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Ancient (Sclerosing) Thymoma: Case Report

Ancient (Sklerozan) Timoma: Olgu Sunumu

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ABSTRACT

A 43-year-old female who had dyspnea and had been diagnosed as myasthenia gravis was found to have a mass lesion of the anterior mediastinum that protruded to the left and contained calcified areas on radiological investigation. The patient was operated on with a preliminary diagnosis of thymoma. Macroscopically the tumoral lesion was 5x4.5 cm in size and was light tan, firm and solid without necrosis or hemorrhage. Histological investigation showed epithelial islands without atypical features scattered within large areas of hyalinized collagenous tissue and the presence of immature T lymphocytes some of which were TdT positive, which led to a preliminary diagnosis of sclerosing thymoma. Sclerosing thymoma is a rare type of thymoma and has first been reported in 1994. Since there are only a few reports in the literature detailed information on clinical features and pathogenesis is needed. The possibility of sclerosing thymoma should always be kept in mind in the differential diagnosis of mediastinal lesions with marked sclerosis that can lead diagnostic difficulties especially when evaluating small mediastinoscopic biopsies.

Key Words: Mediastinum, Thymoma

ÖZ

Solunum sıkıntısı yakınması olan ve myastenia gravis tanısı alan 43 yaşında bayan hastada radyolojik incelemede anterior mediastende sola doğru protrüzyon gösteren, kalsifiye alanlar içeren kitlesel lezyon tanımlanmıştır. Hasta timoma ön tanısı ile opere edilmiştir. Makroskopik olarak solid, sert, gri-beyaz renkli, hemoraji ve nekroz alanları içermeyen, 5X4,5cm boyutlarında tümöral lezyon görülmüştür. Histolojik incelemede geniş alanlarda hyalinize kollajenöz doku içerisinde dağılmış, belirgin atipi göstermeyen epiteliyal adaların ve bir kısmı TdT pozitif immatür T lenfositlerin varlığı nedeni ile olgu sklerozan timoma olarak değerlendirilmiştir. Sklerozan timoma; timomaların ender görülen bir alt tipi olup, ilk kez 1994 yılında yayınlanmıştır. Literatürde bildirilen olgu sayılarının az olması nedeniyle gerek klinik, gerekse patogenezi ile ilgili ayrıntılı bilgiye gereksinim vardır. Özellikle küçük mediastinoskopik biyopsilerde tanısal güçlük yaşanılabilen mediastenin belirgin sklerozis gösteren lezyonlarının ayırıcı tanısında sklerozan timoma olasılığı göz önünde bulundurulmalıdır.

Anahtar Sözcükler: Mediasten, Timoma

INTRODUCTION

Thymomas are neoplasms derived from thymic epithelial cells and show such differentiation. Thymoma classification is difficult and controversial due to the intratumoral histological variability. Various classifications have been developed so far employing the histological findings, histogenesis or immunophenotypic features (1,2). The current World Health Organization (WHO) classification divides thymomas into type A, type B and type AB using three main morphotypical features and type B is further divided into types B1, B2 and B3 according to the dominance of the accompanying non-neoplastic lymphocytic component and atypical epithelial features. Thymomas with unconventional morphological features have been classified under separate headings. These groups consist of micronodular thymoma, metaplastic thymoma and the rare thymoma subtypes (microscopic thymoma, sclerosing thymoma (ST), lipofibroadenoma) (1,2). ST has first been defined by Kuo in 1994 (3). The WHO reports that ST is seen very rarely and makes up less than 1% of the thymomas. There are 14 cases reported as ST in the literature (1,3-5). Most of the mass consists of a stroma rich in collagen in such tumors, making it more difficult to separate it from the non-neoplastic or neoplastic lesions of the mediastinum that have a similar histopathological appearance. Being aware of this rare thymoma type is therefore important in evaluating sclerosing lesions of the mediastinum.

CASE REPORT

The patient was a 43-year-old female with a history of rheumatoid arthritis that was not under follow-up. She presented at another center with symptoms of cough, sputum and intermittent respiratory distress (dyspnea,

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tachypnea) and was treated for a lower respiratory tract infection. However, the difficulty in breathing continued and she was evaluated at the Dokuz Eylül University Emergency Service and admitted to the Internal Medicine Department with preliminary diagnoses of pneumonia and pulmonary embolism. The possibility of pulmonary embolism was eliminated with CT angiography but an anterior mediastinum mass lesion that protruded to the left with internal calcification and consolidated pulmonary areas were observed (Figure 1). The patient was evaluated by neurology with a preliminary diagnosis of myasthenia gravis due to the mediastinal mass and clinical signs such as ptosis and muscle weakness. The symptoms decreased markedly with the neostigmin test together with an increase in the serum acetylcholine antibody level and a diagnosis of myasthenia gravis was made. The mediastinal mass was operated with a diagnosis of thymoma.

The specimen 6.5x4.5x1 cm in size was a solid mass with an irregular shape weighing 30 grams. The cut surface showed a lesion 5x4.5 cm in size that had irregular borders, was solid and fibrotic in appearance and had scattered areas of calcification. There was no necrosis or hemorrhage. Adipose tissue was present around the lesion. Microscopic investigation showed large hyalinized and collagenized areas and focal calcification foci (Figure 2). There was squamoid or oval-spindle type epithelial cell proliferation that lined the microcystic areas between these areas and showed irregular peripheral branching together with accompanying lymphocytes. There were occasional mild cytological atypical features in the epithelial cells (Figure 3,4,5). These cells made up structures similar to Hassal corpuscles in some areas. Immunohistochemical study showed CD20 or CD3 positive T or B lymphocytes and also TDT positive immature T cells. It was not possible to evaluate capsular or extracapsular invasion due to the widespread hyalinization. The clinical symptoms decreased during the 1-year postoperative follow-up period.

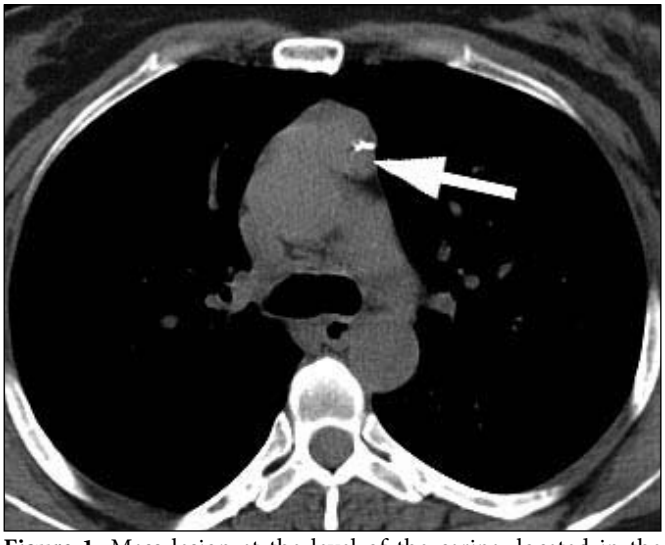

Figure 1: Mass lesion at the level of the carina, located in the anterior mediastinum and containing calcification areas on computed tomography.

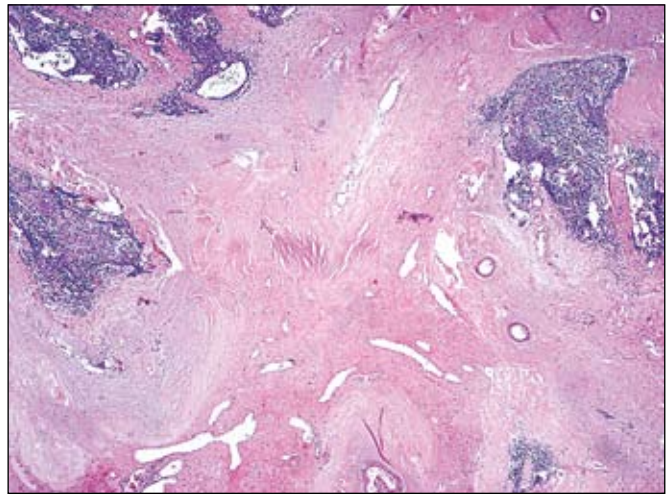

Figure 2: Lesion containing widespread hyalinization and sclerosis on low magnification (H&E, x40).

DISCUSSION

We were able to find 2 cases reported by Kuo, a series of 10 patients reported by Moran CA et al., 1 case reported by Kim YH et al. and 1 case in the World Health Organization (WHO) 2004 thymoma classification book (1,3,4,5). Thymectomy was performed in all these cases and the mean age of the 7 male and 7 female patients varied between 18 and 73.

Two cases reported by Kuo were being followed-up for myasthenia gravis (MG) and the reason for surgery was persistence of disease-related symptoms such as respiratory distress and pneumothorax in one and muscle weakness and difficulty speaking in the other. Only one had a mass lesion on imaging tests. Both cases showed remission following thymectomy (3). Moran CA et al. reported a 10-case series where 5 cases were asymptomatic and the mass was found on routine chest x-ray, 4 cases had symptoms such as dyspnea and chest pain possibly due to pressure from the mass and 1 case had a history of MG. Six of the patient died because of congestive heart failure, pulmonary edema, kidney failure or undefined causes. Two cases were alive and healthy while 2 cases were lost to follow-up (4). Kim YH et al. reported 1 case where a mediastinal mass was found during routine radiography (5). The single case reported by the WHO is

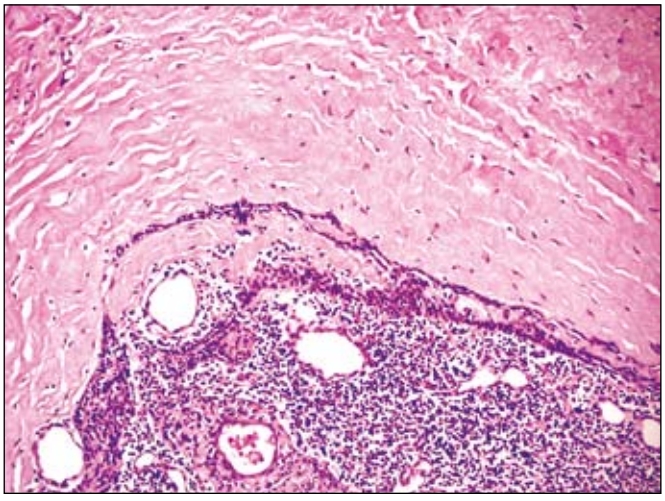

Figure 3: Neoplastic epithelial cells with accompanying lymphocytic component between areas of hyalinization and sclerosis (H&E, x100).

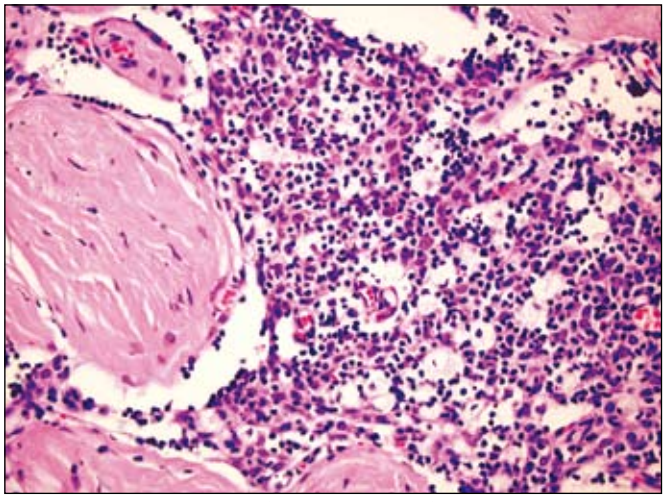

Figure 4: Appearance of areas typical for thymoma on high magnification (H&E, x200).

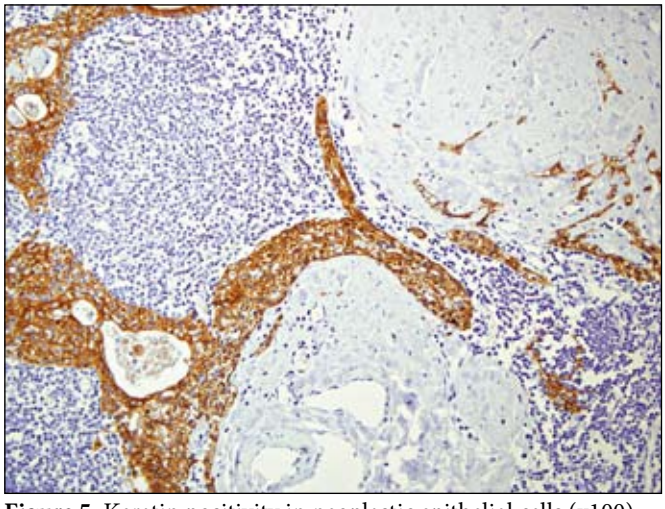

Figure 5: Keratin positivity in neoplastic epithelial cells (x100).

also nonmyasthenic and no detailed information has been provided regarding the clinical symptoms (1).

The tumor size varied from 2 to 18 cm in the reported cases and the tumors were defined as sharply separated, solid nodules. The main tumor mass was 85-90% hyalinized and had a dense fibrocollagenous character in all the cases. There were irregularly arranged epithelial neoplastic areas or neoplastic epithelial cells within myxoid areas within this dense fibrocollagen. A spindle-shaped narrow eosinophilic cytoplasm within the neoplastic epithelial cells with no cellular atypical features or mitotic figures was present in some cases. Focal areas of granulomatous reaction against cholesterol and calcification foci were present in some of these tumors. One case had neoplastic epithelial cell proliferation that dissected the fibrocollagenous bands and gave an appearance of a vascular neoplasm. The cases with MG especially had areas with a loose appearance of hemorrhages and hemosiderin-loaded macrophages together with surrounding sclerotic changes (1,3-5).

There are various hypotheses on the development of the collagen-rich stroma, the main component of ST. Kuo et al. have postulated that this change is caused by spontaneous regression due to apoptosis or vascular insufficiency (3). Suster et al. have stated that the excessive hyalinized fibrosis reflects the "ancient" characteristics that are characterized by the gradual merging of the fibrocollagenous bands surrounding the lobular structures that are the characteristic feature of the tumor, and the decrease of the cellular component (4). The excessive collagenization in the WHO case was reported to be due to the fibrogenic stimulus of neoplastic thymic epithelial cells as there was no accompanying hemorrhage or necrosis (1).

Other mediastinal lesions characterized by marked sclerosis and hyalinization include sclerosing mediastinitis, solitary fibrous tumor and lymphomas (6-10). It may not possible to make a diagnosis if the sclerotic section has been sampled, especially with small biopsies. However, sclerosing thymomas should be considered in the differential diagnosis.

ST can be differentiated from the other lesions included in the differential diagnosis by the presence of two cell types (neoplastic epithelial and nonneoplastic lymphoid component). The acellular necrosis in sclerosing mediastinitis is accompanied by focal inflammatory changes and dystrophic calcification (6). There are hypercellular areas accompanied by hemangiopericytic or various sarcomatous patterns in solitary fibrous tumors and CD34, bcl2-positive and keratin-negative immune profile of the

neoplastic cells also facilitates the differential diagnosis (7, 8). There can be marked sclerosis, especially in Hodgkin's lymphoma and primary mediastinal large B cell lymphoma. The diagnosis in Hodgkin's lymphoma is by the presence of Reed Sternberg - Hodgkin cells (CD30, CD15 positive) on a reactive background containing plasma cells, eosinophilic leukocytes and histiocytes (9,10). Mediastinal large B cell lymphoma (MLBCL) shows a diffuse, moderate or large neoplastic lymphoid infiltration that stains positive for pan B markers. Sclerosis is not an expected finding of MLBCL but it may be seen if there is invasion of the peripheral tissues (10).

In conclusion, we have presented a rare case of ST with controversial etiopathogenesis and emphasized its importance in the differential diagnosis of sclerotic lesions of the anterior mediastinum.

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