Case Report

Multiple myeloma presenting as a mandibular mass: A rare case scenario

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ABSTRACT

Plasma cell dyscrasias are neoplastic proliferation of monoclonal plasma cells encompassing a wide range of entities. Plasmacytoma may present as one of two distinct clinical entities: Multiple myeloma (MM) and solitary plasmacytoma. MM is the most common hematological malignancy accounting for 10% of all hematological cancers. Oral lesions can be seen in up to 70% of MM cases, with the jawbone being involved in up to 30% of cases. The challenge with MM patients is that oral manifestations of myeloma can masquerade as dental or oral pain, swelling, or infection, which if not correctly diagnosed, might lead to a delay in therapy. Here, we present the case of a 45-year-old female complaining of swelling in the left lower gum and multiple loose teeth for 6 months. This case report illustrates the clinical presentation, radiographic, and diagnostic challenges encountered when MM primarily presents in a rare site such as the oral cavity.

Key words: Jaw lesion, Jaw neoplasms, Multiple myeloma, Plasma cells, Plasmacytoma

Multiple myeloma (MM) is a neoplasm characterized by the uncontrolled proliferation of malignant plasma cells derived from a single clone in the bone marrow. It represents 13% of all hematological tumors and is the second most commonly known hematological malignancy [1]. The median age at diagnosis is 70 years and the prevalence increases with age [2]. Data from the surveillance, epidemiology, and end results registry suggest an annual incidence of approximately 7/100,000 men and women per year. As per the Global Cancer Observatory (GLOBOCAN) 2020, the worldwide 5-year prevalence of MM was 5.78/1,00,000, and in India, it was 2.2/1,00,000. MM is characterized by the proliferation of monoclonal plasma cells in the bone marrow in association with excess monoclonal protein production (M-protein). Symptomatic disease is defined by hypercalcemia, renal impairment, anemia, bony disease (CRAB criteria) with the recent addition of ≥60% plasma cell infiltrate, and ratio of the involved and uninvolved light chain ratio of >100 or >1 focal marrow lesions on magnetic resonance imaging (SLiM CRAB) [3] by the international myeloma working group in 2014. The most frequent clinical signs and symptoms of MM consist of anemia, bone pain, fatigue, and infections, and it is characterized by multiple punched-out radiolucent lesions [4]. The clinical features of the disease are due to the proliferation and subsequent replacement of normal bone marrow cells, with a whole monoclonal paraprotein (protein M) and/or its polypeptide subunits, known as Bence Jones proteins [1]. More than 30% of the patients with MM develop osteolytic lesions in the jaws [5]. The angle and the ramus of the mandible are the most common anatomical sites involved. Common manifestations include toothache, loose teeth, paresthesia, and gingival masses [2]. The challenge with MM patients is that oral manifestations of myeloma can masquerade as dental, or oral pain, swelling, or infection, which if not correctly diagnosed, might lead to a delay in therapy [6]. In rare events, osteonecrosis of the jaw may also present with specific dental and oral signs or symptoms. The prognosis of MM has gradually improved, passing from an estimated average survival of 7 months during the pre-chemotherapy era, to an average survival of 24–30 months after the introduction of high-dose chemotherapy with autologous stem cell transplantation [1].

We describe a case of MM involving the mandible in a 45-year-old woman who presented with a swelling in the left mandibular alveolar region along with metastatic lesions involving the ribs, axial, and appendicular skeleton.

CASE REPORT

A 45-year-old female came to the department of head and neck surgery complaining of a swelling of size 5 × 2 cm in the left lower

Access this article online	
Received - 21 November 2024 Initial Review - 09 December 2024 Accepted - 04 February 2025	Quick Response code
DOI: 10.32677/ijcr.v11i3.4922	

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gums for 6 months. It was associated with on-and-off pain with no bleeding. The patient also had multiple bony swelling involving the chest, left side of the abdomen, and scalp for 2 months. The patient had chest pain, low back ache, and generalized weakness. The patient gives a history of tobacco chewing for the past 10 years. The patient is non-diabetic, non-hypertensive, with no known comorbidities. She had no other significant medical or surgical history. The patient's general condition was fair.

On per-oral examination, a soft fleshy mass was noted over the left lower alveolus measuring 5 × 2 cm extending from the incisor to the left 2nd premolar. Multiple loose teeth were noted. There was no evidence of trismus, submucosal fibrosis, or lymphadenopathy.

Positron emission tomography/computed tomography (CT) revealed multiple lytic lesions in the mandible and sternum. Multiple osteolytic bony metastases were also noted in the axial and appendicular skeleton. High-resolution CT of the thorax revealed multiple lytic lesions noted in the ribs with the largest focus noted in the left lower 9th rib.

Biopsy from the left lower alveolus mass revealed a tumor in compact nests and sheets separated by fibrovascular stroma. Cells were round to ovoid having central to eccentric hyperchromatic round nuclei with inconspicuous nucleoli and abundant eosinophilic to clear cytoplasm. Many cells show eccentric nuclei with perinuclear hof (Fig. 1).

With the background of a mass arising in the oral cavity and the above histological findings, a battery of immunohistochemistry (IHC) tests were done. Tumor cells were immunonegative to the following IHCs: p40 (rules out squamous cell carcinoma), PanCK, S100 (rules out Myoepithelial Ca and Epith Myo Ca), Synaptophysin, INSM 1(rules out neuroendocrine tumors), S100 (rules out Paraganglioma and tumors of neural and melanocytic origin) and Myogenin (rules out tumor of skeletal muscle origin). Tumor cells were immunoreactive to epithelial membrane antigen (EMA) and Vimentin (r/o Odontogenic Clear Cell Ca) (Fig. 2). With this histopathological examination and IHC findings, the most common malignancies arising in the mandibular region, that is, odontogenic neoplasm and minor salivary gland neoplasms were excluded from the study.

In the meantime, the patient lost to follow-up briefly and was consulting in another center where a CT-guided trucut biopsy from the lung mass was done and was reported as poorly differentiated non-small cell carcinoma of lung.

Subsequently, the patient again presented to our center. Block and slide from the lung biopsy were received for review in our department. It showed the same morphology as that of the alveolar biopsy (Fig. 3). Further, IHC study was done on the lung biopsy as well as the original alveolar mass which ruled out lung primary, that is, both sites were immune negative to CK 7, Napsin A, and TTF1. CK20 was also negative. Now faced with the dilemma of what IHC to do next as the tumor was negative for most of the common IHCs used in primary workup of a solid malignant neoplasm. The rare possibility of a hematolymphoid malignancy was considered. Further, IHC study was done. Tumor

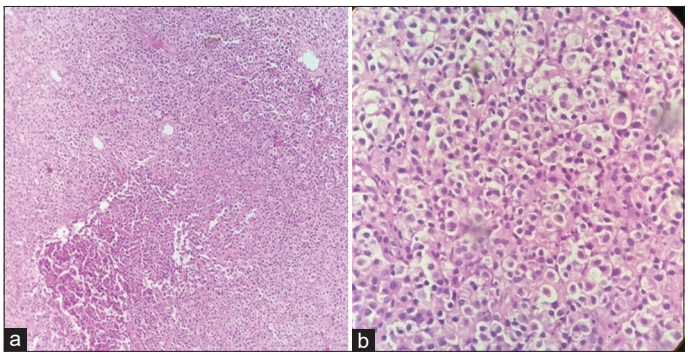

Figure 1: (a and b) Nests and sheets of round to oval cells having central to eccentric hyperchromatic round nuclei with inconspicuous nucleoli and abundant eosinophilic to clear cytoplasm

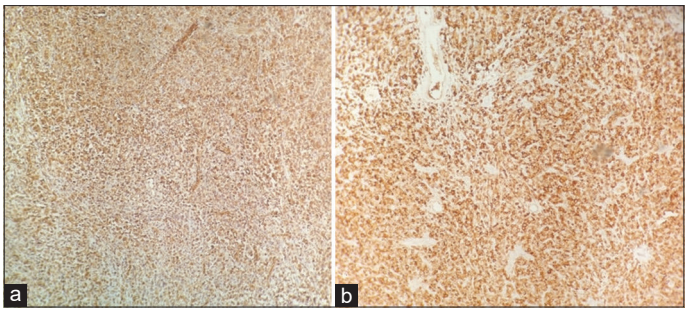

Figure 2: (a) Vimentin-cytoplasmic positivity and (b) epithelial membrane antigen-membranous positivity

cells were immunonegative for CD45, CD5, CD3, and CD20 (rules out lymphoma). Interestingly, it was immunoreactive for CD 138 and MUM 1. Ki 67 index was 60%. Now correlating this result with the earlier findings of EMA and Vimentin positivity, a diagnosis of plasma cell neoplasm was given (Fig. 4). The above IHC findings show monoclonal light chain restriction which confirms a plasma cell neoplastic process.

Considering the histopathological diagnosis of a plasma cell neoplasm with the background of multiple clinical and radiological factors, further evaluation of the patient was carried out. The following tests were done along the lines of MM. B2 microglobulin, free kappa was elevated. Free lambda was decreased. Kappa and Lambda IHC study shows monoclonal light chain restriction (Fig. 5). Serum protein electrophoresis showed the M band to be 2.9 g/dL. In serum immunofixation electrophoresis, the M band was found in the immunoglobulin G (IgG) and Kappa regions. CRAB was present. The patient was thus diagnosed with MM International Staging System III IgG Kappa.

DISCUSSION

MM is the most destructive primary bone malignant neoplasia characteristically affecting the elderly, with a slight tendency to affect men. The most common early signs and symptoms of MM are fatigue, bone pain, fever, anemia, nephropathy, and weight loss [4]. MM can often manifest as lesions in the oral cavity or jaw which might mimic dental or periodontal pathology and might even be the first sign of MM [2]. Our case also

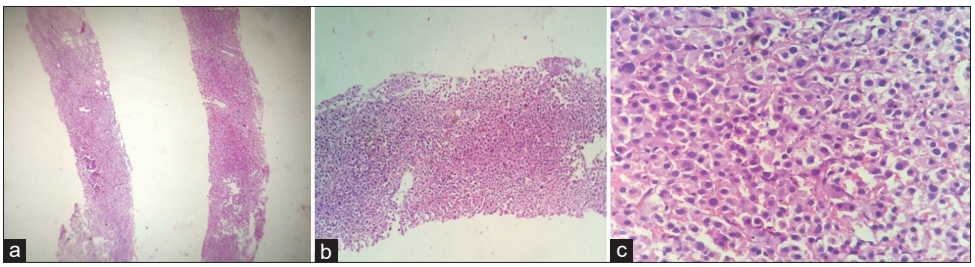

Figure 3: (a-c) Sheets of round to oval cells having central to eccentric hyperchromatic round nuclei with inconspicuous nucleoli and abundant eosinophilic to clear cytoplasm

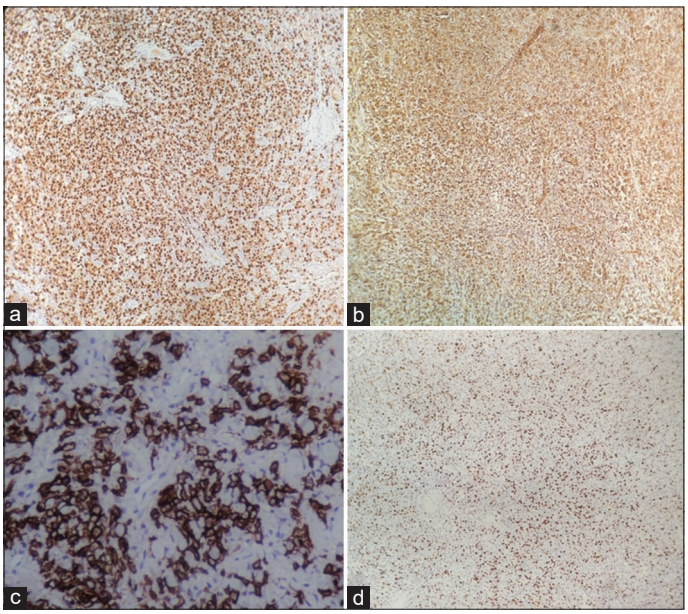

Figure 4: (a) MUM1-Nuclear positivity, (b) vimentin-cytoplasmic positivity, (c) CD 138-membranous positivity, and (d) Ki67 index-60%

presented with jaw swelling which was similar to studies done by Krishnan *et al*. [7,8]. Swelling, orofacial pain, mobility of teeth, paresthesia, hemorrhage, fracture, and root resorption are more frequently found in the mandible than the maxilla. Bony lesions in the jaws are directly attributed to the osteoclastic-activating factor, a lymphokine that is responsible for the development of these lesions.

The bone marrow biopsy demonstrates a large amount of abnormal plasma cells, M protein, and light chain proteins (κ and λ), along with cytokines [9]. Excessive production of M-protein causes hyperviscosity of the blood, which, in turn, leads to renal dysfunction. In serum electrophoresis, M-protein is present in about 93% of the patients. In urine electrophoresis, M-protein is present in approximately 60% of the patients [10]. The diagnosis of MM depends on the identification of abnormal monoclonal plasma cells, a full blood count, a bone marrow biopsy, levels of M-protein in the serum or urine, and a clinical image consistent with MM [10].

Treatment for MM has evolved dramatically over the past few years leading to improved survival [11]. The prognosis of MM is fair with a median survival range between 3 and 10 years [10]. In an advanced stage of myeloma, melphalan-prednisone plus either bortezomib or thalidomide are the novel standards in Europe for

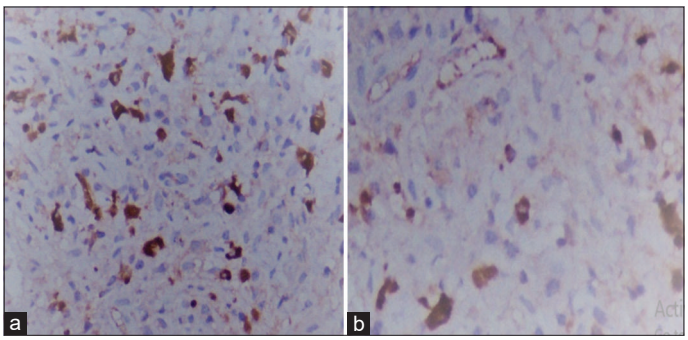

Figure 5: (a and b) Immunohistochemistry-kappa (40×) light chain shows cytoplasmic positivity, lambda (40×) light chain shows negativity

elderly patients. Thalidomide destroys malignant plasma cells directly and has antiangiogenic properties and other effects on the bone marrow microenvironment that can synergize with chemotherapy to stimulate apoptosis [12].

CONCLUSION

MM involving the mandible is quite a unique and rare tumor which is usually mistaken for other more common odontogenic lesions and minor salivary gland neoplasms. The definitive treatment of all resectable solid malignant neoplasms is surgery whereas for hematolymphoid malignancy, it is chemotherapy. Thus, it is of paramount importance not to misdiagnose between these two broad categories. This case report highlights the importance of considering the rare possibility of a hematolymphoid malignancy in the histopathology diagnostic workup of a solid malignant neoplasm especially when most IHC markers come out to be immunonegative. Another important aspect is the undoubtedly clear benefit of how early diagnosis of MM at the jaw level prevents both unnecessary and inadequate treatments.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Beso AP, Kalita U, Sharma JD, Deka M, Bharadwaj BS, Phukan N, *et al*. Multiple myeloma presenting as a mandibular mass: A rare case scenario. Indian J Case Reports. 2025; 11(3):103-106.