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ORIGINAL ARTICLE

Organizing Pneumonia as a Histopathological Term

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Abstract

OBJECTIVES: Organizing pneumonia (OP) is an interstitial lung disease characterized by granulation tissue buds in alveoli and alveolar ductus, possibly accompanied by bronchiolar involvement. Histopathologically, OP may signify a primary disease and be observed as a contiguous disease or as a minor component of other diseases. In this study, the clinical significance of histopathological OP lesions and clinical and radiological features of patients with primary OP were examined.

MATERIAL AND METHODS: Between January 2011 and January 2015, of 6,346 lung pathology reports, 138 patients with OP lesions were retrospectively evaluated. According to the final diagnoses, patients were grouped as reactive OP (those with final diagnosis other than OP) and primary OP (those with OP). Patients with primary OP were classified according to etiology as cryptogenic and secondary OP. Radiological evaluation was conducted within a categorization of "typical," "focal," and "infiltrative."

RESULTS: Of 138 patients, 25% were males and the mean age was 54±14 years. Pathologically, 61% of patients had reactive OP and 39% had primary OP. All reactive OP lesions were reported using surgical specimens, and the most frequent primary diagnoses were malignancy (65%), infection (15%), interstitial lung diseases other than OP (7%), and bronchiectasis (5%). Other diagnoses included bullae, foreign body, hamartoma, bronchogenic cyst, and bronchopleural fistula. Of all the primary OP patients, 48 had cryptogenic OP and six had secondary OP. Radiological involvement was consistent with typical OP in 30%, focal OP in 63%, and infiltrative OP in 7% of the patients. All focal OP lesions were defined using surgical resections. Positron emission computed tomography (PET-CT) was recorded in 28 patients. In 11 patients, lymphadenomegaly was comorbid. The mean widest diameter of focal opacity was 2.7±1.2 (1.2-4.9) cm, and the mean the maximum standardized uptake value (SUVmax was 6.1±3.9 (1.7-16.7).

CONCLUSION: OP lesions generally present as a minor component of other diseases. In patients with OP, cryptogenic OP and radiological focal OP is more frequently observed. Most focal OP lesions are detected using surgical resections because of malignant prediagnosis owing to elevated SUVmax.

KEYWORDS: Interstitial lung disease, malignancy, Masson bodies, organizing pneumonia

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INTRODUCTION

Organizing pneumonia (OP) is an interstitial lung disease, and OP patients present with characteristic clinical, radiological, and histological findings. Histopathologically, there are buds of granulation tissue, which are called Masson bodies and consist of exudative materials including connective tissue components, fibrin, and fibroblasts, in the alveolar ducts and alveoli. Bronchiolar involvement may be present [1,2].

The clinical significance of OP as a histologic finding can vary. It can be found around granulomas or cancer tissues or it can develop as a minor component of diffuse lung diseases such as hypersensitivity pneumonitis and eosinophilic pneumonia. When the OP pattern is detected as a diffuse and major finding, it expresses the disease [3,4]. OP has been investigated in terms of its cryptogenic and secondary forms and its radiological features, but no defnite conclusions can be drawn from these studies [5-7].

In this study, we investigated the Clinical signification of histological OP lesions and the clinical and radiological features of primary OP patients.

The present study was presented as oral presentation in the 19th Turkish Thoracic Society Annual Congress, Antalya, Turkey.
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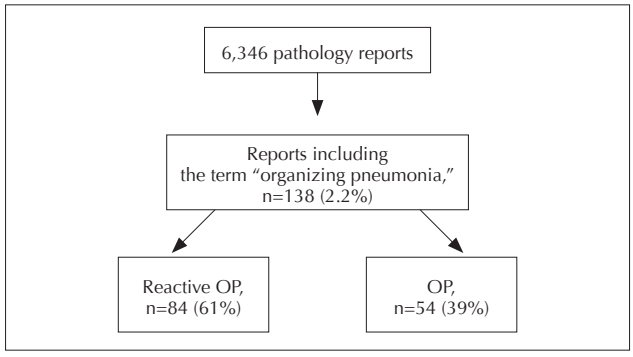


Figure 1. Flowchart of patients

Table 1. Diseases in which reactive organizing pneumonia lesions are detected

Diagnosis	Number of patients
Malignancy	55
NSCLC*	40
Carcinoid tumor	7
SCLC	1
Schwannoma	1
Undifferentiated tumor	2
Malignant epithelial tumor	1
Lymphoma	1
Fibrosarcoma	1
Large cell lung cancer	1
Infections	13
Lung abscess	4
Pneumonia	4
Cyst hydatid	2
Tuberculosis	2
Aspergillus	1
Interstitial lung disease	6
Hypersensitivity pneumonia	3
Usual interstitial pneumonia	1
Cellular non-specific interstitial pneumonia	1
Bronchiolitis	1
Bronchiectasis	4
Bulla	2
Foreign body	1
Hamartoma	1
Bronchogenic cyst	1
Bronchopleural fistula	1

*: squamous cell lung cancer: n=25, adenocarcinoma: n=9. SCLC: small cell lung cancer; NSCLC: non-small cell lung cancer

MATERIAL AND METHODS

The was a single-center, retrospective, observational study.

Our hospital is a chest diseases and chest surgery training and research hospital. For this study, 6,346 pathology reports written in our hospital between January 2011 and January 2015 were reviewed, and 144 patients who were diagnosed with OP were examined (Figure 1). In the first 2 years of the study, lung transplantation was performed at our clinic. Six OP patients undergoing lung transplantation were excluded because they might have changed the rate of reactive OP; thus, the remaining 138 patients were included in the study.

Clinical, laboratory, and radiological findings of the included patients were obtained from their medical records.

The patients were first defined as having reactive or primary OP:

Reactive OP: OP that is found along with a primary disease or as a minor finding of another disease.

Primary OP: OP that is found without another primary disease and not as a minor finding of another disease.

Diseases associated with reactive OP lesions and patient characteristics were recorded. The medical records of primary OP patients were examined, and these patients were divided into two groups according to their clinical findings:

Cryptogenic OP: Patients without any etiological causes.

Secondary OP: Patients developing OP secondary to another cause.

The radiological features of primary OP patients were examined in three groups [8]:

Typical: Multiple, frequently bilateral, patchy alveolar opacities.

Focal: Focal nodular or massive opacities.

Infiltrative: Interstitial involvement with small alveolar opacities.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences version 16.0 (SPSS Inc.; Chicago, IL, USA). The values are presented as mean±standard deviation.

Approval for the study was received from the Local Scientific Ethical Committee of Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was not obtained from the patients because of the retrospective design.

RESULTS

The OP pattern was detected in 138 patients (2.2%) from 6,346 reports in the pathology laboratory of our hospital between 2011 and 2015. Among the 138 patients, 34 (25%) were males and their mean age was 54±14 years (range, 16-80 years). Tissue samples from 132 patients (96%) came from surgical resection, and samples from 6 patients were taken as transbronchial biopsies.

A pathological classification found that 84 (61%) patients had reactive OP and that 54 (39%) patients had primary OP. A total of 69 (84%) reactive OP patients and 35 (65%) primary OP patients were males. The mean ages werewere 53±14 years and 54±14 years, respectively.

Table 2. General features of organizing pneumonia patients according to their radiological features

	Typical OP (n=16)	Focal OP (n=34)	Infiltrative OP (n=4)
Gender			
Male/Female	8/8	24/10	3/1
Mean age, years	51±16	53±14	59±11
Etiology			
Cryptogenic/Secondary	16/0	30/4	2/2
Involvements of lesions on performing PET-CT (SUVmax)	-	6.1±3.9 (1.7-16.7)	-

OP: organizing pneumonia, PET-CT: Positron emission computed tomography, SUVmax: maximum standardized uptake value

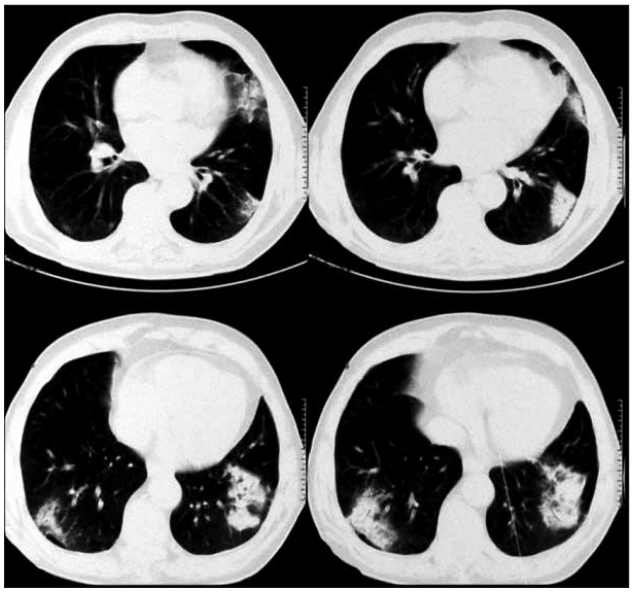


Figure 2. Typical organizing pneumonia

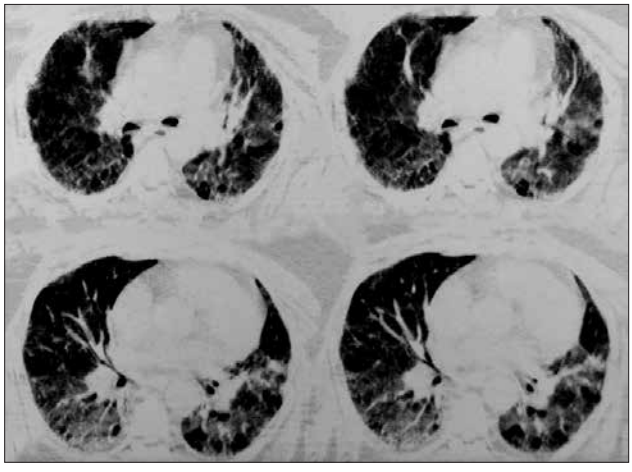


Figure 3. Infiltrative organizing pneumonia

All reactive OP lesions had been defined in surgical resection interventions. Resections had been performed in the right lung in 53 (63%) patients. Primary diagnoses of these 53 patients were mostly malignancies (n=55, 65%) and infections (n=13, 15%). Six (7%) of these patients had non-OP interstitial lung disease and four (5%) had bronchiectasis (Table 1).

Among 54 primary OP patients, 48 (89%) were diagnosed as having cryptogenic OP (COP) and 6 as having secondary OP. In 2 COP patients, the coexistence of eosinophilic pneumonia and OP was observed. The cause of secondary OP was hypersensitivity in 2 patients and connective tissue diseases in 4 patients.

The radiological findings of primary OP patients were classified as typical in 16 (30%) patients, focal in 34 (63%) patients, and infiltrative in 4 (7%) patients (Table 2) (Figures 2-8).

Eight typical OP patients were males, and their mean age was 51±16 years. All were diagnosed with COP, and the typical OP pattern in 6 patients was diagnosed through TBB.

All focal OP patients underwent surgical resection due to the suspicion of malignancy. Twenty-eight focal OP patients had undergone PET-CT, and 11 had accompanying lymphadenomegaly. The widest diameter of focal opacities was 2.7±1.2 cm (range, 1.2-4.9 cm) on average, and the SUVmax at PET-CT was 6.1±3.9 (range, 1.7-16.7).

DISCUSSION

In our study, 54 primary OP patients were evaluated, and reactive OP lesions were reported in 84 patients in the same period.

Organizing pneumonia was first defined 1983, and it was called OP due to the dominant involvement of the alveoli. Two years after that, it was named as "bronchiolitis obliterans organizing pneumonia" considering the involvement in the terminal bronchioles. However, because this term can be confused with "obliterative bronchiolitis", which leads to obstruction in small airways, only the term "organizing pneumonia" is used [1,2].

Organizing pneumonia is the most striking finding in COP. Other than OP disease, t can be seen in vasculitis, bronchocentric granulomatosis, chronic eosinophilic pneumonia, hypersensitivity pneumonia, diffuse alveolar damage, nonspecific pneumonia, lung abscess, pulmonary infarct, and cancers, but as a minor finding [9]. OP can also coexist with fibrotic interstitial pneumonia as small foci [2]. In our study, OP lesions were detected in 84 patients as a minor finding of other diseases. These lesions were mostly reported to occur with malignancy and infections (lung abscess, cyst hydatid, tuberculosis, aspergillus, etc.). Other diseases that occur with the OP pattern include hypersensitivity pneumonia, bronchiolitis and fibrotic interstitial lung diseases, bronchiectasis, bullae and foreign body, hamartoma, bronchogenic cyst, and bronchopleural fistula.

Organizing pneumonia is classified as "secondary OP" when a specific cause is detected and as "cryptogenic OP" when there is no specific cause [10]. The frequency rate of the disease is similar in men and women. Although it is mostly seen between the ages of 50 and 60 years, cases between the ages of 20 and 80 years can also be encountered [2,11]. In our study, there were 54 primary OP patients (88% COP) and the mean age of the patients was 54±14 years.

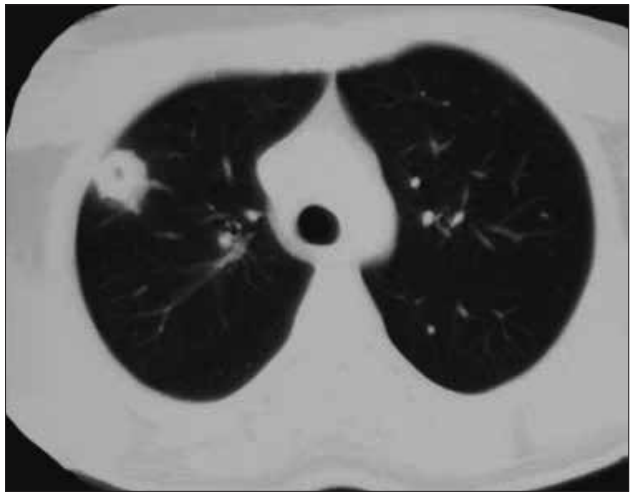
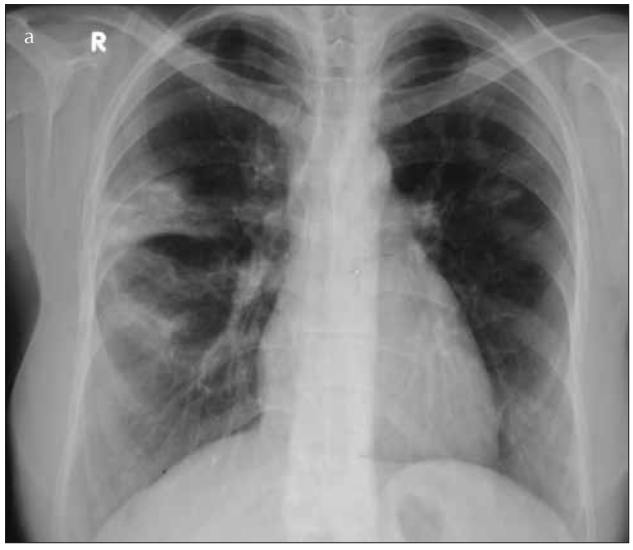


Figure 4. Focal organizing pneumonia in the right upper lobe



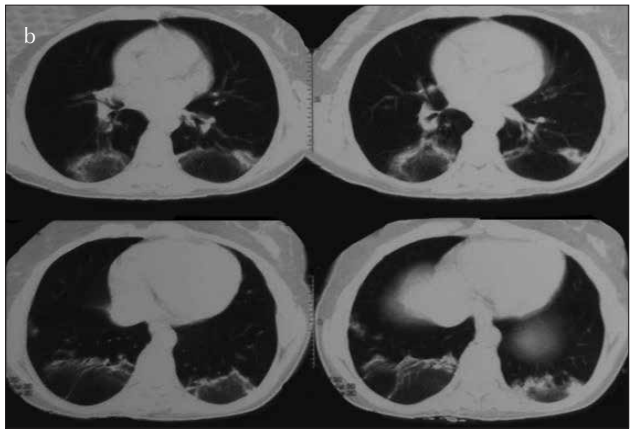


Figure 5. a, b. Typical organizing pneumonia (a). Typical organizing pneumonia (b)

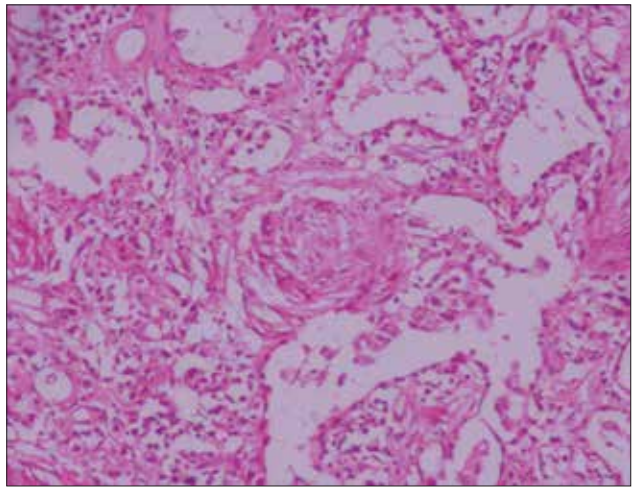


Figure 6. Histology sections that are radiologically consistent with typical organizing pneumonia (H&E, ×10)

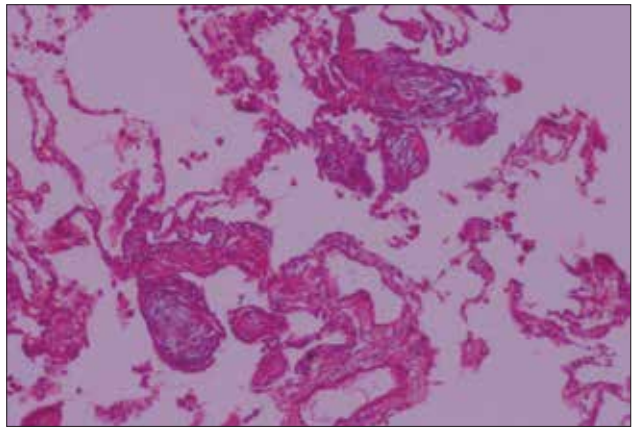


Figure 7. Histology sections that are radiologically consistent with focal organizing pneumonia (H&E, ×10)

Secondary OP can develop secondary to some causes such as heart-lung transplantation, bone marrow transplantation, infections, acute respiratory distress syndrome, drug use, radiotherapy, connective tissue diseases, hypersensitivity pneumonia, and aspiration pneumonia [5]. The series by Sveinsson et al. [6] included 58 cryptogenic OP and 46 secondary OP patients. They reported the causes of secondary OP to be infections (most commonly by *Streptococcus pneumoniae* and *Haemophilus influenza)*, drug use (amiodarone, nitrofurantoin, busulfan, and methotrexate), cancers (breast, lung, and non-Hodgkin lymphoma), connective tissue diseases (rheumatoid arthritis, polymyalgia rheumatica, and Sjögren's syndrome), and radiotherapy in 46% of their patients [6]. The causes defined in 21 secondary OP patients in the series by

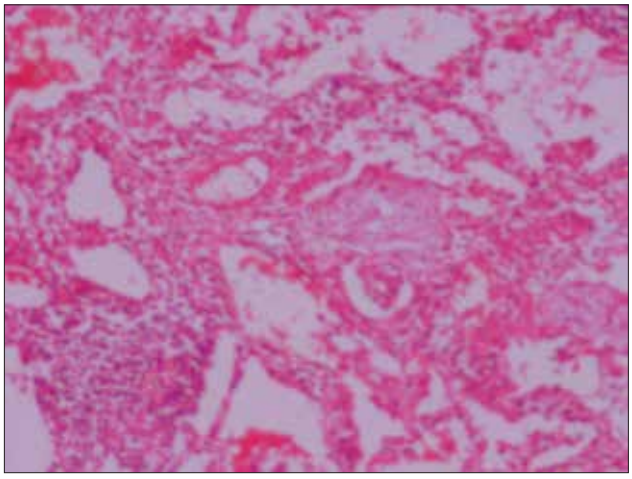


Figure 8. Histology sections that are radiologically consistent with infiltrative organizing pneumonia (H&E, ×10)

Drakopanagiotakis et al. [7] were drug use (29%), rheumatic diseases (20%), breast and colon cancers (24%), lymphoma (14%), renal transplantation (5%), and infections (9%). The frequency of OP was reported to be 2%-4.8% in rheumatoid arthritis patients [12]. In our series, the fact that the number of secondary OP patients was lower than that of COP patients might have resulted from the fact that patients with comorbid diseases less frequently applied to our hospital as ours is a chest diseases hospital. The causes in 6 secondary OP patients were hypersensitivity and connective tissue diseases that were newly diagnosed after investigating the etiology of OP in our study.

Surgical resection or TBB is required for making a diagnosis [13]. The samples in our series were mostly surgical resection materials, and all patients diagnosed through TBB had typical OP radiological findings.

The radiological appearance is frequently multifocal alveolar consolidation with peripheral localization. A reversed halo sign is found at the rate of approximately 20%, and it is indicative of OP [9,14]. It can also appear as a diffuse bilateral infiltration or solitary focal mass lesion [11]. In our study, radiological findings of 54 patients were found to be more consistent with focal OP and less consistent with the infiltrative type.

In lesions occurring as a solitary opacity, OP can also mimic lung cancer by displaying high FDG involvement such as inflammation, granulomatous infections, benign tumors, and autoimmune diseases [3,15]. In the literature, it has been observed that radiological features and metabolic activities of focal OP patients are not enough to rule out a malignancy, and these patients frequently undergo surgery for making a diagnosis [16]. In our series, high FDG involvement at the malignancy level drew attention to focal OP patients, and these patients were mostly operated on due to the suspicion of malignancy. FDG involvements in patients were observed in a range from 1.7 to 16.7. According to our research, there have been no clinical studies on this issue. It was thought that different metabolic activities were been detected in lesions in association with the inflammation stage in OP.

Maldonado et al. [5] evaluated 26 focal OP patients who were diagnosed through surgical biopsies over 8 years. The median age of the patients was 66 years (range, 36-96 years); 42% of the patients were females, and 27% were active smokers. Involvement was reported in all 11 patients who underwent PET, while they were asymptomatic at the time of diagnosis. A history of malignancy and active malignancy was reported in 6 patients. It is specified that irregularity and spiculation could be radiologically observed in lesions, including nodular, massive, and focal consolidation. Three of these 6 cases were evaluated to be secondary to infection, and the others were evaluated to be cryptogenic [5]. Yang et al. [17] reported the involvement of focal OP lesions on performing contrast-enhanced CT. On the other hand, Melloni et al. [18] reported the presence of involvement on performing PET imaging for localized OP defined in 4 patients. In our series, focal OP was detected in 34 patients. Among them, 29% were females and their mean age was 53 years. In PET-CT, SUVmax values showed involvement between 1.7 and 16.7.

In conclusion, OP is found as a minor histological finding with diseases other than OP in pathology reports. An etiological cause is often not found in OP patients. Cryptogenic and radiologically focal OP are more frequently encountered. Focal OP lesions are generally detected in surgical resections with a pre-diagnosis of malignancy.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital.

Informed Consent: Written informed consent was not obtained from the patients because of the retrospective design.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - F.T.A., M.A., A.M., A.A.A., M.Akyıl., T.S.; Design - F.T.A., T.S.; Supervision - F.T.A., M.A., A.M., M.Akyıl.; Data Collection and/or Processing - F.T.A., M.Akyıl.; Analysis and/or Interpretation - F.T.A., T.S.; Literature Search - F.T.A., A.A.A.; Writing Manuscript - F.T.A., M.A., A.M., M.Akyıl.; Critical Review - F.T.A., A.A.A., T.S.

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

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