
A rare association: Castleman's disease and pemphigus vulgaris

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ÖZET

Nadir görülen birliktelik: Castleman hastalığı ve pemfigus vulgaris

Castleman hastalığı, etyolojisi tam olarak aydınlatılmayan, tüm vücutta bulunabilmekle beraber sıklıkla toraksta yerleşen reaktif lenf nodu hiperplazisidir. Genellikle genç erişkinlerde görülür ve asemptomatik seyreder. Sıklıkla ön ve orta mediastende lokalizedir. Pemfigus vulgaris, patogenezinde immün mekanizmaların rol oynadığı büllöz bir deri hastalığıdır. En sık ağız ve orofarenks etkilenir. Epidermal intraselüler yapılara karşı gelişen IgG antikorların varlığı teşhiste gereklidir. Castleman hastalığı ile oral pemfigus vulgaris birlikteliğinin nadir olması nedeniyle, 28 yaşında kadın olguyu literatür eşliğinde tartışmak istedik.

Anahtar Kelimeler: Castleman hastalığı, anjiyofoliküler lenfoid hiperplazi, pemfigus vulgaris, oral ülser.

SUMMARY

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Castleman disease is a reactive lymph node hyperplasia of unknown origin that often involving the thorax although it may involve all parts of the body. It is usually seen in young adults and presents an asymptomatic course. It is usually located to anterior and middle mediastinum. Pemphigus vulgaris is a bullous skin disease in which immune mechanisms take place in the pathogenesis. Mouth and oropharynx are the most commonly involved structures. IgG antibodies against the epidermal intracellular structures are essential in the diagnosis. We have wanted to discuss a 28 years old female with the literature review since the association between pemphigus vulgaris and Castleman's disease is rare.

Key Words: Castleman's disease, angiofollicular lymphoid hyperplasia, pemphigus vulgaris, oral ulcer.

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Castleman's disease is a rare reactive lymphoid hyperplasia. Its synonyms are giant lymph node hyperplasia, angiofollicular lymph node hyperplasia and lymph node hamartoma. A number of terms used to describe this condition indicate the uncertainties in its etiology and pathogenesis (1).

Pemphigus vulgaris (PV) is a rare disease and there have been a few reported cases of association between PV and Castleman's disease (2). PV is a bullous skin disease in which immune mechanisms take place in the pathogenesis. The most common and invariably involved locations are the mouth and oropharynx. IgG antibodies against the epidermal intracellular structures support its immunogenic basis (3).

We have wanted to discuss a subject with both oral PV and Castleman's disease under the light of the literature review.

CASE REPORT

A 28 years old woman presented to outpatient clinic of dermatology department with small wounds lasting for 2.5 months and progressively worsening nutrition due to her oral wounds. On her physical examination, the hairy skin and the hair were normal in appearance, eroded areas which were very extensive on the oral mucosa and tongue with white-yellow membranes on them and an eroded area on the body with a diameter of 3 to 4 mm were found. Tongue biopsy revealed ulceration and neovascularization. Intracellular IgG accumulation at 1/10 titration was found on the indirect immunofluorescence (IIF) test. The patient was diagnosed as oral PV with these findings and she was given a treatment consisting of methylprednisolone (Prednol, 100 mg) and azathiopirine (Imuran, twice daily). The patient referred to our hospital upon observation of homogenous lesion of 3 cm diameter with regular contours on the left hilar region on the postero-anterior (PA) chest graphic was admitted to our hospital (Figure 1). Her medical and family story was not remarkable. No abnormal finding was found on the physical examination apart from her dermatological problems. Her routine laboratory investigations were as follows: erythrocyte sedimentation rate: 50 mm/hour; WBC:

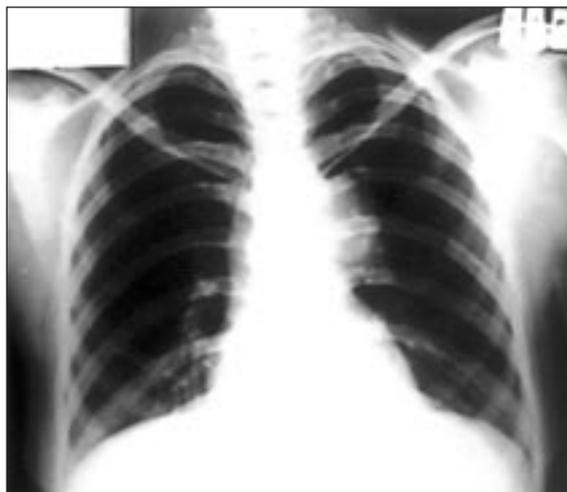


Figure 1. A homogenous lesion 3 cm in diameter with regular margins on the left hilar region on the postero-anterior (PA) chest graphic.

5900 cells/mm³; hemoglobin: 13.6 g/dL, hematocrit: 35.2%; platelet count: 229.000 per/mm³; glucose: 79 mg/dL; urea: 25 mg/dL; creatinine: 0.7 mg/dL; aspartate aminotransferase (AST): 21 IU/L, alanine aminotransferase (ALT): 45 IU/L; total protein: 7.40 g/dL; albumin: 4.6 g/dL; globulin: 2.8 g/dL; hepatitis-B surface antigen (HBsAg): negative; anti-hepatitis C virus antibody (anti-HCV): negative; anti-HIV: negative. Solid mass lesion 5 x 4 x 3 cm in size with paravertebral location on the posterolateral aspect of aorta at the level of arcus aorta on the left side was observed on the contrast enhanced computerized tomography (CT) scans (Figure 2). The lesion was extending to the infra hilar region. The solid lesion was containing 2 calcific foci. Fiberoptic bronchoscopy revealed hyperemia and fragile mucosa on both bronchial systems. Results of pathological examination of the catheter and lavage procedures were reported to be consistent with chronic inflammation. A mass lesion 5 x 2 cm in size with paravertebral location not invading the surrounding tissues and which was in close proximity to the aorta was observed on the posterior segment of upper lobe of the left lung on the thoracic magnetic resonance imaging (MRI) scan (Figure 3). Differential diagnosis was made for exclusion of aneurism by the means of aortography because of being in close proximity and having regular borders of the lesion and disappearance of the fat tissues between the lesi-

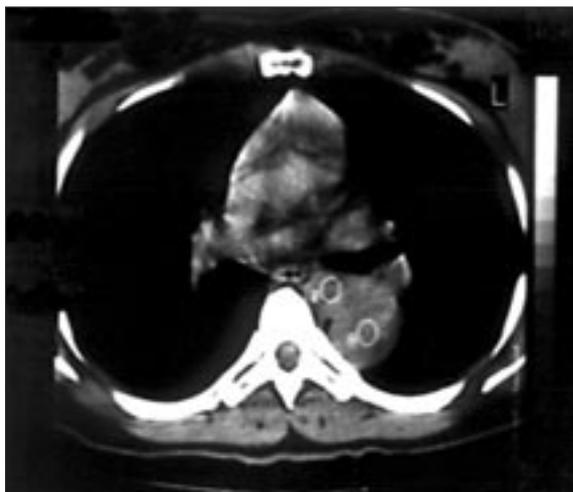


Figure 2. CT scanning showing the solid mass lesion of 5 x 4 x 3 cm with paravertebral location, on the posterolateral aspect of the aorta at the level of arcus aorta on the left side, which extends into infra-hilar level.

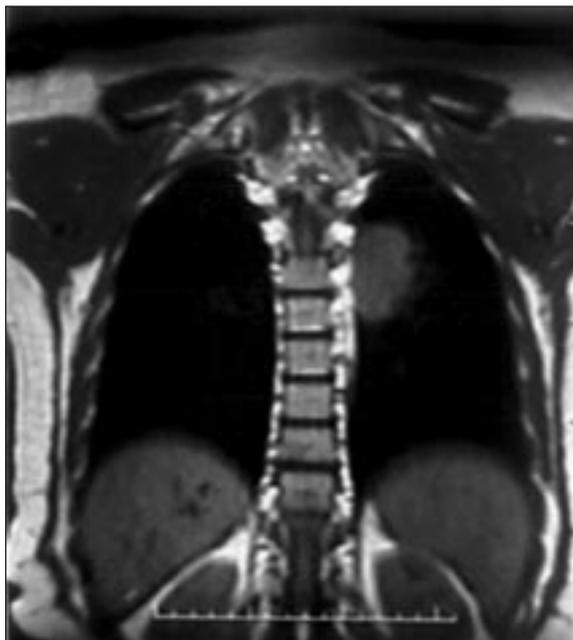


Figure 3. Thoracic MRI scanning showing mass lesion of 5 x 2 cm in the close proximity of the aorta without any invasion into the surrounding tissues that located paravertebrally on the posterior segment of upper lobe of the left lung.

on and the aorta. Aneurismatic filling was not observed in the arcus and descending aorta on the angiography. Paravertebral mass on the upper zone of the left lung was observed to be

hypervascular (Figure 4). The patient underwent transthoracic fine-needle aspiration (TFNA) under the guidance of CT. Microscopic findings were considered as carcinoma metastasis and thyroid investigation was advised for determination of the primary source. T3, T4 and TSH levels were all within normal limits. Thyroid radionuclide scanning revealed bilateral slightly diffuse hyperplasia. Distribution of the activity was normal.

It was decided to perform diagnostic thoracotomy upon these findings and the patient underwent left upper lobectomy. Postoperatively, the patient was diagnosed as angiofollicular hyperplasia of hyaline vascular type (Castleman's disease) (Figure 5). On the immunohistochemical examination, vimentin was (+), factor VIII was positive on the perivascular tissues and cytokeratin was negative. Oral pemphigus of the patient improved rapidly upon resection of the Castleman's tumor. Imuran treatment was discontinued on six months after the diagnosis of pemphigus. Prednol dose was tapered. No antibody of IgG type was found on the repeat-IIF examination 2.5 years after the initial diagnosis and the treatment was discontinued. The patient is currently within the postoperative 5th year and is free-from complaints. Her follow-ups are going on (Figure 6).

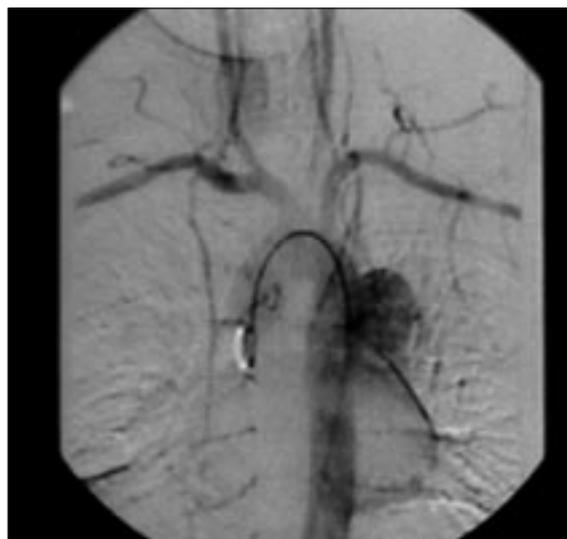


Figure 4. The aortography showing that the paravertebral mass on the upper zone of the left lung to be hypervascular.

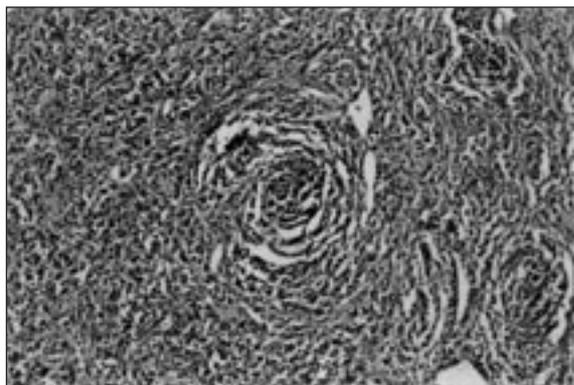


Figure 5. Histological characteristics of hyaline-vascular type. It is characterized by small atrophic or "burnt-out" germinal centers. The germinal centers are surrounded by expanded mantle zones with concentric rings of small lymphocytes and follicular center cells that impart an "onion-skin" appearance. HE, x100.



Figure 6. Normal thoracic CT scanning taken in the 5th postoperative year.

DISCUSSION

Castleman's disease may involve a variety of extranodal tissues including the lungs although it is often localized to the middle mediastinum. Although its etiology has not been completely understood, a chronic inflammatory reaction against an unknown antigen has been implicated in its pathogenesis (4). It is in the form of a gray-red solitary mass in the mediastinum and the lungs with regular margins and soft surfaces. Histologically, it is divided into three types as

hyaline-vascular, plasma cell and mixed type. The most common type is the hyaline-vascular type and this type is responsible for all of the pulmonary cases of Castleman's disease (1). They are usually detected incidentally on the routine pulmonary graphics in the majority of the patients (4,5). Among the commonly observed symptoms are cough, dyspnea and recurrent infections and these symptoms are usually due to compression in the tracheo-bronchial system (6).

Plasma cell type is responsible for 10% of the cases with Castleman's disease. This type of the disease is characterized by hyperplastic germinal center and interfollicular plasma cells. It usually involves the lymph nodes, but not the lungs (1). Abdomen is involved in about 56% of the cases and two thirds of the patients have fatigue, fever and weight loss (4). Almost all of the patients have such hematological abnormalities as anemia, increased erythrocyte sedimentation rate, polyclonal hyperglobulinemia, leukocytosis, trombocytosis or hypoalbuminemia.

Mixed type of Castleman's disease shows the features of both hyaline-vascular type and plasma cell type and is usually multicentric (1).

Clinically, Castleman's disease shows localized or multicentric involvement. Localized type of the disease is usually in the form of mediastinal mass and is seen in young and middle age groups without any sex predilection. Its treatment is surgical resection with complete remission. It has been suggested that radiotherapy is also useful for the localize forms (7). Multicentric type is usually accompanied by the symptoms and usually involves the peripheral lymph nodes. Histologically, it is usually in the form of plasma cell or mixed type and may be associated with myasthenia gravis, malignant lymphoma, Kaposi sarcoma and paraneoplastic pemphigus (8-11). Recently, several studies have been reported on association between multicentric Castleman's disease and human herpes virus-8 (HHV-8) (10-12). Symptoms of the multicentric type may be reduced with systemic chemotherapy and/or steroid treatment. Recently, interferon- α (IFN- α) use has been suggested in the treatment (13,14).

TFNA biopsy is usually not diagnostic in Castleman's disease. It is very likely to confuse it histologically with other lymphoproliferative diseases such as thymoma or lymphoma (15). Cytological examination of TFNA performed under the guidance of CT was confused with thyroid carcinoma in our case.

PV is a rare but serious disease characterized by auto-antibody production against the specific adhesion molecules in the skin and mucosa and clinically by bullae (16). It usually begins 30 to 50 years of age. IgG deposition among the epidermal cells usually in association with C3 deposition is present. A continuous deposition is seen around the keratinocytes along the entire epidermis. Demonstrating the auto-antibodies by direct or IIF methods is diagnostic (17). IgG deposition was found in our patient by IIF method but no C3 deposition was observed. The aim of the treatment in the patients with pemphigus is lowering the levels of circulatory serum auto-antibodies since serum levels of the antibodies are indicative of the disease activity (17, 18). Recently, combination of steroids and azathiopurine has begun to be the standard treatment of PV (18,19). In our patient, serum level of auto-antibodies became zero 2.5 years after the initiation of the treatment.

There have been a few reports in the literature on the association of PV with Castleman's disease. Castleman's disease has been suggested to alter the immune system and might lead to development of such an autoimmune disease as PV (4). Observing simultaneously two rare conditions, Castleman's disease and PV in a subject as well as resolution of the symptoms of PV following the resection of Castleman's tumor clearly indicate that this association is not just a chance.

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