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Lymphnode Involvement in Plasmacytoma

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A case of plasmacytoma of the spine with multiple sites of involvement at presentation is reported. The sites involved were T_4, T_5, T_9 levels and the jugular foramen. The patient had no evidence of bone marrow involvement or paraprotein either in the serum or urine. Resections of the tumour from T_4 and T_5 levels was performed, followed by radiation therapy.

The patient developed a recurrence seven and half years after the initial presentation. The recurrence occurred at the right clavicle and in the soft tissue around it. This was followed by multiple recurrences at the same site with involvement of the supraclavicular lymphnodes inspite of aggressive chemotherapy, radiation therapy and autologous stem cell transplant.

Fine Needle Aspiration cytology and histology showed a typical plasma cell neoplasm with characterstic nuclear features, immunohistochemistry was compatible with a plasmacytoma.

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A plasmacytoma is a discrete, solitary mass of neoplastic monoclonal plasma cells found in either bone marrow or a soft tissue site. These neoplasms can occur as extramedullary solitary plasmacytomas (primary true plasmacytoma of the mucosa with or without affected lymph nodes) and it can be an extramedullary manifestation of multiple myeloma, multiple myeloma, and plasmablastic sarcoma[1].

Plasmacytoma involving lymphnodes is rare. This can occur as a manifestation of regional lymph node involvement in extramedullary plasmacytoma or even more rarely as a primary extramedullary plasmacytoma occurring in lymph node[1].

An unusual case of plasmacytoma of the spine is reported with involvement of the right supraclavicular lymph nodes. The fine needle aspiration cytology and histology are presented and discussed.

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THE CASE

A thirty-six year old male Bahraini patient presented in July 1993 with interscapular pain of three months duration at London Neurology Center. On examination he showed early signs of cord compression with slight weakness of both legs (grade II/1V) and increased deep tendon reflexes and upgoing plantar as well as sensory alteration. He had left hypoglossal nerve palsy leading to deviation of his tongue to the right side. Subsequent investigation by MR and CT showed collapse of his thoracic vertebrae at the T_4 and T_5 levels and erosion around the jugular foramen. He also had changes in the lower thoracic spine (T_9 level).

A CT guided biopsy was done at T_4, T_5 and T_9 levels. A needle biopsy was performed from behind the mastoid on the jugular foramen. The specimen showed presence of plasmacytoma. There was no evidence of blood or bone marrow involvement detected and no evidence of paraprotein seen on immunopheresis. His ESR at that time was 54 mm. The patient thus was diagnosed as having plasmacytoma at three isolated sites.

He underwent thoracotomy and vertebrectomy with reconstruction for his lesion at the T4-T5 level. The tumour mass was resected and the vertebral body removed in total. The khyphotic deformity was corrected and maintained with the use of a moss cage filled with bone graft.

He received postoperative radiotherapy in a total of 5 doses (20 Gy fractions) to the site of surgery followed by three courses of ABCM chemotherapy (Doxorubicin 30 mg/m^2 IV, and BCNU 30 mg/m^2 IV on day one, Melphlan 6 mg/m^2 per day orally cyclophosphamide 100 mg/m^2 per day orally on day 22, 23, 24,and 25 with cycles repeating every 6 weeks). On conclusion of his therapy the patient's peripheral stem cell mass was collected and frozen.

In May 2001, he attended Salmaniya Medical Complex (SMC): He had a recurrence localized to the lateral side of the right clavicle 8x5 cm, where imaging showed a lytic lesion. Fine needle aspiration cytology (FNAC) (Fig 1) showed a plasmacytoma. The peripheral blood smear and bone marrow examination showed no evidence of any plasma cell dyscrasia. No serum or urine paraprotein was detected. The serum calcium and serum creatinine were normal.

Figure 1

B_2 microglobulin was 1.5 µgm/L. Cytogenetic studies on bone marrow showed no abnormality with 46XY karyotype. Localised radiotherapy (20 Gy in 5 fractions over two weeks with 6 mv photons) was given with complete response.

In October 2002, a second recurrence at the right supraclavicular fossa was seen. The lesion was expansile and lytic on imaging and measured 4x3x2cm at the lateral end of the right clavicle with a soft tissue density within. Anteriorly, the bony cortex was broken at

places while posteriorly the cortical shell was completely absent. No calcification was noted. In addition, four lymphnodes were observed in the right supraclavicular region ranging in size from 1-3 cm. Again no plasma cell dyscrasia in bone marrow and no paraprotein in the blood and urine was observed.

FNAC of the lymph nodes was done followed by surgical debulking with removal of the lymph nodes. The lymph node specimen was submitted for histopathology (fig 2 & 3). This showed a plasmacytoma involving lymph nodes and spilling into surrounding fat. Following this localised radiation was given - 30 Gy in 15 fractions over three weeks with six mv photons. The clavicular lesion regressed considerably.

Figure 2 & 3

Fine needle aspiration cytology in May 2001 and October 2002 showed similar appearances - cell rich aspirate with sheets of pleomorphic cells with an eccentric nucleus and moderate amount of opaque cytoplasm. Nuclear chromatin was seen arranged in a clock-wise pattern. An occasional cell showed prominent nucleolus. Bi-nucleate, tri and tetra- nucleated giant cells were seen with nucleomegaly. Cellular fragments were also observed in the spread with a peritheliomatous arrangement of cells around blood vessels contained in minimal stroma. Mitotic figures were noted. (Fig 1)

The aspirated material was also subjected to flow cytometry, which showed a population of abnormal large cells accounting for > than 50% of the total and expressing strong CD38, CD13, CD10 positivity with a weak expression of CD56. The cells lacked expression of CD19 or surface immunoglobulins.

A diagnosis of plasmacytoma was made at cytology.

Histopathology, three lymph nodes removed were matted the largest measured 2 cm. At microscopy, two of these were replaced totally by a neoplasm composed of diffuse infiltrate of plasma and plasmacytoid cells. The infiltrate was seen extending into perinodal fat. Nuclear pleomorphism was seen with most of the nuclei showing the classic clock-wise distribution of chromatin. Multinucleate forms were observed. Some of the neoplastic cells were seen to be distended by eosinophilic material, which pushed the nucleus to an eccentric position. This material probably represented intracellular immunoglobulin but was negative by the periodic acid Schiff stain. Thin fibrous septa rich in blood vessels traversed the entire neoplastic parenchyma. (Fig 2 and 3)

Immunohistochemistry showed common leukocyte antigen negative; CD20 negative; IgG positive; Kappa positive; Lambda negative; CD30 negative; CD5 negative.

In December 2002, the patient however had a recurrence at the same site. He was given four courses of VAD chemotherapy, the response was incomplete and the patient underwent high dose chemotherapy with Melphalan followed by an autologous stem cell transplant in July 2003 with complete response.

In August 2003, the patient had another recurrence within one month of stem cell transplant in the right supraclavicular region, which measured 4x3 cm. He was advised either to repeat the stem cell transplant or to have Thalidomide or Bortezomib therapy. He chose Thalidomide therapy with good response.

Based on the morphology, monoclonal kappa light chain production and a negative surface B-cell antigen (CD20), a histological diagnosis of plasmacytoma was confirmed.

DISCUSSION

Plasmacytoma is a local tumorous collection of monoclonal plasma cells. It can occur as a solitary lesion or as multiple myeloma. A diagnosis of plasmacytoma should prompt further clinical, biochemical and radiologic investigations to determine whether the lesion is truly solitary or in fact a localized presentation of multiple myeloma[2].

In two reported series, solitary osseous and extramedullary plasmacytomas constituted only 6.1% and 8.3% of 822 and 288 patients respectively[2,3]. Solitary plasmacytomas can be classified into two types, they differ in clinical features and behavior. Solitary osseous plasmacytoma is a single bone lesion on radiographs with the histology of plasma cell tumour but without an increase in the plasma cells in a random bone marrow sample. Extramedullary plasmacytoma is a single plasmacytoma at extraskeletal site; the bone marrow and skeletal radiographs are normal, aside from possible bone erosions or damage adjacent to the primary lesion. There may be regional lymph node metastasis.

Extramedullary plasmacytomas commonly occur in the upper aero-digestive tract - the paranasal sinuses, nasopharynx, nose, tonsil, and larynx, presenting as nasal obstruction, epistaxsis, pain, dysphagia or dyspnoea.

Criteria for identifying solitary bone plasmacytoma vary among authors[4-6]. The current accepted criteria for diagnosing these however are:

1. Single area of bone destruction due to clonal plasma cells
2. Normal findings on skeletal survey and MRI of the spine, pelvis, proximal femora and humeri
3. Absence of anaemia, hypercalcaemia or renal impairment attributable to myeloma
4. Low concentrations of serum or urine monoclonal proteins and preserved levels of uninvolved immunoglobulins[7,8].

This case is a unique with three sites of involvement all close to one another but with no evidence of myelomatosis. Cytology and histology confirmed a neoplasm with plasma cell differentiation. The histology showed lymph node involvement. Lymph node involvement in plasmacytomas is rare. The available literature had not more than twenty nine documented cases involving lymph nodes both as a primary or secondary phenomenon[9-11].

In plasma cell tumour of the lymph nodes various differentials have to be considered and ruled out:

a) Castlemans disease of the plasma cell type may sometimes show light chain restriction, but morphology-wise presence of reactive follicles and hyaline vascular follicles is the rule.

b) Lymphoplasmacytic lymphoma is another neoplasm with plasmacytoid differentiation. This lymphoma however is usually disseminated at presentation with lymphadenopathy, splenomegaly and evidence of a hyperviscosity syndrome and paraprotein. Microscopically small lymphocytes mixed with lymphoplasmacytoid cells and plasma cells are seen, with Russel body formation. B cell markers are positive with monotypic Ig (IgM type).

   Plasmacytoma on the contrary and as seen in this case is composed of a monomorphous population of plasma cells instead of mixtures of lymphocytes, plasma cells, and lymphoplasmacytoid cells. The cells showed classic clock-wise nuclear chromatin distribution and some cytoplasmic distension by immunoglobulins.

c) Diffuse large B cell lymphoma with plasma cell differentiation is an aggressive neoplasm. Microscopically, cells vary considerably in size with nuclei, which are round, indented and irregularly folded. Nucleoli are common and B cell markers are invariably positive. This nuclear morphology was not seen in the present case and B cell markers were negative.

d) Plasmablastic lymphoma is a lymphoma, which occurs mostly in a setting of AIDS or sometimes with Castleman's disease. It is limited to the oral cavity and jaw and usually aggressive in nature. Microscopically, it shows large and pleomorphic cells with large nuclei and prominent nucleoli. There is no plasma cell maturation. In the present case the neoplastic cells; however, were plasma cell in nature and nucleoli were inconspicuous. Besides this B-cell markers for surface antigen were negative. Plasmacytomas can be positive for CD56 and this was observed in this case on flow cytometry.

Contrary to the general behavior of plasmacytomas, the disease in this instance involved three sites at initial presentation and behaved aggressively with multiple recurrences. The biological determinants of an aggressive behavior of plasma cell neoplasms is poorly understood and molecular genetic differences may be responsible for this. The present case illustrates this.

CONCLUSION

An unusual case of plasmacytoma with multiple sites of involvement is presented. Though multiple site involvement was seen yet it failed to fulfill all criteria for a multiple myeloma even after eleven years of the onset of the disease. Most plasmacytomas

respond well to therapy, in particular solitary ones. Inspite of adequate therapy and stem cell transplantation, multiple recurrences were seen and the disease persisted; possibly due to unfavourable features, which included spine lesions, multiple lesions, large size of the lesion (8cm). Lymph node involvement in this case occurred late in the disease and the general condition at eleven years of follow up appeared to be fairly good in spite of recurrences.

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