Case Report

Multiple Myeloma Presenting at Unusual Sites

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Abstract

Objective: To report unusual presentations of multiple myeloma and to highlight that early detection of these unusual features will encourage early investigation, diagnosis and appropriate management and consequently better prognosis of this difficult disease.

Patients and Methods: Three consecutive cases of plasmacytoma reported at histopathology department of Foundation University Medical College which were later on diagnosed as multiple myeloma are presented. The clinical features and lab investigations were extracted from the patients' files. The hematoxylin and eosin stained slides were retrieved and reviewed.

Results: Three cases comprising a surgically excised chest wall mass (presternal), trucut biopsy of a mediastinal mass and a surgically excised extra dural mass along D7-D8 vertebrae were received in histopathology lab. All the patients were females. The ages of the patients were 63, 55 and 47 years respectively. On initial view of slides the diagnosis of plasma cell tumor, plasmacytoma and non-Hodgkin's lymphoma (lymphoplasmacytic type) was made respectively although the differential of large cell lymphoma with plasmacytic differentiation was also kept in mind. Surprisingly all three cases turned out to be multiple myeloma after bone marrow aspiration, serum protein electrophoresis and skeletal x-rays.

Conclusion: Plasmacytoma with coexistent multiple myeloma must be kept in the differential of mediastinal and vertebral masses and further lab and radiologic assessment must be done before starting the treatment.

Keywords: Multiple myeloma, plasmacytoma.

Introduction

Multiple myeloma also known as myelomatosis or plasma cell myeloma is a bone marrow based, multifocal plasma cell neoplasm associated with M-protein in serum or urine. It is the most common plasma cell neoplasm. Other plasma cell neoplasms include monoclonal gammopathy of undetermined significance (MGUS), plasmacytomas and monoclonal immunoglobulin deposition diseases. Multiple myeloma constitutes 1% of malignant tumors and 10-15% of hematopoietic neoplasms. About 20% of deaths from hematologic malignancies are due to it and the median age at diagnosis is 70 years. Only 2-3 percent of cases are younger than 30 years. Employment in the nuclear industry, sheet metal and agricultural occupations and jobs in which workers are exposed to wood dust are the risk factors of multiple myeloma.

Plasmacytoma represents a localized form of plasma cell neoplasm. This may be osseous (medullary) or extraosseous (extramedullary) and primary or secondary to disseminated multiple myeloma. It is also included in the diagnostic criteria of symptomatic plasma cell myeloma. Other criteria are bone marrow clonal plasma cells, M-protein in the serum or urine and related organ or tissue impairment (CRAB: hypercalcemia, renal insufficiency, anemia, bone lesions).

Multiple myeloma is difficult to diagnose clinically because of the range of initial presentations that vary from asymptomatic type to swellings at unusual sites including, skull, cutaneous swellings and spinal cord swellings. From the histopathologist’s perspective, it is difficult to diagnose because of the lack of evidence of systemic disease. Many lymphomas that exhibit plasmacytic differentiation and clonal reactive plasma cell proliferations make this task even more challenging. It is important to report any case of multiple myeloma with unusual site of initial presentation so that both clinicians and the pathologists investigate the suspicious patient and start early therapy because this improves the survival.

Patient 1

A 63 years old female patient (housewife) presented with soft tissue swelling in chest of three months duration involving the ends of both clavicles, upper end
of sternum and cartilaginous ends of both first and second ribs. The swelling gradually increased in size caused pain. There was no history of anorexia, weight loss or trauma. The mass was excised along with a part of medial end of clavicle which bled profusely during surgery and sent for histopathological examination. On microscopy, the sections showed a malignant tumor composed of sheets of monotonous cells with eosinophilic cytoplasm and eccentric round nuclei and inconspicuous nucleoli. The overlying skin, left lateral margin and deep margin were involved by the tumor. The incorporated bony tissue was free of tumor (Figure 1). The diagnosis of plasmacytoma – chest was made with a note to investigate the patient for multiple myeloma. The patient was referred to hematology department where the diagnosis of multiple myeloma was established based on bone marrow findings. Further investigations showed a monoclonal spike on serum protein electrophoresis and multiple osteolytic lesions on radiograph of spinal cord. The patient however lost the follow-up.

**Patient 2**

A 55 years old female patient (housewife) presented with progression to complete paraplegia in neurosurgery outpatient department over past seven months. She also had pain and numbness of legs and loss of bladder function of 2 days duration. Physical examination revealed absence of bilateral lower extremities reflexes, lower extremity weakness (1/5), upper extremity weakness (3/5). Sensation to pain and temperature as well as proprioception was absent in her lower extremity while upper extremity sensation were intact. MRI scan of lumbar spine revealed extrudal mass at D8-D10 showing homogeneous enhancement on post-contrast, compressing the cord along with multiple foci of abnormal bone marrow signal enhancement. Patient underwent laminectomy and excision of the mass which was sent for histopathological examination. The slides examined revealed fragments of tumor comprising sheets of cells having round hyperchromatic nuclei (Figure 2). At one focus these cells exhibited abundant cytoplasm and eccentric nuclei (plasmacytoid features). The diagnosis of nonhodgkin’s lymphoma (lymphoplasmacytic type) was made. The patient was referred to hematology department for further workup. Her bone marrow aspiration revealed 18% plasma cells with binucleated and trinucleate forms and flame cells (Figure 3). The diagnosis of multiple myeloma/plasma cell leukemia was confirmed after bone marrow trephine biopsy which showed infiltration by plasma cells. Skeletal survey revealed multiple lytic lesions in skull and pelvis. Bence Jones protein in urine was negative. The patient was treated with chemotherapy and is well now.

**Patient 3**

A, 47 years old female patient presented with severe pain in her right leg after fall. Her X-ray of right femur and pelvis revealed fracture of neck of femur along with multiple osteolytic lesions in ileum and pubis. Her chest X-ray revealed a lobulated soft tissue mass in upper mediastinum. Trucut biopsy of this mass was performed which revealed a tumor composed of plasma cells with dysplastic features focally. The treating surgeon was advised to investigate for multiple myeloma so further laboratory investigations were done. Peripheral film examination revealed myelocytes and metamyelocytes with 3% reticulocytes. ESR was raised (35mm at the end of first hr) as well as urea and creatinine. The bone marrow aspiration revealed 4% plasma cells. Later it was found on detailed history that she was diagnosed as multiple myeloma three years back. She was put on chemotherapy and dialysis and responded well to treatment.

**Discussion**

About 90% of cases of multiple myeloma occur over the age of 50. 1 In our first and second case report the ages of the patients were above 50 years however in our third case, patient was only 47 years old. Multiple myeloma cases in younger ages have been reported in Pakistan.8,10 It is more common in men than in women (1.4:1); however all of our three cases were females. Multiple myeloma usually presents with recurrent infections resulting from immune deficiencies or with bone pains caused by osteolytic lesions. Other common presentations are due to systemic sequelae such as renal insufficiency due to light chain deposition, anemia, fatigue and hypercalcaemia.8 About 30% of patients are diagnosed incidentally during routine investigations.11 Our first two cases were a diagnostic dilemma since they presented as chest swelling and spinal cord compression. It was the histological report which first gave clue to the diagnosis in the first case while in the second case bone marrow aspiration pointed towards the surprising diagnosis. In the third case report, routine chest x-ray revealed mediastinal swelling which was diagnosed as plasmacytoma on histopathology. On review of recent articles case reports of plasmacytoma as initial presentation of multiple myeloma at unusual sites were retrieved. These reported masses were found at the clivus with extension towards the petrous apices and the sigmoid sinus,5 the mandible,12 the orbit,13 intracerebrally,14 the skull base,15 cystic swellings at chest16 and the mediastinal swelling.17,18 Vertebral plasmacytomas comprise 5% of the presentations of multiple myeloma.8 Mediastinal plasmacytoma are also rare comprising only 5% of cases. Only 5% of patients with extramedullary plasmacytomas have coexistent multiple myeloma.15 There is only one recent case report in the literature in which the vertebral plasmacytoma provided clue to the diagnosis of multiple myeloma 8 and two
case reports in which mediastinal plasmacytoma provided early hint to the diagnosis of multiple myeloma. Only one case report of multiple myeloma presenting as cutaneous chest swellings was found. Despite identifying such masses as plasmacytoma, additional tests are mandatory to distinguish between extramedullary plasmacytoma and the systemic disease since extramedullary plasmacytomas have better overall prognosis than multiple myeloma. Cutaneous involvement associated with multiple myeloma varies from 5 - 10%. It can be due to direct spread from underlying osteolytic lesion or can also be seen distinct from the bony focus as was in our case. It can even be an initial manifestation of the disease. Some patients have presented with solitary lesions but multiple nodules may be present. In our case it was a single swelling. Histologically cutaneous plasmacytomas can have two patterns: nodular or interstitial. Our case had interstitial pattern characterized by cords of neoplastic plasma cells arranged between collagen bundles and infiltrating the muscle fibers too. The epidermis was spared while the subcutaneous tissue was involved. Few Russell bodies were also seen. In the cases with cutaneous and mediastinal masses, the neoplastic cells were readily identified as plasma cells with variable maturation, and some of them were binucleated or multinucleated. Some of the cells were large with pleomorphic vesicular nuclei and prominent nucleoli but it was difficult to label them as plasmablasts. The neoplastic plasma cells can also be seen as sheets of spindle shaped cells in the cutaneous mass and it usually represents advanced form of a disease. Mitotic figures were not seen in the cutaneous mass but seen in the mediastinal mass. In the slides of extradural mass most cells looked like lymphoblasts with dense chromatin, and scanty cytoplasm and slight pleomorphism. Some of the cells were comparatively of large size. There was only one area of plasmacytic differentiation (eccentric nuclei and perinuclear halo). Many lymphomas exhibit plasma cell differentiation including marginal zone lymphoma of MALT type, lymphoplasmacytic lymphoma and immunoblastic or plasmablastic large cell lymphoma. The diagnosis of non-Hodgkin’s lymphoma (lymphoplasmacytic type) was made on predominant morphology but the differential of large cell lymphoma with plasmacytic differentiation was also kept in mind before applying the immune-histochemical markers which showed positive staining for CD38 and CD138. The peripheral film examination of same patient showed 18% plasma cells with binucleated and trinucleated forms and mott cells. Even if immunohistochemistry was not performed, the bone marrow aspiration and radiological findings were enough to fulfill the diagnostic criteria of plasma cell leukemia which is a rare clinical variant of multiple myeloma.
immunohistochemistry is sometimes necessary to establish monoclonality of plasma cells since reactive plasmacytic proliferations can also be misdiagnosed as plasmacytoma especially when the plasma cells are mature looking.20

Conclusion

Failure to recognize the presentations of multiple myeloma leads to delay and even errors in diagnosis. Although multiple myeloma may not be kept at the forefront in the differential diagnosis of spinal, mediastinal and cutaneous masses especially when tuberculosis and lymphomas are more common, but extensive investigations are needed to rule out the possibility. The histopathologist has more responsibility in this regard to correlate the findings with clinical data and stress on further investigations.

References