

Solitary Plasmacytoma of Mandible Transforming to Multiple Myeloma? - A Rare Case Report

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ABSTRACT

Background: Plasma cell dyscrasias is proliferation of the plasma cells that typically produces monoclonal immunoglobulin. Solitary plasmacytoma, multiple myeloma, and extramedullary plasmacytoma are their three distinct clinical entities. The most common among the plasmacytoma is the solitary bone type which accounts for less than 450 cases annually and constitutes only 2% to 5% of all plasma cell malignancies

In case of solitary plasmacytoma, it is significant to make dissimilitude of whether minimal bone marrow clonal plasmacytosis are there or not, solitary bone lesion or soft tissue, negative whole-body imaging for further lesions, anemia and renal dysfunction. Almost 50% Solitary plasmacytoma cases shows transformation into multiple myeloma.

Case Presentation: A 58 years old female patient with single, diffuse tumour mass in the left mandibular region of oral cavity was subjected for clinical, radiological, histopathological, immunohistochemical and biochemical investigation. The diagnosis of solitary plasmacytoma was done. But with correlation of all the investigation a suspect of transformation into multiple myeloma arise.

Discussion: Despite of the excellent local control rates, majority of solitary plasmacytoma will eventually progress to multiple myeloma. Previous studies on solitary plasmacytoma had shown 5-year overall survival rate as 70% and 5-year of disease-free survival rate as 46%, with median time for development of multiple myeloma as 21 months, with a 5-year probability of 51%.

Conclusion: Solitary plasmacytoma being a rare plasma cell malignancy with high potency to transform into multiple myeloma, a thorough investigation is needed before diagnosis. Early diagnosis and appropriate treatment is the key to increase disease free survival rate of the patient.

Keywords: Multiple Myeloma, Plasmacytoma, Plasma cell dyscrasias, monoclonal immunoglobulin

INTRODUCTION

Plasma cell dyscrasias are a unique group of entities which is characterized by neoplastic monoclonal proliferation of the plasma cells that typically produces monoclonal immunoglobulin.¹ Plasmacytoma exhibits three distinct clinical entities namely solitary plasmacytoma, multiple myeloma (MM), and extramedullary plasmacytoma (EMP).²

Most of these lesions are encountered centrally within single bone. They are present most frequently in femur, spine, vertebrae and pelvis.^{3,4}

Rarely, they are encountered in soft tissue, and those cases are termed as extramedullary plasmacytoma. Upper respiratory tract viz, nasal cavity, nasopharynx, oropharynx and sinuses are involved frequently, and it has quite longer survival rate.^{5,6}

However, extramedullary plasmacytoma can transform into plasmacytoma of bone and myeloma, which is associated with poor prognosis.^{7,8}

Solitary plasmacytomas accounts for less than 5% of all plasma cell disorder. They are subclassified as solitary bone

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plasmacytoma or solitary extramedullary plasmacytoma which is hinge on the site of involvement whether in bone or soft tissue.⁵

In case of solitary plasmacytoma, it is significant to make dissimilitude of whether minimal bone marrow clonal plasmacytosis are there or not, solitary bone lesion or

soft tissue, negative whole-body imaging for further lesions, anemia and renal dysfunction.⁵

Table 1: Shows additional systemic investigations and their results along with reference value.

Other investigations:

INVESTIGATIONS	RESULT/IMPRESSION	
RADIOGRAPH		
SKULL	Expansion of diploic spaces giving hair on end appearance.	
MRI OF WHOLE SPINE	Disc desiccation changes noted at all levels.	
Cervical spine		
Dorsal spine	Well defined T2 hyperintense areas noted in D6 and D12 vertebral bodies	
Lumbar spine	Disc desiccation changes noted at all lumbar levels. L4-5 Level: Diffuse disc bulge noted causing indentation on thecal sac, significant narrowing bilateral lateral recess. No nerve root compression. Note: No lytic lesion owing to plasma cell dyscrasia is evident.	
Abdomino-Pelvic Ultrasound Scan	Mild Hepatomegaly	
HEMATOLOGY	RESULT	Normal range
Prothrombin time Test	14.6 sec	9.4-12.5
INR	1.23	
Haemoglobin	6.2 gm%	12-15
RBC	3.2 million/	3.8-4.8
PCV	cu.mm	36-46
MCV	21.9%	63-101
MCH	67.6%	27-32
MCHC	19.1pg	31-34
RDW	28.3%	11.6-14
WBC	23.5%	-11
	4.86 thousand/ μ l	4
BIOCHEMISTRY		
Liver Function Test		
Total protein	9 g/dl	6.3-8.2
ALP	153 U/L	38-126
Renal Function Test		
Random blood sugar	92 mg/dl	75-140
Urea	15 mg/dl	15-36
Creatinine	0.7 mg/dl	0.5-1.04
Uric acid	7.8 mg/dl	2.5-6.2
Bence Jones Protein	PRESENT	

*NOTE: To be precise only the blood and biochemical investigation with positive results were mentioned here

Almost 50% Solitary plasmacytoma cases shows transformation into multiple myeloma.

Axial skeleton, particularly vertebrae is the primary site of involvement and long bones are secondarily involved. However, incidence in jaw is very rare. Based on the previous literature evidence, till date only 2% of solitary plasmacytoma of bone case shows incidence in mandibular region. (Table 2) Their predilection for mandible is high especially in bone marrow-rich areas of mandible like angle, body, ramus and retromolar trigone.⁶ The presented case report is one among those rare incidence, presenting in the body of mandible. The predilection for male is high with the average age of incidence 60 years. Radiation therapy, extensive radical surgery or combination of both is recommended as the primary treatment.⁹

CASE REPORT

A 58-year-old female patient complains of swelling in her lower left side of face since 5 months. There is no history of pain or discharge associated with the swelling. Patient was apparently normal before 5 months and she noted a sudden onset of a pea sized swelling which increased gradually to the present size. Also she complains of loosening of teeth in the same region since 1 month. No history of trauma, pain, fever or swelling anywhere else in the body. The medical history reveals that patient is under medication for hypothyroidism for past 1 year and proteinuria for past 6 months. Also patient gives history of body and joint pain and not under medication for the same. Patient has undergone extraction of 36 due to caries before 10 years. No relevant personal history. On extraoral examination, a gross facial asymmetry noted on lower left side of face. A single diffuse swelling of size approx. 3.5x2.5cm extending anteroposteriorly from 2 cm anterior to the tragus to 1cm posterior to the corner of mouth, superoinferiorly 1cm below the ala tragus line to the lower border of mandible. On palpation, the swelling is soft in consistency in upper one third and bony hard consistency in lower third. (Figure1A)

Lymphnodes: Non-tender, Well defined, solitary lymph nodes are palpable in submandibular region bilaterally of size approximately 0.5x0.5 cm which is soft in consistency and tender.

On intraoral examination, a well defined solitary swelling noted buccally of size 4x3x0.5cm extending from mesial aspect of 35 to distal aspect of 38. Mucosa over the swelling appears normal. Swelling is non tender and non fluctuant. Grade III mobility was noted in 37,38.

Radiograph reveals well defined radiolucency of size

Table 2: Sites of localization of solitary plasmacytoma of bone.²⁰

Anatomic site	Percentage
Vertebral column	28.9%
long tubal bone	28.9%
sternum and ribs	24.4%
craniofacial bone	8.9%
Clavicle	6.7%
Mandible	2.2%



approx. 6cm x5cm extending from apical region of 35 to distal surface of 38 & superiorly from 0.5cm above alveolar ridge to lower border of mandible.(Figure 1B)

The associated tooth 37 shows knife edge root resorption upto cervical 1/3rd of root. 38 shows knife edge root resorption upto level of apical third of root. Margins are well defined with ridging at lower border of mandible & there is blurring of trabeculae at center.(Figure 1C)

Along with biopsy, other investigations mentioned in table 1 were also performed.

Incisional biopsy was done and the soft tissue bits of size approximately 1.7 x 1.2 x 0.4 cm which is irregular in shape with rough surface, greyish white in color and soft in consistency. (Figure 1D)

Histopathological examination

The hematoxylin eosin stained sections showed parakeratinised stratified squamous epithelium and underlying connective tissue. The subepithelial connective showed moderate amount of inflammatory cells along with few proliferating blood vessels. The deeper connective tissue showed sheets of plasma cells proliferating in varying degrees of differentiation. (Figure 2A) In few cells perinuclear hof adjacent to nuclei was noted. Numerous pleomorphic, bizarre, binucleated and trinucleated plasma cells are noted with hyperchromatic nuclei. (Figure 2B and C) Few mitotic figures were evident. In few areas Russell bodies (Figure 2D) and Mott cells were also seen. The surrounding stroma was eosinophilic, granular owing to the extruded immunoglobulin from the neoplastic plasma cells.

Immunohistochemistry investigations:

CD 45 and 138 showed diffuse and strong positivity. Lambda chain showed diffuse and strong positivity. Kappa

chain showed weak and focal positivity. With kappa and lambda chain ratio monoclonality of plasma cell was confirmed.

NOTE: Exclusive expression of anti-Lambda light chain antibody (polyclonal antibody) proving monotype. Absence of expression of anti-Kappa light chain antibody (polyclonal antibody).

Correlating clinically, radiographically, histopathologically and with other investigations(table 1), final diagnosis of solitary Plasmacytoma was given. But hematological and biochemical investigation had given the suspicion of transformation towards multiple myeloma.

DISCUSSION

Plasmacytoma is referred as a lymphoid neoplastic proliferation of B cells. Their incidence can occur alone inside the bone as a solitary bone plasmacytoma or within the soft tissue as an extramedullary plasmacytoma. The multifocal disseminated form of plasmacytoma is referred as multiple myeloma (MM).¹⁰

The most common among the plasmacytoma is the solitary bone type.

Solitary bone plasmacytoma: They accounts for less than 450 cases annually and constitutes only 2% to 5% of all plasma cell malignancies.¹¹ The etiology of solitary bone plasmacytoma remains uncertain and several hypotheses were proposed which involves the role of radiation, viruses, chemical exposure and genetic factors. The Cytogenetic studies had revealed that the principal growth factor in pathogenesis is mainly attributed to a gain in chromosome 19p, 9q, 1q and loss in 13, 1p, 14q and interleukin-6.¹²

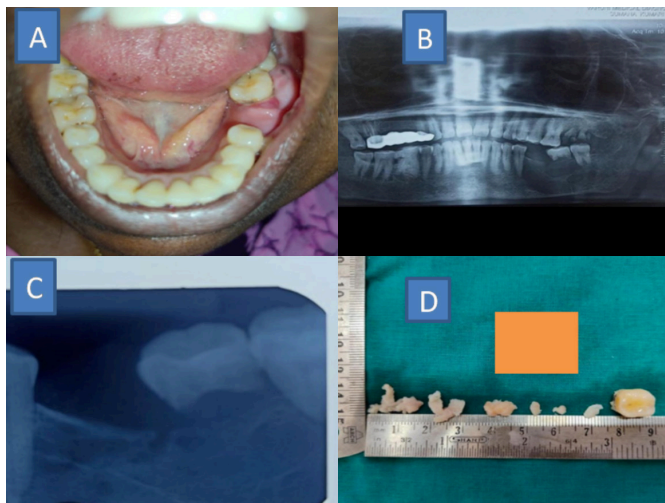


Fig.1: A. Solitary swelling extending from mesial aspect of 35 to distal aspect of 38. B and C. Well defined radiolucency extending from apical region of 35 to distal surface of 38 & superiorly from alveolar ridge to lower border of mandible. 37 and 38 showing knife edge root resorption. D. Grossing specimen of incisional biopsy.

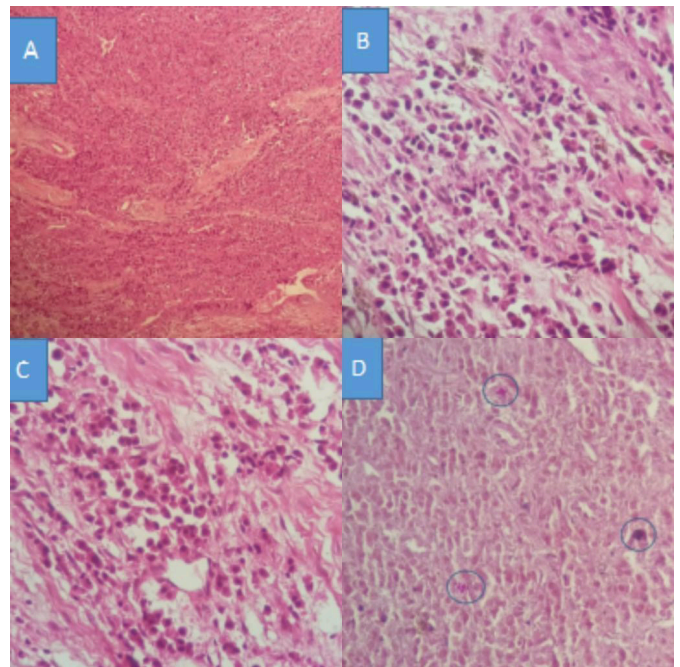


Fig.2: A. 10x showing sheets of plasma cells. B. Mott cells, mitosis, perinuclear hof (40x) C. Pleomorphic plasma cells, binucleated cells (40x) D. PAS stain showing Russell bodies. (40x)

Solitary bone plasmacytoma occurs most frequently between the ages of 50 and 80 years with a mean age of occurrence of about 60 years. Their incidence is rare before 40 years.²

The clinical presentation of solitary plasmacytoma in mandible (SPM) is not specific. The most common clinical signs include tooth mobility, facial swelling and sensory disturbances. Rarely, their incidence in mandible may be revealed during pathological fracture, TMJ dislocation, post-extraction bleeding.¹³

In the present case main complaint was swelling along with loosening of teeth. The diagnosis of solitary bone plasmacytoma depends on the biopsy evidence of sheets of plasma cell proliferation along with the absence of evidence of involvement of the other bones.¹⁴

The radiographic and clinical aspects of solitary plasmacytoma of mandible are variable.¹⁵ In our case, a well defined multilocular radiolucency with destruction of cortical bone and widespread to the surrounding tissues is evident.

The current criteria for diagnosis of solitary plasmacytoma is to confirm with both histopathological and immunohistochemical (IHC) analysis along with definite systemic investigation support.

Microscopically, plasma cells display varying degrees of differentiation along with sparse stroma. Plasmacytomas can be graded from minimal to severe dysplasia.¹⁰ The nucleus can be binucleated. Spherical nuclei are seen eccentrically and shows irregular or regular margination of chromatin showing a cart-wheel pattern.¹⁶ The chromatin may coarsely clumped to show a clock-face pattern. Sometimes para nuclear globular,

pale-staining, cytoplasmic space called hof may be noted. Giant cell formation, pseudo-angiomatous areas, myxoid change and amyloid deposition can be evident in some cases. The plasma cells may display intracytoplasmic (Russell body) and nuclear inclusions referred as Dutcher bodies. The immature plasma cells will have larger or more irregular nuclei with less condensed chromatin. The immature cells are usually larger and irregular along with ample slightly basophilic cytoplasm.⁵ Microscopic examination of our case (discussed under histopathological examination of case report) is completely in accordance with these findings.

Immunohistochemistry staining showing monoclonal plasma cell population is very characteristic. In our present case the immunohistochemistry analysis showed exclusive expression of anti-Lambda light chain antibody and absence of expression of anti-Kappa light chain antibody proving monoclonality.

The additional systemic investigation viz isolated areas of bone destruction owing to clonal plasma cells, plasma cell infiltration of bone marrow not exceeding 5% of all nucleated cells, absence of other osteolytic bone lesions and absence of other systemic pathological features like anemia, hypercalcemia, renal impairment due to myeloma, low concentrations of serum or urine monoclonal protein are done.²

The diagnosis of solitary plasmacytoma of mandible was given based on histopathological and immunohistochemical analysis addition with other systemic investigation (as mentioned in the table 1).

No therapeutic advances exist in the treatment of solitary plasmacytoma over the years. Treatment methods such as local surgical excision, systemic chemotherapy, local irradiation or a combination of these methods are followed. Among these radiation is the mainstay therapy for plasmacytoma as the lesion is highly radiosensitive. The local control rates can be achieved in 80–90% of cases by providing radiation therapy alone.¹⁷ The optimal radiotherapy dose for treatment of plasmacytoma is still under debate, and most of the published series suggested a dose range of 30 to 60 Gy.²¹

The surgical resection is usually not recommended due to their radiosensitive nature. Mostly surgical excision is preferred for the cases where there is destruction of anatomic structural integrity or presence of emergent decompression.¹⁸

If surgery is to be performed, it is usually done prior to radiation therapy and as an adjunct to the definitive radiation. The radiotherapy can be delayed but it is still necessary as excision of tumor without subsequent radiotherapy will result in a very high rate of recurrence.¹⁹

According to the latest recommendation, the role of adjuvant chemotherapy following the radiation therapy in treatment of solitary plasmacytoma of bone remains controversial.¹⁸

Many investigations were attempted to optimise the appropriate diagnostic criteria and treatment strategy for plasmacytoma of bone but still it is impoverished.

Despite the excellent local control rates, majority of solitary plasmacytoma will eventually progress to multiple myeloma. In our present case, though there is absence of multiple bone lesion, the presence of anemia, increased alkaline phosphatase

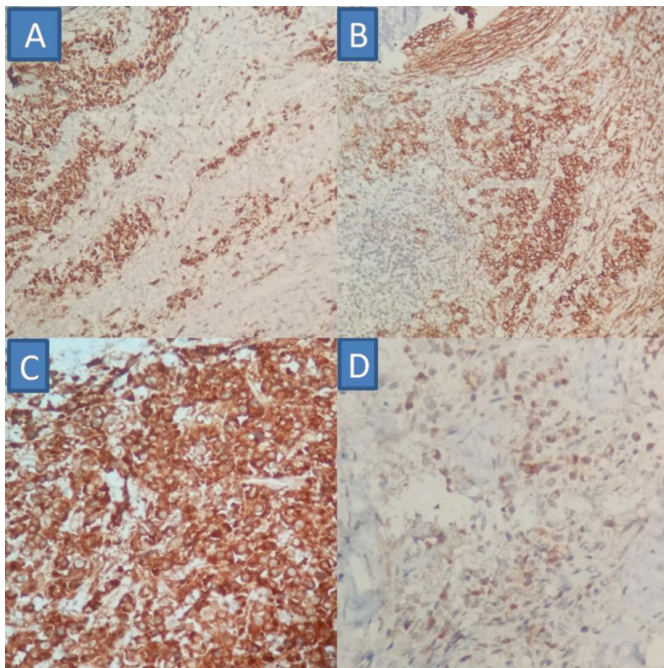


Fig. 3. A. CD45 showing diffuse positivity (10x) B. CD138 showing diffuse positivity (10x) C. Lambda chain showed diffuse and strong positivity (40x) D. Kappa chain showed weak and focal positivity (40x)

level and mainly presence of bence jones protein suggests that there might be a transition phase where solitary plasmacytoma is progressing into multiple myeloma.

Previous studies had shown 5-year overall survival rate as 70% and 5-year of disease-free survival rate as 46%, with median time for development of multiple myeloma as 21 months, with a 5-year probability of 51%.¹⁹

CONCLUSION

Solitary plasmacytoma being a rare plasma cell malignancy with high potency to transform into multiple myeloma, a thorough investigation is needed before diagnosis. Early diagnosis and appropriate treatment is the key to increase disease free survival rate of the patient.

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