

MULTIPLE PRIMARY EXTRAMEDULLARY PLASMACYTOMAS: AN UNUSUAL PRESENTATION

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ABSTRACT

Extramedullary plasmacytoma (EMP) is a rare neoplasm of soft tissue which usually arises in the respiratory tract, nasal cavity, sinuses and nasopharynx. Multiple extramedullary plasmacytomas are extremely rare, especially those that are not associated with multiple myeloma. We describe multiple primary EMP in a 37 year old man, without involvement of bone or bone marrow. EMP usually has a good prognosis but our patient survived only 15 months after diagnosis.

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INTRODUCTION

Plasma cell neoplasms represent a spectrum of diseases characterised by clonal proliferation of immunoglobulin producing cells that are terminally differentiated B cells. The clinical spectrum includes clinically benign conditions, such as MGUS to more malignant entity plasma cell myeloma.⁸ Extramedullary plasmacytoma (EMP) may precede, be followed by, or be concurrent with multiple myeloma. EMP more frequently occurs in association with active disease (bone marrow involvement by multiple myeloma). Since some have presented as solitary lesions without systemic disease, they are considered as primary EMP.⁵

Primary plasmacytoma was mentioned by Unna in 1891 and first described by Schiddle in 1905. Since then EMP affecting almost any organ of the body has been reported, although the upper respiratory tract and oral cavity are most commonly the site of involvement.⁹ We report a case of multiple EMP that had a long history of progressive soft tissue disease without a detectable systemic myelomatous process.

CASE REPORT

A 37 year old male shepherd presented with a lump on the right side of the trunk of 24 month's duration. He had felt rapid growth of the mass recently. Chest wall

lesion excisional biopsy revealed a 16×11×8 cm fragile mass composed of extensive infiltration of skin and subcutaneous tissue by plasma cells. Focal anaplastic changes consisting of sheets of immature plasmacytoid cells with frequent mitosis were seen. Epidermis was intact. He denied any other therapy.

Two months later he was admitted to our institute with a huge mass on the right side of the anterior chest and abdominal wall (Fig. 1), a large mass in the lateral aspect of the thorax extending to the axilla and a fungating ulcerated mass in the oral cavity without constitutional symptoms or bone pain. There was a strong family history of cancer; his father and grandfather had died of advanced cancer before their fifties. The patient's karyotype is presented in Fig. 2.

CT scan of the thorax revealed two large soft tissue masses without bone destruction. Axial brain CT scan showed a soft tissue mass in the nasopharynx and around the hard palate and in the sinuses. Biopsy of the lateral chest wall mass confirmed the diagnosis of plasmacytoma with anaplastic changes. Immunohistochemically the cells were diffusely and strongly positive for kappa light chains, plasma cell Ag, CD138, IgG, but negative for IgM, lambda light chain, LCA, CD20, CD30, CD3, S100, Vimentin, Epithelial membrane Ag and actin. The work up for multiple myeloma including CBC, ESR, Ca, uric acid, creatinine, serum and urine protein electrophoresis, skeletal survey, MRI of the axial skeleton and

Multiple Primary Extramedullary Plasmacytomas



Fig. 1. Extramedullary plasmacytoma of abdominal wall.

bone marrow aspirate and biopsy was negative (Figs. 3,4,5 and 6).

Overall this was a very aggressive presentation of extramedullary plasmacytoma, and we reasoned that it should be treated as multiple myeloma. After 4 cycles of chemotherapy (C-VAD) the oral cavity mass disappeared, but the chest wall mass remained. Radiation to the chest wall removed that; but some weeks later hundreds of cutaneous nodules occurred in his right arm, all parts of the back and thoracoabdominal area. Although radiotherapy and salvage chemotherapy was continued, he did not have any response and 15 months after his first presentation he died. An autopsy was not permitted.

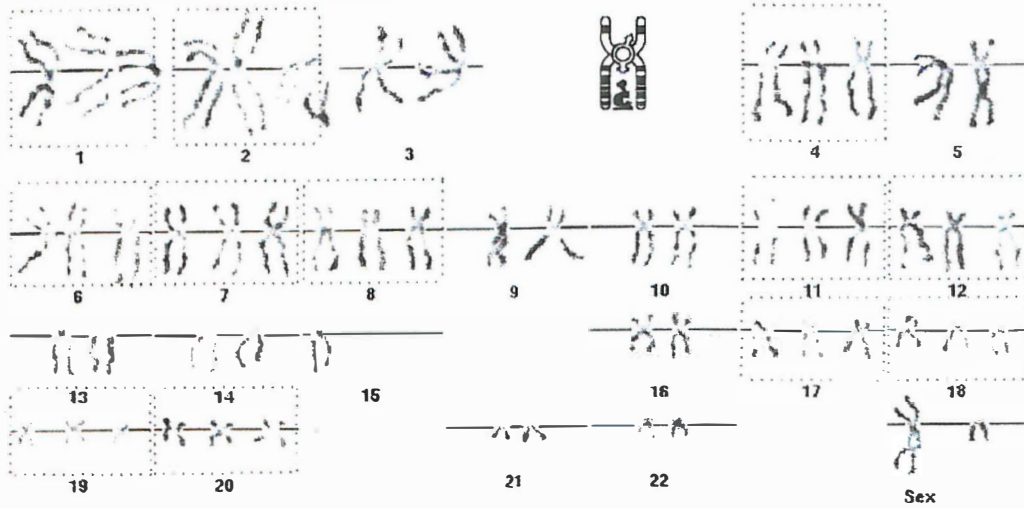


Fig. 2. Cytogenesis study of bone marrow.

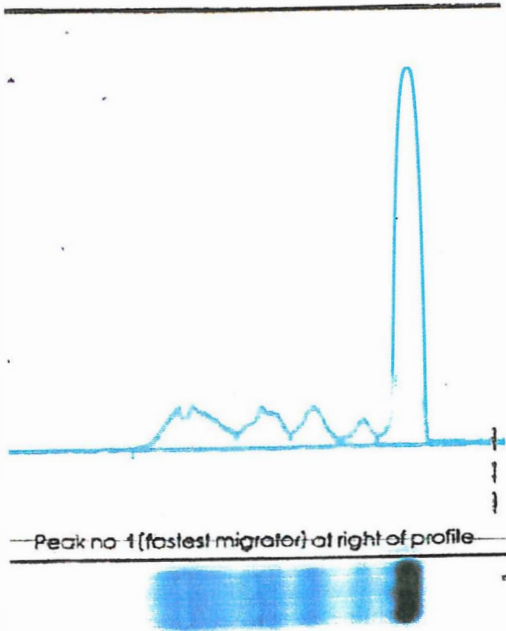


Fig. 3. Serum protein electrophoresis.

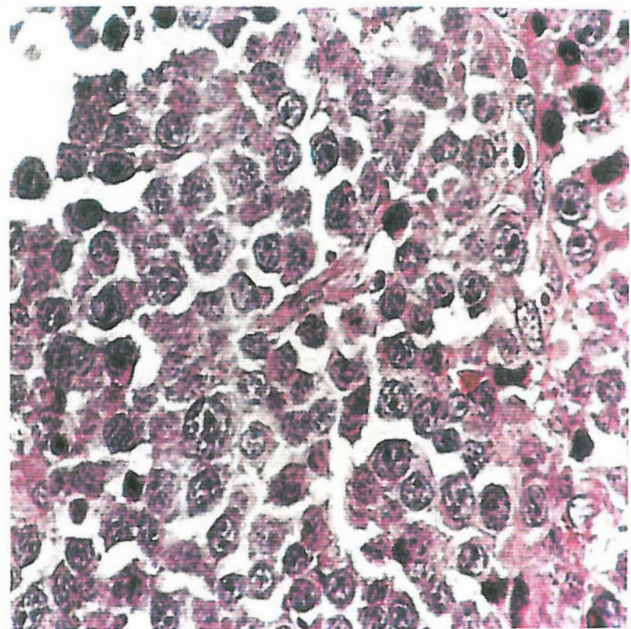


Fig. 4. Extramedullary plasmacytoma (H&E stain).

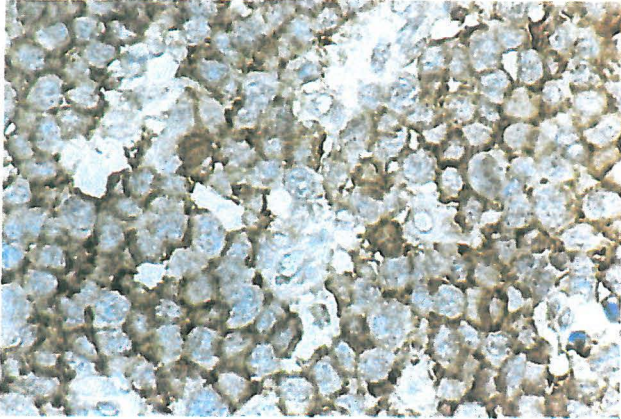


Fig. 5. Immunostaining for kappa light chain.

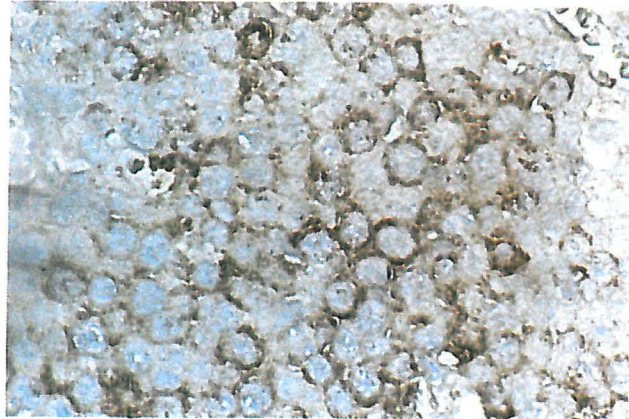


Fig. 6. Immunostaining for plasma cell antigen.

DISCUSSION

Primary EMPs, account for 1-2% of the total number of plasma cell growths. EMP occurs predominantly in males at a ratio of 3:1. The majority of patients are between 50 and 70 years. Disease in almost all patients is solitary and 85% originate in the head and neck area. In contrast to multiple myeloma, long term Disease Free Survival (DFS) and cure is possible.⁴

The youth of our case, multiple sites of disease, and presentation with cutaneous nodules long before involvement of mucosal layers of the upper airway is unusual. Is the diagnosis correct?

Histologic differential diagnoses of plasmacytoma include reactive processes, marginal zone B cell lymphoma with plasmacytoid differentiation,¹ malignant epithelioid melanoma because of the eccentric location of the nucleolus and abundant cytoplasm, and soft tissue sarcoma, especially fibrosarcoma that may mimic plasmacytoma.²

Anaplastic changes, frequent mitosis, light chain restriction in addition to an aggressive course, rules out reactive processes. Immunohistochemically we found no marker for lymphoma, melanoma, or sarcoma but all features of a plasma disorder could be seen.

It is interesting to speculate why the marrow and skeleton were not involved despite widespread involvement of soft tissue. Possibly this is related to the presence of adhesive molecules on malignant plasma cells and their respective ligands on the endothelium and permissive growth factors.³

Progression Free Survival (PFS) of patients with EMP after treatment is significantly better than solitary osseous plasmacytoma and/or multiple myeloma.⁷ Treatment of choice is local radiotherapy. In one study on 46 cases of EMP treated by radia-

tion, 85% had complete response, 7.5% relapse and 78% had 15 years survival. In other references the median survival was 8.3 years.⁴ Our patient had 15 months survival from diagnosis and 39 months from his first symptom. What is the reason of this downhill course? He did not receive local therapy at the best time and at the time of therapy had huge masses. Size of the EMP has been mentioned as an independent predictor of survival at least in one study.

Is there any way to predict the behavior of clinically benign entities such as solitary plasmacytoma?

The evaluation of peripheral blood clonal B cells and serum neural adhesion molecules level and biologic and radiologic studies of the bones have proven useful in differentiating a solitary plasmacytoma from an occult systemic disease with aggressive behaviour.^{3,12}

Jackson suggested that osteopenia and low levels of uninvolved immunoglobulins were adverse prognostic factors for EMP. Low levels of uninvolved immunoglobulins usually indicate occult multiple myeloma, but our patient had a normal bone survey and normal immunoglobulins, even on the last days of his life.¹⁰

There are numerous characteristics that set EMP apart from multiple myeloma, such as its behaviour, predisposition and presentation. Our case with sequential presentation of EMP in different tissues without multiple myeloma is distinctly unusual.

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Fetal Death and Mental Retardation in Progenies of Chemical Warfare Victim

The son (a three-year old boy), was born after a difficult vaginal delivery. He has had multiple seizures since the day of birth; he was hospitalized several times because of his respiratory problems and uncontrolled seizures. His swallowing had been impaired and aspiration pneumonia had also set in.

At present, from the point of development, he is severely retarded; no head control, unable to speak and sit. His height is 85 cm, weight 9.5 Kg, head circumference 44 cm, which are all lower than the 5th percentile of normal range. It means that he has severe growth and mental retardation. He has severe spasm in his upper and lower extremities and has spastic cerebral palsy. The father, aged 34, has chronic respiratory problems and has dyspnea in polluted air. His chest X-ray reveals a reticular pattern. The spirometry test reveals restrictive pattern and interstitial fibrosis. His scrotum itches in cold weather and becomes xerotic and lichenoid.

Pour-Jafari and his colleague in a serial investigation on a population of more than one thousand Iranian chemical warfare victims, showed that chemical injury with mustard gas can lead to increased fetal deaths,⁴ increase in risk of congenital deformity⁵ and changing the birth order.⁷ The results of the present case, once again, clearly show that sulfur mustard has genetic consequences and it is truly a crime against humanity.

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