Case Report / Olgu Sunumu

Mediastinal epithelioid angiosarcoma arising in schwannoma: The first case in the literature

Schwannomda gelişen mediastinal epitelioid anjiosarkom: Literatürdeki ilk olgu

Ş. Mustafa Demiröz¹, Göktürk Fındık¹, Koray Aydoğdu¹, Barış Hekimoğlu¹,
Funda İncekara¹, Funda Demirağ², Sadi Kaya¹

¹Department of Thoracic Surgery, Atatürk Chest Diseases and Chest Surgery Training and Research Hospital, Ankara, Turkey

²Department of Pathology, Atatürk Chest Diseases and Chest Surgery Training and Research Hospital, Ankara, Turkey

ABSTRACT

Angiosarcoma arising in a long-standing schwannoma is extremely rare and only a few cases were reported in the English literature. Besides tumors arising from vagus, sciatic or adrenal nerves, tumors growing on neck, foot or kidney were also described. To the best of our knowledge, in this article, we report the first mediastinal case occurring in long-standing schwannoma in a 53-year-old female patient. The patient was admitted to our clinic with severe dyspnea and palpitation. Her medical history showed a progressive right-sided paramediastinal mass which was first diagnosed in 2002. Three transthoracic needle biopsies performed in 2002, 2015 and 2016 were all non-diagnostic. An operation was suggested since 2002, but the patient has not accepted. Thorax computed tomography and magnetic resonance imaging revealed a huge mediastinal mass nearly fulfilling the right hemithorax. A diagnosis of "malign spindle cell tumor" was established with the last transthoracic biopsy and total surgical resection via posterolateral thoracotomy was performed. Microscopically, tumor was composed of two components: a benign schwannoma and an epithelioid angiosarcoma. Endothelial and neural cell differentiations were confirmed immunohistochemically.

Keywords: Angiosarcoma; chemotherapy; mediastinum; schwannoma; thoracotomy.

Öz

Uzun süreli schwannomda anjiosarkom gelişimi oldukça nadir olup İngilizce literatürde sadece birkaç olgu bildirilmiştir. Vagus, siyatik sinir veya adrenal sinir kökenli tümörlerin yanı sıra boyun, ayak ve böbrekte gelişen tümörler de tanımlanmıştır. Bildiğimiz kadarıyla, bu yazıda, 53 yaşında bir kadın hastada uzun süreli schwannomda gelişen ilk mediastinal olgu sunuldu. Hasta ciddi solunum güçlüğü ve çarpıntı ile kliniğimize başvurdu. Tıbbi öyküsünde ilk olarak 2002'de tanı konulan, progresif, sağ taraflı bir paramediastinal kitle olduğu görüldü. 2002, 2015 ve 2016'da uygulanan üç transtorasik iğne biyopsisi tanısal değil idi. 2002'den beri ameliyat önerilmekte, fakat hasta kabul etmemekte idi. Toraks bilgisayarlı tomografi ve manyetik rezonans görüntülemeye sağ hemitoraksı neredeyse tamamen dolduran büyük bir mediastinal kitle izlendi. Son transtorasik biyopsi ile "malign işi hücreli tümör" tanısı konuldu ve posterolateral torakotomi yoluyla total cerrahi rezeksiyon uygulandı. Tümör mikroskopik olarak iki bileşenden oluşmakta idi: benign schwannom ve epitelioid anjiosarkom. Endotelyal ve nöral hücre farklılaşmaları immünhistokimyasal olarak teyit edildi.

Anahtar sözcükler: Anjiosarkom; kemoterapi; mediasten; schwannom; torakotomi.

Schwannoma is a well-known benign peripheral nerve sheath tumor and malignant transformation is extremely rare. Such malignant transformation was defined as malignant peripheral nerve sheath tumor (MPNST).^[1] There are only several reports about angiosarcoma arising in a schwannoma in the English literature. To the best of our knowledge, in this article, we describe the first case of an epithelioid angiosarcoma arising in a mediastinal long-standing schwannoma.

CASE REPORT

A 53-year-old female patient with severe dyspnea and palpitation was admitted to our clinic. Her medical history showed a right-sided paramediastinal mass which was first diagnosed in 2002 (Figure 1). Transthoracic needle biopsy was not diagnostic, an operation was suggested but the patient has not accepted. She was asymptomatic until 2015, since then, her dyspnea progressed. Renewed transthoracic needle

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Correspondence: Ş. Mustafa Demiröz, MD. Atatürk Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Göğüs Cerrahisi Kliniği, 06280 Keçiören, Ankara, Turkey. Tel: +90 312 - 567 72 47 e-mail: demirozsm@gmail.com

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Figure 1. Chest X-rays in 2002 (a), 2005 (b) and 2015 (c).

biopsy was also non-diagnostic. Her thorax computed tomography and magnetic resonance imaging revealed a huge right-sided mediastinal mass nearly fulfilling the hemithorax (Figure 2). A final transthoracic biopsy was performed, which revealed a “malign spindle cell tumor”. The tumor was immunohistochemically positive for epithelial membrane antigen (EMA) and pankeratin while negative for CD45, HMB45, CD34, actin, WT-1, S100 protein and calretinin. The respiratory function tests revealed a forced expiratory volume 1 of 42% of the predicted by a value of 1.2 L. A written informed consent was obtained from the patient.

Surgical treatment was performed via posterolateral thoracotomy. The mass and adjacent mediastinal pleura and pericardium were totally excised. Postoperative course was uneventful. All symptoms improved immediately.

In pathologic examination, 18×15×7 cm, fragile, mostly encapsulated mass consisting of multiple components was evaluated. The main tumor was represented by rounded large cells with reduced amphophilic cytoplasm and large polymorphous hyperchromatic nuclei layering small pseudovascular spaces. Tumor cells realized a scarcely small network occupied by erythrocytes (Figure 3a). In the immunohistochemical examination, the tumor was diffuse positive for CD31 and CD34 while focally positive for D2-40 and CD68 and negative for actin, keratin 8/18, desmin and CD99 (Figure 3b). Some areas of the tumor consisted of uniform spindle cells with elongated wavy nuclei and pale cytoplasm. Antoni A and Antoni B areas were detected. This component was diffusely positive for S100 protein and focally positive for EMA and also grossly negative for CD31 and CD34 (Figure 3c, d). The vascular tumor component

Figure 2. Mass on (a) 18F-fluorodeoxyglucose positron emission tomography and (b) mediastinal magnetic resonance imaging.

Figure 3. (a) Anastomosing vascular structures covered by atypical cells with intraluminal erythrocytes (H-E×400). (b) Tumor cells positive for CD31 staining (CD31, ×400). (c) Antoni A and Antoni B areas were seen near angiosarcoma (H-E×200). (d) S100 protein positivity in schwannoma component (S100, ×200).

was dominant in mass. With trichrome staining, while the spindle component was rich of collagen, the epithelioid parts were not. Areas of vascular structures were rich of reticulin. Excised mediastinal pleura and pericardium were infiltrated with the tumor. Based on clinical findings and the medical history, the final pathologic diagnosis was “epithelioid angiosarcoma arising from a schwannoma”.

The patient was consulted to medical and radiation oncology for adjuvant therapy. Because the tumor had invaded both the adjacent pleura and the pericardium, it was not found eligible for adjuvant radiotherapy. So, the patient only received four cycles of Doxorubicin + Ifosfamide + Mesna (2500 mg/m² Ifosfamide + 2500 mg/m² Mesna + 60 mg/m² Doxorubicin) chemotherapy and follow-up tomography and also positron emission tomography/computed tomography scan where there was no evidence of malignant tissue. On the 22nd month of follow-up, the patient was free of any signs of disease.

DISCUSSION

Neurogenic tumors are the most common posterior mediastinal masses (95%) and, in adults, the most

common subtype is nerve sheath tumors. Among these, schwannoma is the most common benign peripheral nerve sheath tumor.^[2] In a review in 1994, nine cases of MPNSTs arising in benign schwannomas were reported.^[3] The first authors reporting an angiosarcoma arising in a schwannoma were Trassard et al.^[4] Then, Mentzel and Katenkamp^[5] have reported two additional cases. In a series of 17 patients, only four cases were diagnosed as angiosarcoma.^[6] To the best of our knowledge, we described the first case of an epithelioid angiosarcoma arising in a mediastinal long-standing schwannoma.

The pathologic pathway leading to the angiosarcoma transformation is unclear. While some authors suggest that the angiosarcoma arise directly from the vascular structures of the schwannoma, some others suggest that chronic vascular stasis and edema is the triggering factor.^[6,7] Three cases immunoreactive for vascular endothelial growth factor caused some others think that it may have a role in the pathogenesis.^[1]

Differential diagnosis for these extremely rare cases includes epithelioid malignant peripheral nerve sheath tumor and the schwannoma variants; therefore, immunohistochemistry is helpful in diagnosis.

Factor VIII, CD31 and CD34 are common markers for endothelial differentiation. The benign neural component of the tumor was consisted of uniform spindle cells. Presence of Antoni A and Antoni B areas enabled differentiation from normal anatomic cells.

Malignant tumors of mediastinum are highly challenging for the surgeon. However, it is known that the only curative treatment of soft tissue sarcomas is complete surgical resection. In complete resection, capsule penetration, invasion of the adjacent tissues and large tumor size were shown to be related to poor prognosis.^[1] On the other hand, local tumor control can improve survival in mediastinal sarcomas, particularly when the disease is limited in thorax.^[8] It is mostly hard to achieve tumor free surgical margins for these types of tumors so neoadjuvant and adjuvant therapy had come into scene in recent years.

In conclusion, malignant transformation in a benign schwannoma is a rare condition, while development of an angiosarcoma in this ground is extremely rare. Treatment of these tumors is controversial in the literature. The main goal of therapy is total excision of the tumor for limited disease in selected patients; however, if not possible, adjuvant treatment including chemotherapy and/or radiotherapy may be the only chance. Unfortunately, none of these attempts seem to achieve satisfactory overall survival rates.

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REFERENCES

1. Li C, Chen Y, Zhang H, Zheng X, Wang J. Epithelioid angiosarcoma arising in schwannoma: report of three Chinese cases with review of the literature. *Pathol Int* 2012;62:500-5.
2. Occhipinti M, Heidinger BH, Franquet E, Eisenberg RL, Bankier AA. Imaging the posterior mediastinum: a multimodality approach. *Diagn Interv Radiol* 2015;21:293-306.
3. Woodruff JM, Selig AM, Crowley K, Allen PW. Schwannoma (neurilemoma) with malignant transformation. A rare, distinctive peripheral nerve tumor. *Am J Surg Pathol* 1994;18:882-95.
4. Trassard M, Le Doussal V, Bui BN, Coindre JM. Angiosarcoma arising in a solitary schwannoma (neurilemoma) of the sciatic nerve. *Am J Surg Pathol* 1996;20:1412-7.
5. Mentzel T, Katenkamp D. Intraneural angiosarcoma and angiosarcoma arising in benign and malignant peripheral nerve sheath tumours: clinicopathological and immunohistochemical analysis of four cases. *Histopathology* 1999;35:114-20.
6. McMenamin ME, Fletcher CD. Expanding the spectrum of malignant change in schwannomas: epithelioid malignant change, epithelioid malignant peripheral nerve sheath tumor, and epithelioid angiosarcoma: a study of 17 cases. *Am J Surg Pathol* 2001;25:13-25.
7. Rückert RI, Fleige B, Rogalla P, Woodruff JM. Schwannoma with angiosarcoma. Report of a case and comparison with other types of nerve tumors with angiosarcoma. *Cancer* 2000;89:1577-85.
8. Turbendian H, Seastedt KP, Shavlade N, Port J, Altorki N, Stiles B, et al. Extended resection of sarcomas involving the mediastinum: a 15-year experience†. *Eur J Cardiothorac Surg* 2016;49:829-34.