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Original Research Article

Extramedullary Presentation of Multiple Myeloma: A Retrospective Study Series of Unsuspected Cases

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Abstract

Context: Multiple myeloma is a malignant neoplasm of plasma cells involving the bone marrow. Before entering into aggressive phase, there is a frequent occurrence of extramedullary manifestations. The sites of predilection for extramedullary plasmacytoma are nasopharynx, larynx and upper respiratory tract. *Aims:* The aim of this present study is to highlight the importance to have high index of suspicion to consider a diagnosis of plasmacytoma based on histomorphological features even in the absence of classical clinical findings. *Settings and Design:* This study was done as a retrospective study in Coimbatore Medical College Hospital, Coimbatore over a period of 6 months from November 2017 to April 2018 in cases diagnosed as plasma cell lesions. *Methods and Materials:* 14 Cases of incidentally diagnosed plasma cell myeloma in a period of 6 months were taken. Out of these, 6 cases presented as soft tissue lesions, 3 cases as viscera - organ involvement and 5 cases as lytic lesios of bone. Immunohistochemical confirmation was done with CD 138, kappa and lambda. *Results:* Fine Needle Aspiration was done for all soft tissue lesions and was reported as plasmacytoma. Subsequently biopsies also proved the same. CD 138 was positive in all cases, kappa in 3 cases and lambda in 11 cases. Two cases were non secretory myeloma with negative serum M protein and urine Bence Jones protein. *Conclusions:* Soft tissue lesions in patients over the age of 50years should always include a diagnosis of plasmcytoma when sheets of plasma cells are seen. CD 138 showed 100% sensitivity, with lambda expression in plasma cell myeloma with multiple bony and subcutaneous lesions. Kappa was positive in cases with visceral involvement.

Keywords: Plasma Cell Lesion; Incidental; Uncommon Presentation; Imunohistochemistry.

Introduction

Plasma cell neoplasms and related disorders are clonal proliferations of immunoglobulin producing plasma cells or lymphocytes that make and secrete a single class of immunoglobulin or a polypeptide subunit of a single immunoglobulin that is usually detectable as a monoclonal protein (M protein)[1].

Plasma cell myeloma is a bone marrow based, multifocal plasma cell neoplasm associated with M protein in serum or urine. Other organs may be secondarily involved. Any patients having multiple myeloma may develop extramedullary soft tissue lesions (4%), that presents as the most prominent clinical history [2].

Extramedullary spread in multiple myeloma is poorly understood. VLA - 4 and CD 44 which facilitate dissemination and ultimately the tetraspanins expressions are down regulated and increase in angiogenesis have been considered [3].

Materials and Methods

Cases diagnosed as plasma cell lesions in histopathological examination; Fine needle aspiration cytology study of soft tissue lesion; Peripheral smear, bone marrow aspiration study and bone marrow biopsy, were taken in the study.

Subsequently these were supplemented with biochemical tests and skeletal survey.

Inclusion criteria

*Biopsies from extramedullary swellings

*FNAC smears from soft tissue swellings

*Peripheral smear study in incidental cases

*Patients age >50yrs

Exclusion criteria

*Known case of Plasma cell neoplasm

*Patients age <50 yrs

FNAC was done with 26 gauge needle. Aspirates were spread evenly and stained with harris hematoxylin and eosin stain and also with Leishman's stain. Sections were cut at 4 microns thickness, stained with hematoxylin and eosin stain. Coated slides were used and the slides kept in incubation at 58 degrees, overnight for immmunohistochemistry by two step indirect technique.

Fine needle aspiration cytology smears were stained by Harris Hematoxylin and Eosin stains. Leishman's stain was also used.

Peripheral smear study, Bone marrow aspiration study were stained by leishman's stain. Bone marrow biopsy was fixed in 10% buffered formalin and processed to obtain sections at 4 microns and stained with hematoxylin and eosin stain.

Results

Total of 14 cases were diagnosed as plasma cell myeloma. Out of these, 6 cases were reported on fine needle aspiration cytology followed by histopathological examination, 3 cases were reported on biopsy from viscera and confirmed with immunohistochemistry as extramedullary myeloma. 5 cases were diagnosed by bone marrow aspiration study and bone marrow biopsy. Immunohistochemistry confirmed the diagnosis with CD 138, kappa/lambda, showing 100% sensitivity.

The cytological smears from 6 cases were cellular and showed numerous plasma cells in varying degrees of maturity (Figure 1).

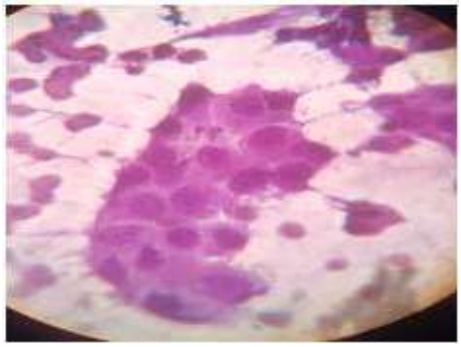

Fig. 1: Fine Needle Aspiration smear showing plasma cells with eccentrically placed nucleus. (40X Leishman stain)

Subsequently histopathological samplings showed sheets of plasma cells with similar findings (Figure 2).

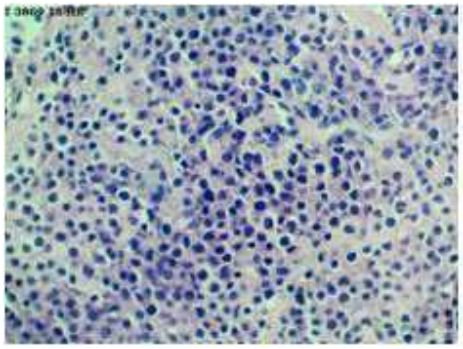

Fig. 2: Sheets of plasma cells are seen with eccentrically placed nucleus. (40X H & E stain)

The diagnosis was confirmed with Immunohistochemistry showing CD 138 positivity and Lambda chain restriction (Figure 3 and Figure 4)

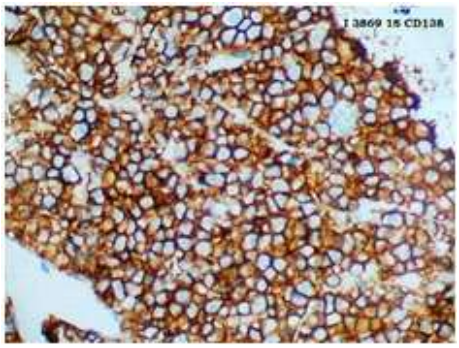

Fig. 3: Plasmacytoma showing intense cytoplasmic CD138 positivity in tumour cells

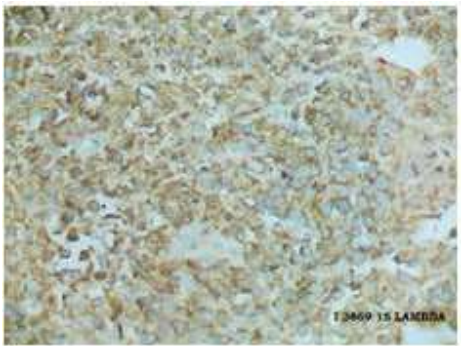

Fig. 4: Tumour cells in plasmacytoma showing monoclonal Lambda positivity

Biopsies from 3 cases , one from bladder growth, one from liver mass and the other from nasal mass showed kappa positivity. Out of these 9 cases, 2 cases were Non secrectory myeloma showing negative for Serum M protein and urine Bence Jones protein.

5 cases diagnosed by bone marrow aspiration studies and bone marrow biopsy showed plasma cells >10% in the bone marrow in all forms of maturation.

The results of immunohistochemistry are shown in table 1.

Table 1: IHC marker study of 14 cases in the present study.

Biopsies	CD138	Kappa	lambda
Soft tissue 6 cases	+		+
Viscero – organ 3 cases	+	+	
Trephine 5 cases	+		+

Discussion

Plasma cell neoplasms are categorized as multiple myeloma, solitary plasmacytoma of bone and extramedullary plasmacytoma [1]. Extramedullary plasmacytomas have an incidence of 7% to 17% in patients at the time of diagnosis and 6% to 20% during the course of the disease [14]. In the present study the incidence was >60% at the time of diagnosis, signifying the dissemination of the disease at its earliest [15].

Extramedullary plasmacytoma shows male predilection, occurring above 40 yrs. 80% of extramedullary plasmacytomas occur in head and neck, especially the nasopharynx and paranasal sinuses. The first case of extramedullary plasmacytoma was reported in 1905 by Schridde [13]. In the present study, the sites of manifestations were soft tissue mass – anterior chest wall swelling, skull, supraclavicular region, nasal mass, liver nodule, bladder mass, jaw mass and inguinal lymph node. In 6 cases Fine needle aspiration study was done the smears showed plasma cells in sheets with varying stages of maturity. Similar study was done by Bangerter M et al. who performed Fine needle aspiration study in 13 out of 18 cases [7]. Goel et al. in 2010, did Fine needle aspiration study in 3 out of 8 patients [8] and in a study by Radha R Pai, Fine needle aspiration was done in 4 out of 6 cases. In all these cases, sheets and scattered neoplastic plasma cells were seen in the smears.

Subsequently they were complemented by histopathologial examination and confirmation was done with CD 138 positive with lambda light chain restriction.

3 cases with visceral organ involvement was reported on biopsies and confirmed by CD 138 positivity and with kappa positivity [13].

5 cases were evaluated for anaemia, pancytopenia, multiple lytic lesions skull and weakness of both upper and lower limbs. Bone marrow aspiration and trephine biopsy showed >10% of plasma cells in varying stages of maturity. Confirmation with immunohistochemistry was done showing CD 138 and lambda light chain positivity [14].

The British society for Haematology issued a set of guidelines for the diagnosis and treatment of extramedullary plasmacytoma

Diagnostic criteria for solitary extramedullary plasmcytoma (Guidelines working group of the UK myeloma forum) [15]

1. Single extramedullary mass of clonal plasma cells
2. Histologically normal marrow aspirate and trephine.
3. Normal results on skeletal survey, including radiology long bones
4. No anemia, hypercalcemia or renal

impairment due to plasma cell dyscrasia.

5. Absent or low serum or urinary level of monoclonal immunoglobulin.

One case fits these criteria in the present study which presented as liver mass.

Conclusion

Through this case series studied for six months, we create an awareness of the extramedullary presentation of plasma cell myeloma and to stress upon the need of Fine needle aspiration which has proved a rapid tool in early diagnosis.

Interestingly kappa chain restriction was seen in extramedullary visceral involovement. As the literature quotes that plasmacytoma with extramedullary manifestations at the time of diagnosis has a bad prognosis than the extramedullary plasmacytoma which has prognostically better survival rate.

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