

A Case of Thyroid Angiosarcoma and Multiple Pleuropulmonary Metastasis Diagnosed at Autopsy

Otopside Tanı Konulan Tiroid Anjiyosarkoma ile Multipl Plevrapulmoner Metastazi

İbrahim Meteoğlu¹, Emel Ünal¹, Serdar Şen², Emel Dikicioğlu Çetin¹, Musa Dirlik³

¹Adnan Menderes University, Faculty of Medicine, Pathology, Aydın, Turkey

²Adnan Menderes University, Faculty of Medicine, Thoracic Surgery, Aydın, Turkey

³Adnan Menderes University, Faculty of Medicine, Forensic Medicine, Aydın, Turkey

ABSTRACT

A 74 year old male patient with the history of hypertension, diabetes mellitus and 50 years of nodular thyroid presented at the emergency unit with shortness of breath, and pleural effusion was detected after physical and laboratory examination. Imaging studies demonstrated bilateral pleural fluid, slightly more in the left and several intrapulmonary nodules. The patient died of cardiac arrest at the 4th day of hospitalization. At autopsy, hemorrhagic fluid in the thoracic cavity and hemorrhagic nodules on the right and left pleural surfaces were detected. On microscopic examination of the hemorrhagic cystic nodules of left thyroid lobe and pulmonary nodules; anastomosing angiomatous structures formed by large fusiform epitheloid cells and large eosinophilic cytoplasm, showing partial papillary or solid islet structures were observed. In the immunohistochemical, examination, staining was negative for cytokeratin and thyroglobulin and positive for CD31 CD34 and F VIII. Based on these findings, the case was diagnosed as "thyroid angiosarcoma and multiple pleuropulmonary metastasis".

(*Tur Toraks Der* 2010;11: 41-3)

Key words: Thyroid angiosarcoma, pleuropulmonary metastasis, autopsy

Received: 22. 02. 2008

Accepted: 23. 05. 2008

ÖZET

Nefes darlığı nedeniyle acil servise başvuran 74 yaşındaki erkek hastada hipertansiyon ve diabetes mellitus öyküsü olduğu ve 50 yıldır tiroid nodülleri bulunduğu saptandı. Fizik muayene ve laboratuvar çalışmaları ile plevral efüzyon saptanan hastada, görüntüleme yöntemleri ile bilateral plevral efüzyonu ve sol tarafta daha fazla olmak üzere her iki akciğerde çok sayıda intrapulmoner nodül olduğu gözlemlendi. Hasta hastaneye yatırılışının dördüncü gününde kardiyak arrest nedeniyle öldü. Uygulanan otopsi sonucunda, toraks kavitesinde kanamalı sıvı ile her iki plevral yüzde kanamalı plevral nodüller tespit edildi. Sol tiroid lobunda bulunan kanamalı kistik nodül ve akciğer nodüllerinin mikroskopik incelemesinde, solid adalar ve yer yer papiller yapılar oluşturan, geniş eozinofilik sitoplazmalı, büyük iğsi epitelioid hücrelerden oluşan anastomoz damar yapıları izlendi. İmmunhistokimyasal çalışmada bu hücrelerin sitokeratin ve tiroglobulin ile negatif olduğu, CD31, CD34 ve FVIII ile pozitif olduğu bulundu. Bu bulgular ile olguya "tiroid anjiyosarkomu ve multipl plevrapulmoner metastaz" tanısı kondu.

(*Tur Toraks Der* 2010;11: 41-3)

Anahtar sözcükler: Tiroid anjiyosarkom, plevrapulmoner metastaz, otopsi

Geliş Tarihi: 22. 02. 2008

Kabul Tarihi: 23. 05. 2008

INTRODUCTION

Angiosarcomas constitute fewer than 1% of all sarcomas and most frequently involve the skin-soft tissue [1]. Thyroid angiosarcoma is very rare and its incidence is higher in the Alpine region of Europe. Thyroid angiosarcoma forms 2-10% of all thyroid malignancies in the North Italy, Austria and Switzerland region [2]. It is rarely observed in the other regions of the World. The mean age of diagnosis is 66 years and the male/female ratio is reported as 1.2/1 [3]. Most of the thyroid angiosarcomas arise from a long-standing nodular goiter [4]. The rate of local recurrence (36%) and metastasis (80%) is high. Most common spread patterns are regional lymph

nodes and pulmonary metastasis. The majority of cases are incidentally diagnosed during the investigation of symptoms caused by metastasis, and 79% of the patients die within 5 years after the diagnosis. Multiple regimens consisting of surgery, radiotherapy and chemotherapy are used for treatment [5].

In this adult autopsy, a case of thyroid angiosarcoma and pleuropulmonary metastasis is presented.

CASE

A 74 year old male patient who was referred to the emergency unit with the complaint of shortness of breath, had a history of hypertension, diabetes mellitus and

a nodular thyroid which has been present for 50 years and showing progressive expansion in the previous two years. Shortness of breath had also been progressively increasing in the last two years. His thorax radiograph revealed massive pleural effusion, more on the left side, and a nodular lesion on the right lung. Computerized tomography revealed bilateral pleural fluid, more on the left side and several intrapulmonary nodules (Figure 1A). Hemorrhagic fluid was drained by thoracentesis and his laboratory results were hemoglobin: 7.8 mg/dl, hematocrit: 23.7%; triiodothyronine (T3): 0.912ng/ml, thyroxine (T4): 8.05ug/dl and free triiodothyronine (fT3): 3,12tg/ml, thyroid stimulating hormone (TSH): 0.024uIU/ml. The patient was hospitalized and a total of 4000 cc of pleural hemorrhagic fluid was drained within 4 days. The patient died of cardiac arrest at the 4th day despite close monitoring and massive blood transfusion.

Autopsy was performed with the suspicion of pulmonary embolism in the 8th post-mortem hour. At autopsy, macroscopic findings were as follows: cerebrum and cerebellum were normal, 2500 cc hemorrhagic fluid was observed in the thoracic cavity and there were hemorrhagic nodules on the right-left lung pleural surfaces; cystic expansion observed in the left lobe and there were nodular structures on the right lobe of thyroid, and abdominal organs were normal. All organs were examined both macroscopically and microscopically.

The thyroid weighed 235 g. on macroscopic examination, dimensions of the right lobe were 7.5x4x2.5 cm and left lobe 10x5.5x4.5 cm. The right lobe was nodular and the left lobe had a blood-filled cystic cavity. (Figure 1B). Multiple hemorrhagic nodular lesions, the largest measuring 3 cm in diameter, were observed on both pleural surfaces (Figure 1B). The aorta, coronary arteries and basilar artery had modest atherosclerotic plaques. Other organs were normal.

On microscopic examination of samples, obtained from the hemorrhagic cystic nodule of 10 cm diameter found on the left lobe of thyroid and from the pulmonary nodules, revealed anastomosing angiomatous structures formed by large fusiform epithelioid cells with a vesicular nucleus and large eosinophilic cytoplasm showing partially papillary or solid islet structures (Figure 1C, 1D, 1E). Also extensive hemorrhage and necrosis were observed. Immunohistochemical staining was negative for cytokeratine and thyroglobulin, and positive for CD31 (Figure 1F), CD34 and FVIII. In other regions of the thyroid, nodular findings were determined. Reactive hyperplasia findings were observed in 17 of the peribronchial, paraaortic and cervical lymph nodes which were dissected for regional lymph node metastasis. Based on these findings, the case was diagnosed as "thyroid angiosarcoma and multiple pleurapulmonary metastasis".

DISCUSSION

Primary angiosarcoma is a rare tumor of the thyroid gland. It usually arises from a long standing nodular goiter [5]. Endothelial proliferations after recurrent intranodular hemorrhages occurring in a long standing nodular

goiter have been considered to initiate neoplastic transformation [6]. It is more common in the Alpine region of Europe and incidence is about 2-10%[2]. Cases are sporadic in other regions of the world and the exact incidence is unknown [7]. History of a nodular goiter of more than half a century is in accordance with tumor development mechanism described above. This case is the first Turkish autopsy case which has been described in English literature as thyroid angiosarcoma and multiple pleurapulmonary metastasis.

Thyroid angiosarcoma with aggressive characteristics metastasizes early to the lungs, regional lymph nodes and brain [5]. It may also cause gastrointestinal bleeding due to small and large intestinal metastases and anemia due to bone marrow metastasis [8,9]. The majority of the patients present with symptoms due to metastasis [5,10]. Autopsy also revealed that the presenting symptom of this case, shortness of breath, was due to the hemothorax caused by lung metastasis.

Differential diagnosis of primary thyroid angiosarcoma includes benign vascular lesions such as hemangioma and sclerosing hemangioma and malignant tumors such as thyroid anaplastic carcinoma [3,11]. It is differentiated from benign lesions by nuclear atypia and necrosis. Negative staining for keratin, thyroglobulin and positive staining for endothelial cell markers (CD31, CD34, Faktör VIII, Ulex europaeus) in immunohistochemical examinations differentiates it from anaplastic (undifferentiated) carcinoma of the thyroid [2]. However, epithelioid findings observed in some angiosarcomas and immunohistochemically determined cytokeratin and epithelial membrane antigen positivity may cause difficulty in differentiation from angiomatoid anaplastic carcinoma. Some authors suggest that these two entities are not different from each other. Although differentiation of these entities is supposed to be for academic purposes only, there are some indications signifying that angiosarcoma is a different entity. The presence of Weibel-Palade bodies, geographic distribution of angiosarcomas, and absence of thyroglobulin mRNA in tumor cells are some of these. Also, the absence of well differentiated regions, such as papillary or follicular carcinoma in angiosarcomas, in contrast to anaplastic carcinomas, is another characteristic that is used for differentiation.

Thyroid angiosarcoma has a poor prognosis, like anaplastic carcinoma. Some cases with an early stage without extrathyroidal spread may demonstrate less aggressive behavior. Surgery seems to be the first choice in the early stages of thyroid angiosarcomas, where clinical prognosis is determined by the stage of the disease at the time of surgery.

In conclusion, although it is considered to be an analogue of carcinosarcoma observed in various systems and a transitional tumor which shows epithelial and endothelial differentiation, thyroid angiosarcoma is accepted as a different entity with a poor prognosis. Although diagnosis can be made by autopsy, as in this case, there are cases in the literature diagnosed by fine needle aspiration biopsies. Specific and sensitive markers such as CD31,

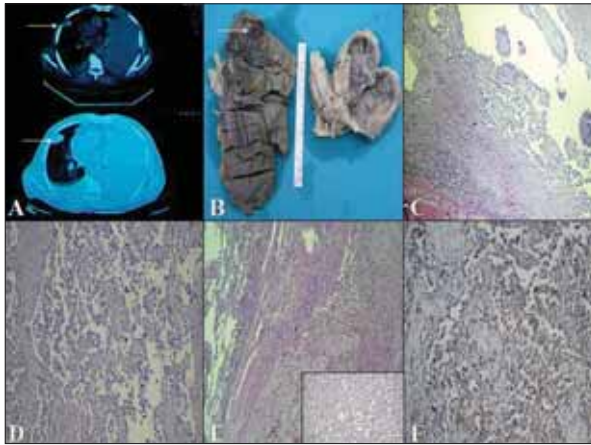


Figure 1. CT image showing intrapulmonary nodule (arrows), **A:** Gross photograph show pleuropulmonary nodule (arrow) and cystic mass of thyroid, **B:** Photomicrograph shows anastomosing angiomatous structures and large fusiform epithelioid cells and large eosinophilic cytoplasm showing partially papillary structure (**C:** Thyroid, x40, hematoxylin-eosin, **D:** Thyroid, x200, hematoxylin-eosin, **E:** Lung x100, hematoxylin-eosin, insert: Lung x200, hematoxylin-eosin), **F:** Photomicrograph shows Anti-CD 31 positivity of anastomosing structures (Thyroid, x100, anti-CD31)

which confirms endothelial differentiation, should be used for the diagnosis of the tumors which have thyroid anaplastic carcinoma for differential diagnosis. This tumor has been incidentally diagnosed in Turkey outside its typical geographical location, by means of an autopsy performed to determine the unknown cause of death. However, larger series are required to establish its diagnosis, treatment, prognosis and pathogenesis.

REFERENCES

1. Weiss SW, Goldblum JR. Malignant vascular tumors. In: Weiss SW, Goldblum JR, eds. *Enzinger and Weiss's Soft Tissue Tumors*. 4 th ed. St Louis, Mo: Mosby; 2001:917-54.
2. Ryska A, Ludvikova M, Szepe P, et al. Epithelioid angiosarcoma of the thyroid gland. Report of six cases from a non-Alpine region. *Histopathology* 2004;44:40-6.
3. Christopher D, Fletcher M. Tumors of the thyroid and parathyroid glands. In: *Diagnostic Histopathology of Tumors*. 2 th ed. United Kingdom, 2000, p:1018-9.
4. Papotti M, Volante M, Negro F, et al. Thyroglobulin mRNA expression helps to distinguish anaplastic carcinoma from angiosarcoma of the thyroid. *Virchows Arch* 2000;437:635-42.
5. Astl J, Duskova J, Limanova Z, et al. Haemangiosarcoma of the thyroid gland. A case report. *Neuroendocrinology Letters* 2000;21:213-6.
6. Eusebi V, Carcangiu ML, Dina R, et al. Keratin-positive epithelioid angiosarcoma of the thyroid: A report of four cases. *Am J Surg Pathol* 1990;14:737-47.
7. Maiorana A, Collina G, Cesinaro AM, et al. Epithelioid angiosarcoma of the thyroid. Clinicopathological analysis of seven cases from non-Alpine areas. *Virchows Arch* 1996;429:131-7.
8. Bandorski D, Arps H, Jaspersen D, et al. Severe intestinal bleeding caused by intestinal metastasis of a primary angiosarcoma of the thyroid gland. *Z Gastroenterol* 2002;40:811-4.
9. Yilmazlar T, Kirdak T, Adim S, et al. A case of hemangiosarcoma in thyroid with severe anemia due to bone marrow metastasis. *Endocrine Journal* 2005;52:57-9.
10. Tacheci I, Ryska A, Cap J, et al. Epithelioid hemangiosarcoma of the thyroid gland. *Cas Lek Cesk* 2002;141:291-3.
11. Lamovec J, Zidar A, Zidanik B. Epithelioid angiosarcoma of the thyroid gland. Report of two cases. *Arch Pathol Lab Med* 1994;118:642-6.