Testicular Plasmacytoma: Case Report

Testiküler Plazmasitoma

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ABSTRACT Testicular plasmacytomas are rare tumors presenting in most cases with painless testicular swelling. Testicular involvement may occur as a first manifestation of plasma cell disorder or following diagnosis of systemic plasma cell myeloma. We report a case of a 49-year-old man who was found to have IgG-λ type multiple myeloma and spinal cord compression at Th 7-9 level. After spinal radiotherapy, he was treated with VAD chemotherapy. Just before the second cycle of VAD he admitted with left testicular swelling. Surgical orchiectomy of his left testis was performed. Histological and immunohistochemical studies of surgical material established massive interstitial plasma cell infiltration with strong anti-IgG and anti-λ antisera staining. Soon after the surgery he died of worsening renal failure and progressive myeloma. We present here a fatal case with an aggressive form of plasma cell myeloma with widespread bone disease along with extramedullary involvement of testis.

Key Words: Testicular neoplasms; plasmacytoma; multiple myeloma

ÖZET Testiküler plazmasitomalar çoğu olguda testiste ağrısız şişliğe neden olan nadir tümörlerdir. Testis tutulumu plazma hücre hastalığının ilk belirtisi olabilir veya sistemik myelom tanısı sonrasında gelişebilir. Bu yazımızda IgG-lamda tipi multipl myelom tanısı konan ve Th 7-9 düzeyinde spinal kord basısı saptanan 49 yaşında bir erkek hastayı bildiriyoruz. Hasta spinal radyoterapi sonrası VAD kemoterapisi ile tedavi edildi. İkinci kurs VAD tedavisinin hemen öncesinde hasta sol testiste şişlik yakınması ile başvurdu. Sol testise cerrahi orşiektomi uygulandı. Cerrahi materyalin histolojik ve immunhistokimyasal analizinde anti-IgG ve anti-lamda antiserumu ile güçlü boyanan, yoğun interstisyel plazma hücre infiltrasyonu saptandı. Hasta cerrahi sonrasında ağırlaşan renal yetmezlik ve ilerleyici myelom nedeniyle öldü. Burada yaygın kemik lezyonları ile birlikte testiste ekstramedüller tutulum izlenen, fatal seyirli bir agresif plazma hücreli myelom olgusunu sunuyoruz.

Anahtar Kelimeler: Testiküler neoplaziler; plazmasitom; multipl myelom

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Plasma cell myeloma (PCM) is a fatal and clonal plasma-cell disorder. Plasma cell infiltration is mainly observed in the bone marrow and bone lesions, but soft tissue and organ infiltration also occurs. Extramedullary plasmacytomas (EMPs) may involve a wide variety of anatomic sites and in most cases they are observed in the context of terminal, progressive phase of the disease.

EMPs are most frequently found in the upper respiratory tract, nasopharynx, lymph nodes, and gastrointestinal tract.[1] Testicular involvement

in multiple myeloma, however is a very rare clinical entity. In their review Anghel et al.[2] stated that since the first description in 1939, as few as 51 cases of testicular plasmacytomas had been published. In most cases testicular plasmacytomas were observed after the diagnosis of or concurrent with systemic myeloma. However isolated testicular plasmacytomas without bone marrow disease were also reported.

We report here the clinical course of a 49-year-old-man with testicular plasmacytoma and previous systemic myeloma.

CASE REPORT

In May 2004 a 49-year-old Caucasian man admitted to our hospital because of back pain, double vision, left-sided sudden onset hearing loss, weight loss of 24 kilograms in the last two months, hypercalcemia and renal failure. He had back pain for almost one year, but he was treated with various non-steroidal anti-inflammatory drugs without etiologic investigation. His physical examination revealed pain induced by pressure on the right clavicle and dorsolumbar vertebral bodies. He also had a painless right supraclavicular soft tissue mass approximately 10×4 cm in size. His audiometric examination showed diminished hearing on the right ear and total hearing loss on the left ear. Ophthalmologic examination detected right-sided abduscent nerve paralysis.

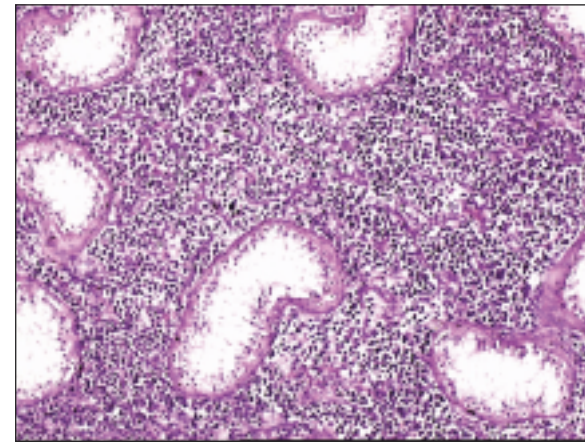

FIGURE 1: Diffuse plasma cell infiltration between seminiferous tubules of left testicular tissue (H&E, original magnification X50).

Laboratory findings included a complete blood cell count with Hb 9.4 g/dL, Htc 26.5%, MCV 82.9 fL, WBC 6×10^9/L, and platelets 91×10^9/L. Erythrocyte sedimentation rate in 1 hour was 57 mm, serum creatinine, corrected calcium, LDH, and β_2-microglobulin values were 6.9 mg/dL (normal: 0.6-1.1 mg/dL), 14.6 mg/dL (normal: 8.9-10.3 mg/dL), 350 U/L (normal: 98-192 U/L) and 16292 ng/mL (normal: 1010-2200), respectively. Serum creatinine clearance was measured as 17.2 ml/min. Serum total protein and albumin levels were found to be 7.2 g/dL (normal: 6.1-7.9 g/dL) and 3.2 g/dL (normal: 3.5-4.8 g/dL), respectively. Serum protein electrophoresis showed an M-protein spike in the α-2 region. Serum immunofixation assay with spe-

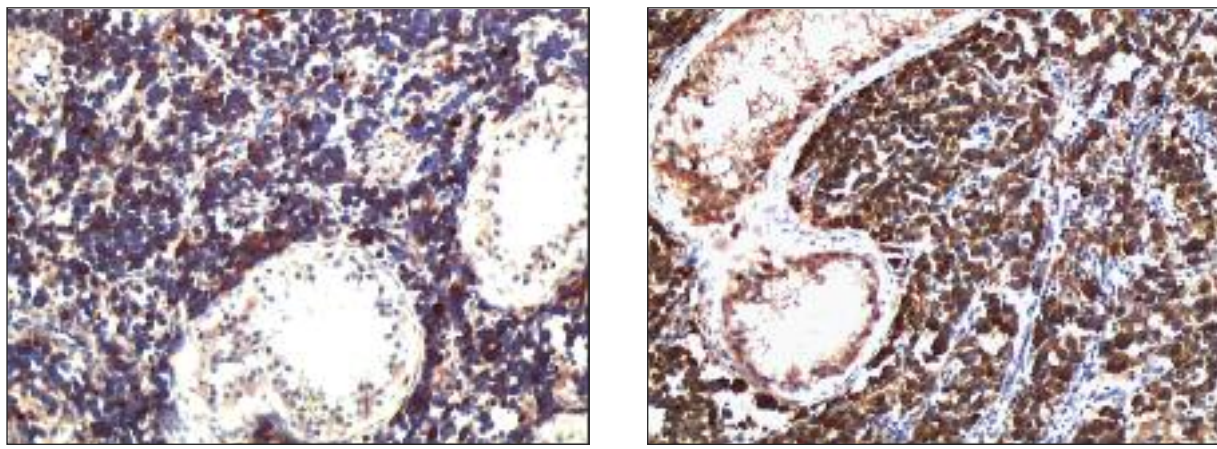

FIGURE 2: Strong intracytoplasmic staining with anti-IgG (A) and anti-λ (B) antisera (Streptavidine-biotin peroxidase X100).

cific antisera demonstrated an IgG-λ monoclonal protein. Serum levels of immunoglobuline classes were as follows IgG, 1980 mg/dL (normal: 694-1618 mg/dL); IgA, 9.35 mg/dL (normal: 82-453 mg/dL); IgM, 31.8 mg/dL (normal: 60-263 mg/dL). λ-type Bence Jones proteinuria was measured as 19.2 g/24h.

Bone marrow aspiration was unsuccessful on several occasions. Histology of bone marrow trephine biopsy showed diffuse monoclonal pleomorphic plasma cell infiltration with round-shaped eccentric nuclei, abundant basophilic cytoplasm and a marked perinuclear hof and histochemically grade III reticulin fibrosis. Antisera to heavy (IgG, IgA, and IgM) and light chains (κ and λ) were used to stain plasma cells. Immunohistochemical findings showed strong intracytoplasmic staining with the IgG and λ. Congo red staining of bone marrow specimen was found to be negative. He was diagnosed as having IgG-λ type multiple myeloma. Durie-Salmon stage and International Prognostic Score were found to be IIIB and III, respectively.

Magnetic resonance imaging (MRI) studies revealed expansive osteolytic lesions in calvarium, clivus and bilateral petrous bones, widespread destruction of vertebral bodies, paravertebral soft tissue mass and spinal cord compression at Th 7-9 level. MR images also showed destructive soft tissue mass at the medial portion of right clavicle (13×10 cm in diameter). The patient was treated with radiotherapy (25 Gy in 10 fractions) on Th 5-9 area. Thereafter monthly VAD chemotherapy courses consisting of vincristin 0.4 mg/day IV for 4 days, doxorubicin 9 mg/m^2/day for 4 days and dexamethasone 40 mg/day po for 12 days (days 1-4, 9-12, and 17-20) were started. He was also commenced on monthly intravenous zolendronic acid (4 mg) after successful treatment of acute renal failure without necessitating renal replacement therapy.

Just before the second course of VAD chemotherapy he was admitted again with left testicular swelling and dyspnea. His physical examination showed left testicular mass and bilateral decreased breath sounds. Plain chest film showed bilateral pleural effusion. He had no sign of plasma cell leukemia. The evaluation of exudative pleural fluid revealed no sign of plasma cell infiltration or infection. He refused pleural biopsy. He responded well to bilateral therapeutic thoracentesis. Ultrasound examination confirmed a diffuse mass lesion involving whole left testicle.

Before planned operation the patient received only the first four days of his second VAD course because of concern about poor wound healing. Then, surgical orchiectomy of his left testicle was performed. Macroscopic evaluation of left orchiectomy material revealed gray white solid tumor infiltration in testicular tissue (2×1.5×1.2 cm in size). Histologic and immunohistochemical studies were performed on paraffin-embedded tissue. Microscopic examination of surgical material established massive interstitial infiltration of pleomorphic, atypic looking plasma cells with strong anti-IgG and anti-λ antisera staining (Figure1, Figure 2A and 2B).

One day before the planned third VAD course the patient admitted to our emergency department with severe dyspnea as a result of pleural effusion recurrence. As he refused pleural sclerotherapy, therapeutic thoracentesis procedures were performed as needed. Approximately two months after the first VAD chemotherapy serum IgG, Bence-Jones proteinuria, and creatinine levels were measured as 319 mg/dL, 2.9 g/24h, and 1.5 mg/dL, respectively. Thorax computerized tomography (CT) showed that his right supraclavicular soft tissue mass was diminished in size (10×7 cm). But approximately 3 months later after the first course of VAD the course of the disease became progressive. The patient died of worsening renal failure and progressive myeloma.

DISCUSSION

PCM is a bone marrow-based, multifocal plasma cell neoplasm characterized by a serum monoclonal protein and skeletal destruction with osteolytic lesions, pathologic fractures, bone pain, hypercalcemia and anemia.[3] A minority of patients (<5%) with plasma cell malignancies are presented with either a single bone lesion, or less commonly, a soft

tissue mass of monoclonal plasma cells.[4] Extramedullary involvement may occur as an occasional finding during autopsy, as a primary clinical manifestation, called primary extraosseous plasmacytoma (PEP), or as a metastatic lesion in patients with PCM or plasma cell leukemia.[5-7] In almost 90% of cases PEP arises in the head and neck, especially in the upper respiratory tract including the nasal cavity, sinuses, oropharynx, salivary glands and larynx.[4] Although in its early phases PCM is usually restricted to the bone marrow, terminal phase of the disease is frequently characterized with disseminated plasma cell infiltration of various organs.

In autopsy studies 65% to 71% of myeloma patients have shown extraosseous involvement.[8] However plasma cell infiltration of testis in the course of myeloma is quite rare. Levin et al.[8] reported only seven cases of testicular plasmacytoma among 6000 cases of testicular tumors, indicating an incidence of about 0.1%. In one review only five cases were found to have testicular involvement among 182 patients with extramedullary myeloma, and in another study of EMPs, one of 161 cases involved the testis.[9] If we only consider patients with PCM, the incidence of plasmacytoma infiltrating the testis ranges between 0.6 and 2.7% of the total.[2] Most cases, reported in the literature, are observed in the setting of advanced disease.[8] Although very unusual, cases of solitary testicular plasmacytoma without evidence of systemic myeloma have been reported.[2,10] Hou et al.[10] reviewed the outcome of 15 patients with primary testicular plasmacytoma. Except one patient, progression to myeloma or dissemination was not observed. However six patients (40%) died of their disease. In another review 51 patients with testicular plasmacytoma were reported.[2] Among the whole cohort 34 patients had previous or concurrent PCM or EMP. Outcome data of three patients were not available. The majority (20 patients) of the remainder 31 patients had a fatal outcome with progressive disease. On the other hand, six patients presented with primary testicular plasmacytoma. After a median follow-up of 15 months, all patients were alive with no evidence of disease following orchiectomy. In view of these findings, it seems logical to put forward that the prognosis of primary testicular plasmacytoma is better than secondary testicular involvement in the course of PCM.

We present here a fatal case with an aggressive form of PCM with testicular plasmacytoma. As previously reported painless testicular swelling is the most common chief complaint of testicular involvement, as the patient examined.[11] Neuroophtalmologic signs like hearing loss and double vision were probable related to expansive lytic lesions of head bones. Although not biopsy proven we also strongly suspect that the right supraclavicular soft tissue mass also represented a plasmacytoma.

In PCM the degree of bone marrow fibrosis tends to correlate with the magnitude of plasma cell infiltration and is a poor prognostic sign. Myeloma patients with progressive disease were found to have significantly higher levels of serum aminoterminal propeptide of type III procollagen as a marker of marrow fibrogenesis and disease activity than responding patients.[12] So grade III reticulin fibrosis in our present case could reflect the behavior of an aggressive plasma cell clone and is the explanation of unsuccessful marrow aspirations. Our patient had almost a partial M-protein response and improvement of azotemia after near two courses of chemotherapy and therefore could be regarded as chemosensitive. However three weeks after the establishment of M-protein response, he died with progressive disease. This reflects the fact that there is not always a correlation between M-protein response and the clinical course of disease.

EMPs occurring in the course of multiple myeloma confer a poor prognosis and indicate aggressive disease compared with primary plasmacytomas without bone marrow involvement.[1,2,13] Testicular plasmacytomas could be managed with orchiectomy or radiotherapy, but in most instances this maneuver doesn't change the course of systemic disease.

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