castleman disease) were considered in differential diagnosis. There is no specific distinguishing characteristic in cardiac lesions. Echocardiography is generally used in diagnosis [4,5]. While the ones located in the left atrium may lead to pulmonary edema, the ones located in the right atrium may cause vena cava inferior thrombosis, liver congestion or vena cava superior disease [4,5].

Bronchoscopy and transthoracic needle biopsy (TTNB) are mostly not helpful in diagnosis. In the series of Fabre et al. [2], diagnosis was made with bronchoscopy in 16% of the patients and with TTNB in 8% of the patients. Therefore, surgery is generally necessary in diagnosis and treatment [1]. Videothoracoscopic surgical resection with stable surgical margins is a good option in solitary pulmonary nodules [7]. Surgical excision is a diagnostic and treatment option in the ones with cardiac origin [5].

Some cases may progress locally invasive and invade the chest wall and mediastinal structures [1,2,7]. IMT, which is a rare tumor of mesenchymal origin, can be seen in nearly everywhere in the body [8]. Macroscopic findings of our case suggested that it may have been resulted from RIPV (Figure 3). No matter where it originates from, the main treatment of IMT is surgical excision [1-3,8]. The efficiency of nonsurgical treatments has not been established [3]. Local recurrence is very low in IMT of pulmonary origin; however, up to 25% recurrence can be seen in extrapulmonary IMT [4]. Survival is poor in both cardiac and pulmonary recurrences [1,3,4].

In conclusion, IMT is a rare neoplasm that may show radiologic resemblance to both benign and malignant lesions of the lungs with regard to localization, characteristics and size of the lesion. Despite being seen rarely and the low number of cases in series, the consensus is that a complete surgical resection is necessary for long-term survival.

Written consent was obtained from the patient for all interventions performed. The consent also include the use of findings and images related to his disease for scientific and educational purposes.

Author Contributions: Concept - Ü.A.; Design - E.U.; Supervision - G.Y.; Resources - F.T.; Materials - F.B.; Data Collection and/or Processing - E.U.; Analysis and/or Interpretation - Ü.A.; Literature Search - F.T.; Writing Manuscript - Ü.A.; Critical Review - F.B., G.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial supports.

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