Alopecia Areata Associated with Thymoma Presenting as a Diffuse Pleural Dissemination Mimicking Mesothelioma: Rare Concomitant Presentation

Mezotelyomaya Benzer Diffüz Plevral Yayılımla Seyreden Timoma ve Alopecia Areata Birlikteliği

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ABSTRACT A 42-year-old man presented with dyspnea, left-sided chest pain and sudden onset of hair loss. Multiple pleural masses were found on computed tomographic scans which were highly suggestiveof malignant pleural mesothelioma or pleural metastases. After open pleural biopsy, pathological examination showed the lesion to be a metastatic pleural thymoma or primary pleural thymoma with an exceptional localization. Clinical signs and symptoms of myasthenia gravis (MG) were absent and anti-acetylcholine -receptor antibodies were in normal range. Electromyogram was normal. PET-CT showed anterior-superior hypermetabolic partially calcified mass (malignant thymoma, SUV: 4-4. 2) located to the thymus. The patient was diagnosed as alopecia areata (AA) in the view of dermatological findings. Association of AA and thymoma was previously reported in the presence of MG as individual cases. Nevertheless, this case represents an unusual form of metastatic thymoma with diffuse pleural dissemination mimicking malignant mesothelioma associated with AA, but not accompanied by MG. It should be emphasized that dermatologists must be aware of the clinical findings of a pulmonary disease such as thymoma in patients with AA.

Key Words: Thymoma; mesothelioma; alopecia areata

ÖZET Kırkiki yaşında erkek hasta ani başlayan saç dökülmesi, dispne ve göğüs ağrısı yakınmaları ile Göğüs Hastalıkları polikliniğine başvurdu. Olgunun akciğer bilgisayarlı tomografisinde diffüz plevral mezotelyoma veya plevral metastaz ile uyumlu multiple plevral kitleler mevcuttu. Myastenia gravis' in klinik semptom ve bulguları yoktu ve asetilkolin reseptor antikoru normal sınırlarda idi. Elektromyogram sonuçları normaldi. Plevra biyopsisi primer veya metastatik plevral timoma ile uyumlu idi. Pozitron emisyon tomografide (PET) anterior-süperior mediastende timus lokalizasyonunda malign timoma (SUV: 4-4.2) ile uyumlu kalsifiye kitle mevcuttu. Dermatolojik bulgular açısından hasta alopecia areata olarak değerlendirildi. Alopecia areata ve timoma birlikteliği literatürde sıklıkla myastenia gravis'in eşlik ettiği timoma olgularında bildirilmiştir. Olgumuz, alopecia areata ile birlikte olan timomanın, mezotelyomaya benzer yaygın plevral tutulumla seyretmesi ve eşlik eden myastenia gravis bulgularının olmaması nedeniyle ilginçtir. Dermatologlar, alopecia areata olgularında timoma gibi pulmoner hastalıkların klinik bulgularından haberdar olmalıdırlar.

Anahtar Kelimeler: Timoma; mezotelyoma; saç dökülmesi

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Alopecia areata (AA) A is characterized by a sudden and patchy loss of hair, and known to be a T-cell mediated autoimmune disorder. AA is frequently associated with several autoimmune disorders such as type 1 diabetes mellitus, pernicious anemia, atopic dermatitis, and autoimmune thyroid disease.[1]

Thymoma is the most common primary tumor of the anterior mediastinum and some cases may present with local invasion to adjacent structures. Pleural dissemination causing total collapse, via circumferential pleural thickening which encases the entire lung, is typical of malignant pleural mesothelioma but it is unusual for thymoma.[2]

Patients with thymoma may present with symptoms related to one or more of the autoimmune diseases and typically MG, hypogammaglobulinemia, pure red cell aplasia, and non-thymic malignancies.[3] Moreover, few cases of thymoma associated with MG and AA have been reported.[4,5]The role of thymoma in the development of these autoimmune diseases is largely unknown. To our knowledge, up to date a unique case of alopecia universalis has been reported to be associated only with thymoma.[6]

CASE REPORT

A 42-year-old male was admitted with excessive hair loss, dyspnea and left-sided chest pain. There was no other significant family or past medical history, such as asbestosis, atopy, arthritis, skin changes, Raynaud's phenomenon, systemic lupus erythematosus, pernicious anemia, thyroid disease, irradiation and/or chemotherapy. No autoimmune diseases or AA were noted in his family. Physical examination revealed tachycardia and decreased breath sounds at the base of left lung, with dullness on percussion; no axillary lymph node enlargement was found. Neither ptosis nor generalized muscle weakness or dysphonia suggesting MG was observed on neurological examination.

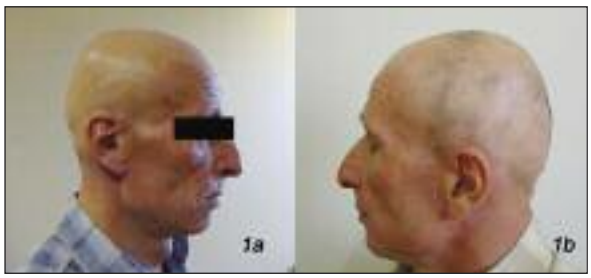

FIGURE 1A: Total loss of scalp hair, eyelashes and eyebrows.
1B: Growing hair in patchy pattern one year later.

When he was first referred to the dermatology outpatient clinic, he had patchy areas of alopecia on the entire scalp, but he did not benefit from topical and systemic steroid (50 mg/day, orally for 2-3 weeks) treatments. No involvements of the nails were observed. The hair loss in the scalp progressively increased and presented as alopecia totalis complicated with gradual loss of the eyelashes, eyebrows (Figure 1a) and whole body hair within two months. PUVA therapy was started for alopecia universalis, but the patient did not complete the treatment.

Complete blood count, routine biochemical analysis, thyroid function tests, total IgE, ANA, anti-acetylcholine receptor antibody and urinalysis were in normal limits. Erythrocyte sedimentation rate was 36mm/h. Electromyogram was normal. Chest X-ray and computerized tomography (CT) on admission showed multi-focal large pleural masses encasing the entire lung. CT also showed an anterior mediastinal calcified mass, which was at the same density with the pleural masses, and was indistinguishable from the pleural masses or malignant adenopathy. Based on radiological findings, the expected diagnosis was malignant pleural mesothelioma or pleural metastases from another malignancy. Bronchoscopy demonstrated no endobronchial lesion.

Pleural effusion was serous in appearance. Cytological examination showed only lymphocytosis, and was negative for malignant cells and tumor markers (CEA, AFP, β-HCG). Open- pleural biopsy was performed. On histological examination, the individual epithelial cells were large and polygonal with open nuclei and prominent nucleoli. Perivascular spaces were frequent. Epithelial cells showed strong reactivity for CK19 and CK5/6. Lymphoid cells showed strong reactivity for CD3 and CD1a consistent with thymic origin. Immunohistochemical stainings for TTF-1, calretinin, CD15, Ber-EP4, MOC31, CEA and CD20 were negative implicating a low possibility of thyroid, lung or mesothelial origin. Histopathological findings were consistent with type B2/B3 primary or metastasizing pleural thymoma (Figures 2a, 2b). PET-CT showed anterior-superior hypermetabolic, partially

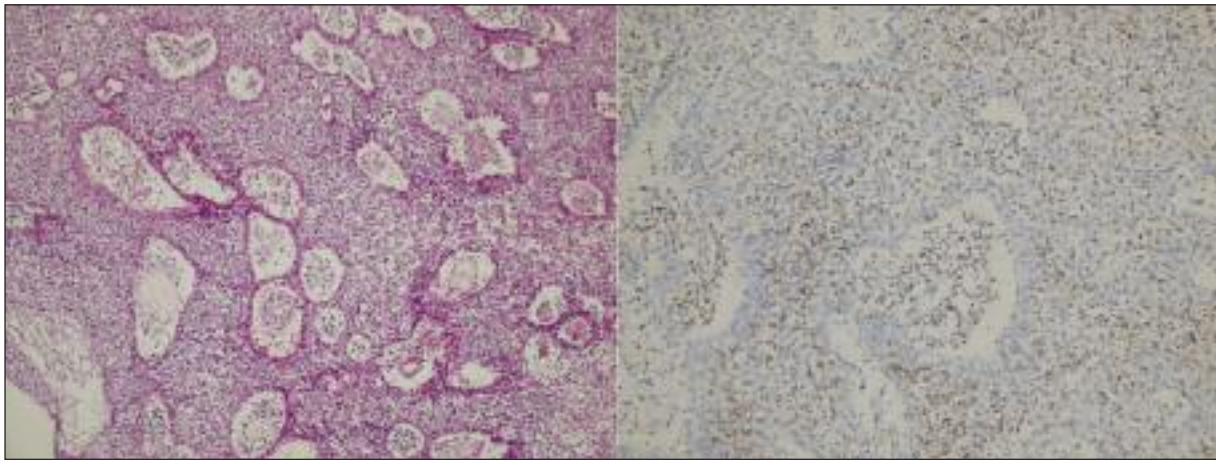

FIGURE 2A: Epithelial tumor cells palisading around blood vessels and perivascular spaces characteristic of thymoma. Note the lymphocytes partially obscuring epithelial cells (H&E). **2B:** CD3 positive lymphocytes infiltrating epithelial cells.

calcified mass (malignant thymoma, SUV: 4-4. 2) located in the thymus (Figure 3).

When the patient was reevaluated in the dermatology department one year later, it was noted that he underwent an explorative thoracotomy at a different hospital. The lesions invaded adjacent tissues and were unresectable. A combination chemotherapy regimen (ADOC, including adriamycin 50mg/m^2 on day 1, cisplatin 70mgr /m^2 on day 1, cyclophosphamide 700mg/m^2 on day 4, vincristine 0.6mg/m^2 on day 2 in 21-day cycles) was begun thereafter. After four cycles, follow-up was continued under oral cyclophosphamide 50mg /day and oral etoposide 100 mg/day on two days weekly. The patient stated that his hair started to grow since then. We observed that the growing hair were mainly on the scalp (Figure 1b) and minimally in eyelashes, the eyebrows and the whole body. He also had pitting of the right forth and fifth fingernails.

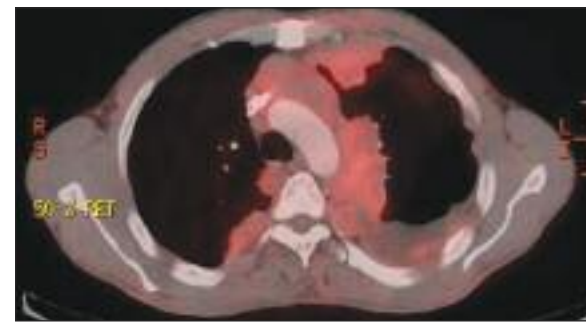

FIGURE 3: ^{18}F-FDG PET/CT fusion images demonstrate an anterior mediastinal partially calcified mass (maximal standard uptake value [SUV max: 4-4.2]).

DISCUSSION

Thymoma presented with diffuse pleural dissemination mimicking malignant mesothelioma in this case. Radiologically, it is often difficult to differentiate mesothelioma from thymoma extending into the pleural cavity ending with total collapse which is typical of malignant pleural mesothelioma, but rare for thymoma[2] as seen in our patient.

Association of AA and thymoma was also reported in the presence of MG[4, 5]. In the case of Wakata et al.[4] AA and MG appeared one and a half years after the patient was diagnosed as thymoma. Likewise, Sander et al.[6] reported thymoma to be preceded by alopecia universalis whereas thymoma was diagnosed six months later than AA in the case of Kamada et al[5] However, in our patient, presentation was with sudden onset of hair loss and a few symptoms of intrathoracic spread were present suggesting that AA and thymoma started simultaneously, and no symptoms of MG were observed.

Skin diseases are considered as rare complications of thymoma. Few definitive cases of AA were stated to be accompanied by thymoma[4, 5] mentioned as multiple disease associations, mainly with MG. The co-occurrence of multiple autoimmune conditions is not described in the present case except for thymoma. The role of thymoma in the

development of AA may be attributed to autoimmune nature of both diseases.

Alopecia totalis and universalis are severe forms of AA[1] as observed in our case. To our knowledge, this is the second case of alopecia universalis associated with thymoma but not accompanied by MG or any other autoimmune disorder. Although the patient could not be effectively treated for AA, observation of growing hair one year later is a satisfactory result. This shows that the course of alopecia areata ran parallel with the activity of thymoma in our case. It may also be attributed to the patient's emotional condition after receiving chemotherapy for thymoma.

In conclusion, concomitant presentation of AA with thymoma supported the existence of increased risk of autoimmune disorders in patients with AA. This case also represents that thymoma may present as pleural masses mimicking mesothelioma. It should be underlined that dermatologists must be aware of the clinical findings of a pulmonary disease such as thymoma in patients presented with AA.

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