Case Report

Multiple myeloma as a mandibular primary - Dilemma in diagnosing rare tumours of the mandible

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Abstract

Multiple myeloma (MM) is a plasma cell malignancy, and its typical radiographic presentation includes punched-out radiolucency of the skull. It is a bourgeois description of myeloma and often holds good in most cases. However, the diagnosis can get tricky when a patient walks into the clinic with non-specific signs and symptoms. Many suspicions arise when we examine a well-defined mandibular swelling, but the real picture is revealed with thorough screening. This article presents a rare mandibular swelling diagnosed as MM, emphasizing important differential diagnoses for maxillofacial surgeons and pathologists.

Keywords: Differential diagnosis, mandible, multiple myeloma, rare tumours

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INTRODUCTION

Rare tumours of the mandible are diagnostic challenges as they are often misleading due to the lack of specific clinical characteristics. Due to this, ordering the array of diagnostic tests becomes difficult and may result in the patient not getting the desired treatment.

Multiple myeloma (MM) is the most common bone malignancy with a lymphoid neoplastic proliferation of plasma cells in the bone marrow.[1] The monoclonal immunoglobulins are traceable in urine and serum. Elderly males with bone pain, anaemia, renal insufficiency and hypercalcaemia with characteristic punched-out radiolucent bone lesions are typical presentations.[2] The head and neck manifestations of MM occurs usually at an advanced stage of the disease, with a prevalence of 14-30%.[1] It is rare for a mandible swelling to be the primary presenting lesion, and if it occurs, the angle and ramus are the most commonly involved.[3,4] Since the lesion does not have specific clinical features, it is diagnosed when elevated protein levels are found in the blood or urine. This report aims to describe a rare case of MM of the mandible as the primary presenting lesion, emphasizing the differential diagnosis of rare mandibular tumours.

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CASE REPORT

A 71-year-old female patient reported to the Oral Surgery Department due to a one-month-old diffuse swelling on the left mandibular ascending ramus. It was sudden in onset without pain, paraesthesia or other systemic symptoms. The swelling was firm and non-tender with no involvement

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of overlying skin or cervical lymph nodes [Figure 1]. The patient was edentulous, with the lesion extending from tooth 38 region posteriorly and obliterating the maxillary and mandibular gingivo-buccal sulcus. It was firm on palpation without any discharge or local rise of temperature. The overlying and surrounding mucosa were normal [Figure 2]. A contrast-enhanced computed tomography (CT) scan of the face revealed a heterogeneous expansile lesion with a soft tissue component arising from the left mandibular ramus and destroying the outer and inner cortices [Figure 3a]. An orthopantomogram was also ordered which revealed an ill-defined, unicystic osteolytic lesion with irregular borders extending from the left sigmoid notch superiorly to the mandibular inferior border, and extending up to the left second mandibular molar anteriorly [Figure 3b]. After radiographic evaluation, aspiration was performed which was inconclusive. A differential diagnosis of ameloblastoma, odontogenic myxoma, PIOC (primary intraosseous carcinoma), osteogenic sarcoma and primary non-Hodgkin's lymphoma (NHL) of mandible was made. An incision biopsy of the lesion yielded a pale white firm tissue suggestive of a tumour. Histopathological analysis revealed the presence of atypical plasma cells showing a high nuclear-cytoplasmic ratio, prominent or eccentric nucleoli and dense cytoplasm, indicating a potential plasma cell malignancy [Figure 4]. Additionally, an immunohistochemical analysis was conducted to exclude the possibility of MM.

The analysis showed positive for CD 138 (Cluster of Differentiation), lambda light chain, MUM-1 (multiple myeloma oncogene-1) and high Ki 67 (50%) immunostaining suggestive of plasmacytoma [Figure 5]. The patient was then referred to the oncologist for a detailed evaluation and treatment planning. A bone marrow aspiration revealed a hyperplastic marrow with a myeloid to erythroid ratio of 4.6:1 and 27% atypical plasma cells. Comprehensive myeloma protein panel detection with gel electrophoresis showed myeloma band in the gamma globulin region corresponding to immunoglobulin G with lambda light chain (1040 mg/L) along with high beta-2 microglobulin (5.7 mg/ml) and normal serum albumin (3.57 g/dL) was suggestive of monoclonal gammopathy characteristic of MM. The serum lactate dehydrogenase level was measured and found to be within the normal range (163 U/L). As per the revised

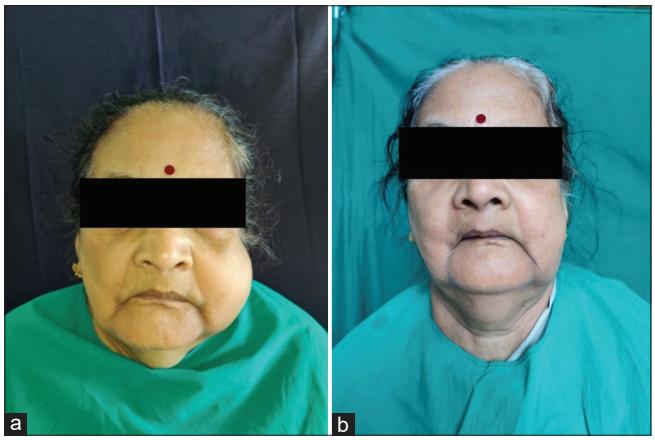

Figure 1: (a) Patient photograph before treatment shows swelling on the left mandible (b) Post-treatment photograph shows reduced size of swelling

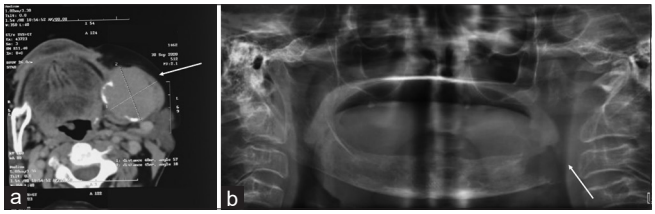

Figure 3: (a) CT axial section shows a heterogeneous expansile lesion arising from the left mandibular ramus (white arrow) (b) Panoramic view of the mandible shows an ill-defined, unicystic osteolytic lesion on the left mandibular ramus (white arrow)

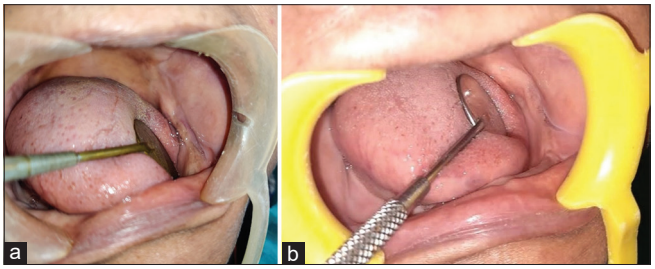

Figure 2: (a) Intraoral photograph before treatment shows diffuse swelling involving buccal mucosa, alveolar ridge and obliterated buccal sulcus (b) Post-treatment photograph shows reduced swelling and a more clearly defined buccal sulcus

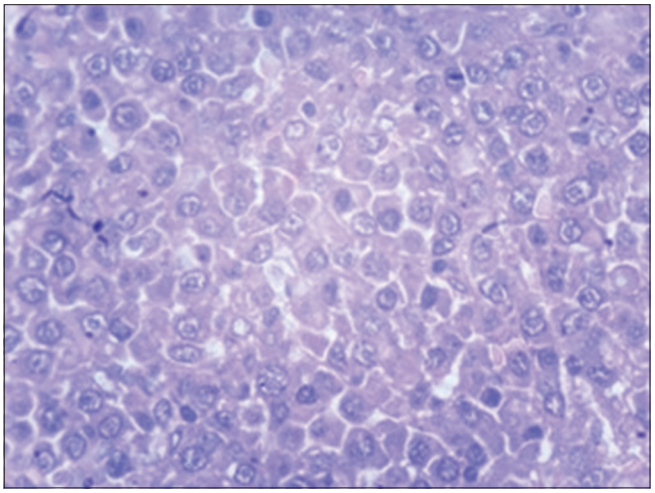

Figure 4: Histopathological microphotograph of multiple myeloma showing a diffuse population of atypical plasma cells having prominent nucleoli, eccentric nuclei and abundant cytoplasm (plasmablasts) (H&E stain X 40x)

ISS (International Staging System) for MM, the patient was diagnosed with Stage III disease. A whole-body MRI (magnetic resonance imaging) diffusion-weighted sequence with MRI spine screening showed evidence of a lytic lesion in the right acetabulum and T12 vertebral body for which the patient was asymptomatic [Figure 6]. Appropriate chemotherapy involving a three-drug regimen was initiated with bortezomib 1.3 mg/m^2 intravenous injection and tablet dexamethasone 40 mg on days 1, 8, 15, 22 and thalidomide capsule 50 mg oral daily along with herpes zoster prophylaxis. The patient was followed up every six weeks with the oncologist, and in the Oral and Maxillofacial Surgery Clinic, tumour remission was noted [Figures 1, 2 and 7].

DISCUSSION

MM is a plasma cell malignancy accounting for 10-15% of neoplasms of haematologic origin.[5] MM has an incidence rate of 6-7% worldwide and 8-15% among jaw lesions, more frequently seen among men of 60-70 years of age.[6,7] It is associated with hypercalcaemia, renal failure, anaemia and bone destruction (CRAB). The criteria for diagnosis include the presence of a proportion of 10% plasma cells in bone marrow aspirate or biopsy specimen, serum or urine monoclonal protein, and end-organ damage.[8] Diagnostic workup constitutes a multidisciplinary approach comprising body biochemical analysis, bone marrow cytology and radiological investigation to detect osteolytic lesions.[6]

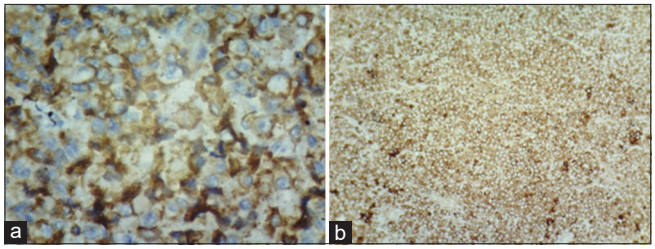

Figure 5: (a) Immunohistochemistry image showing strong lambda cytoplasmic positivity (Lamda X 5x) (b) CD138 membranous positivity (CD138 X 45x)

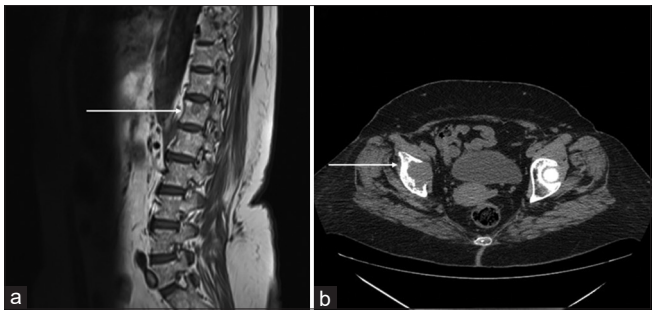

Figure 6: (a) Diffusion-weighted sagittal spine MRI shows T12 lytic lesion (white arrow) (b) CT section shows evidence of a lytic lesion in the right acetabulum (white arrow)

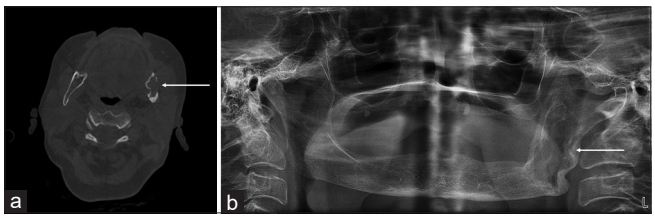

Figure 7: Post-treatment radiographic imaging (a) CBCT axial slice shows bone healing in the left mandibular ramus region (white arrow) (b) Panoramic view shows bone healing in the left mandibular ramus region (white arrow)

A mandibular lesion as the first clinical presentation is rare but not the first of its kind. The skull and mandible are the most common presentation sites in the craniofacial skeleton. Most lesions occur in the mandible and rarely in the maxilla due to the amount of active haematopoietic marrow in the mandible.[7,9] The clinical presentation is usually pain, paraesthesia, tooth mobility, pathological fracture, tongue enlargement[7] or simply a firm swelling without other symptoms. Due to this non-specificity of symptoms, it may go unnoticed. Tooth removal can trigger the spread of the disease due to additional marrow spaces. In edentulous patients, lesions are more common in association with the mandibular canal due to wide marrow spaces.[10]

Imaging studies have described MM in jaws as multiple smaller lesions infiltrating adjacent bone to form a 'larger lesion with irregular osteoporotic margins'[7,9] or as 'multiple punched out radiolucency having well-defined borders', which is due to the action of 'osteoclast activating factor'.[11] Uncertainty exists regarding the onset and spread of the disease, if it begins simultaneously at various bony sites or from a solitary local lesion to metastasizes to other areas. Evidence of cortical erosion may be seen in a few, while others may present with an expansile lesion.[10] Imaging should help identify the extent of the lesion and distant metastasis.

An expansile lesion developing on the posterior mandible can be of varied aetiology like inflammatory, developmental, neoplastic or reactionary pathoses. After careful examination, differential diagnoses of ameloblastoma, odontogenic myxoma, PIOC, osteogenic sarcoma and NHL were made. The clinical presentation and behaviour of the tumour were comparable to an odontogenic tumour. The presence of unilocular or multilocular radiolucency with significant expansion, cortical destruction and soft tissue swelling is seen with ameloblastoma,[12] which was primarily suspected. However, the absence of a honeycomb or soap-bubble appearance on the radiograph

and a negative aspiration test ruled out the disease. The absence of perpendicularly oriented internal trabeculations characteristic of odontogenic myxoma helped rule out the possibility of its existence.[13]

PIOC is a rare lesion assumed to originate from the odontogenic epithelium in the posterior mandible in the sixth decade of life or later. It is defined as 'having no initial connection with the oral mucosa' and should not be a metastasis from a distant primary, which was precisely the pattern when the patient reported the lesion. The absence of invasion of buccal mucosa was strongly predictive of PIOC. The criteria to differentiate this lesion from PIOC was the presence of lytic lesions with irregular cortical borders. A PIOC will have well-defined borders, and the histopathology reports were negative for an epithelial tumour.[14]

Primary NHL of the mandible frequently goes undiagnosed since it is uncommon in this area (8%), distant soft-tissue or lymphatic involvement is absent and exhibits no distinctive symptoms. Imaging studies also suggested the possibility of NHL due to the painless and rapid enlargement of the mandible with the presence of cortical destruction. Lab findings confirmed it to be of plasma cell origin and, the absence of common symptoms like pain and paraesthesia helped rule out the possibility of lymphoma.[15]

Osteogenic sarcoma of the jaws comprises 15% of primary bone tumours. The clinical presentation is usually a destructive lesion with ill-defined margins and is of the lytic, sclerotic or mixed radiographic pattern. The characteristic 'sun-ray' effect is pathognomonic but not necessarily found in all lesions and lymph node metastases are rare. These were suggestive of its existence, but the age of presentation, mostly the fourth decade, made the diagnosis questionable. There was no increase in the levels of lactate dehydrogenase (LDH - 163 U/L) or alkaline phosphatase (ALP - 135 U/L) to support the diagnosis.[16]

Clinicians order imaging for various purposes, but accurate interpretation and comprehensive evaluation of scans are crucial, as incidental findings are frequently reported on cone beam computed tomography (CBCT) scans. There have been reported instances of misdiagnosing myeloma as periapical inflammatory lesions, odontogenic cysts and temporomandibular disorders which results in delayed or inappropriate treatments. A delayed diagnosis can be harmful, as oral symptoms often signal disease progression in haematologic malignancies.[17] Finally, a chest radiograph and CT of the thorax are mandatory to rule out any other existing lesions.

CONCLUSION

Solid lesions in the mandible are myriad and common. Detailed evaluation of these lesions may reveal many signs and symptoms, which can be misleading. It is easy to diagnose when the pathognomonic features are evident. However, things get tricky when the lesion reveals no specific features. In such instances, there is a need to evaluate the differential pathoses likely to arise, site- or age-specific. Once we single out a lesion, the array of tests and the appropriate treatment can be ordered.

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Conflicts of interest
There are no conflicts of interest.

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