Extramedullary progression of multiple myeloma despite a good response in the bone marrow in a patient following autologous stem cell transplantation

MUSTAFA KÖSE1, MEHMET SÖNMEZ2, ÜMİT ÇOBANOĞLU3, MUSTAFA YILMAZ2, S. SAMİ KARTI2, ERCÜMENT OVALI2, YAVUZ ÖZORAN3
Karadeniz Technical University, School of Medicine, 1Department of Internal Medicine, 2Division of Hematology and 3Department of Pathology, Trabzon-Turkey

ABSTRACT
Extramedullary plasmacytomas may be seen in the course of multiple myeloma. However, extramedullary progression despite good response in the bone marrow to therapy is extremely rare. Recently, two cases of multiple with extramedullary progression despite continued response to thalidomide in the bone marrow has been reported. In the present case, we did not use thalidomide for treatment of myeloma, moreover we observed extramedullary progression of the disease despite the continued marrow response and lack of the M-protein in serum or urine. Therefore, we think that not only thalidomide, but other chemotherapeutics also may change expression of adhesion molecules causing extramedullary progression of myeloma. [Turk J Cancer 2003;33(2):102-103]

KEY WORDS:
Extramedullary plasmacytoma, multiple myeloma

INTRODUCTION
Multiple myeloma is a plasma cell disorder, representing 1% of cancers and 10% of hematologic malignancies. Diagnosis can be achieved by demonstration of increased marrow plasmocytes, monoclonal protein in serum or urine and osteolytic bone lesions on direct X-ray graphies (1). Extramedullary plasmacytomas may be seen in the course of multiple myeloma (2). However, extramedullary progression despite good marrow response to therapy is extremely rare (3). Here, we present a patient, with multiple extramedullary plasmacytomas, who formerly showed good response to chemotherapy and autologous stem cell transplantation.

CASE REPORT
A 50 year old woman was referred to hematology clinic with plasmacytoma of mandibula for evaluation of multiple myeloma. She was evaluated by a dentist with pain of the lower chin of two month duration and had been diagnosed as plasmacytoma of the mandibula with an incisional biopsy. On admission, she had fatigue and pain on the right lower chin. On physical examination she had a 2x2 cm tender mass lesion on the right first molar teeth. Examination of chest, cardiac and neurologic systems were normal. Laboratory investigation on admission showed a hemoglobin of 11.3 g/dL, white blood cell count of 9.7x10³/µL, platelet count of 389x10³/µL. Erythrocyte sedimentation rate was increased (75 mm/h). Serum protein profile showed increased gamma globulin with IgA and lambda monoclonal gammopathy. Bone marrow aspiration smear showed 73% plasmacytic infiltration. Cranial X-rays revealed multiple lytic lesions. She was diagnosed as IgA, λ multiple myeloma with these clinical and laboratory findings and VAD (vin-
cristine, 0.4 mg/day on days 1-4; adriamycin 9 mg/m²/day on days 1-4; dexamethasone 40 mg/day on days 1-4, 9-12 and 17-21) was instituted. She was accepted to be unresponsive to following 3 courses of VAD regimen. Cyclophosphamide (C) 750 mg/m² on day 1 and dexamethasone (D) 40 mg on days 1-4 were administered. After administration of 3 courses of CD regimen, reevaluation of the patient revealed 1% plasmacytes in the bone marrow. No M-protein was detected in serum or urine. On X-ray survey of the bones there was no progression of the lytic lesions. Intensive chemotherapy with high dose intravenous melphalan (100 mg/m²) was administered followed by autologous peripheral stem cell support. The patient was quite well with normal physical and laboratory findings until the 3rd month following the autologous transplantation, until she was admitted to hematology clinic with a subcutaneous nodule on her right forearm. Histopathological examination revealed severe plasma cell infiltration (Figure 1). Postero-anterior chest X-ray revealed pleural effusion on the right side. Cytological examination of the pleural fluid showed plasma cell infiltration (Figure 2) and on abdominal CT multiple intraabdominal masses obstructing ureters were observed. The patient died due to septic shock and uremic encephalopathy on the end of the 4th month of autologous transplantation.

**Fig 1. Plasma cell infiltration seen in the subcutaneous nodule (H&E, x40)**

**Fig 2. Plasma cells seen in the pleural fluid (H&E, x40)**

**DISCUSSION**

Extramedullary plasmacytomas have been observed in lymph nodes, skin, liver, and occasionally kidney and meninges in the course of multiple myeloma (4). These patients usually have a poor prognosis even with aggressive treatment approaches (5,6). However, extramedullary progression despite good marrow response to therapy is extremely rare (3). Recently, Avigdor et al (3) reported 2 cases of multiple myeloma with extramedullary progression despite continued response to thalidomide in the bone marrow and they assume that a change in the expression of some adhesion molecules on myeloma and/or stromal cells due to thalidomide may be responsible for this phenomenon. In our case, we did not use thalidomide, moreover we observed extramedullary progression of the disease despite the continued response in the bone marrow and lack of the M-protein in the serum or urine. Therefore, we think not only thalidomide, but other chemotherapeutics also may change the adhesion molecules causing extramedullary progression of the myeloma cells.

In conclusion, multiple myeloma patients with good response to chemotherapy and/or autologous stem cell transplantation may progress as multiple extramedullary plasmacytomas and treatment of such patients may be difficult due to resistance to chemotherapeutic agents.

**References**