Oral Manifestations of Malignant Immunoglobinopathy Hidden in Plain Sight - A Rare Case Report

Naresh Kumar Sharma, Akhilesh Kumar Singh, Mehul Shashikant Hirani, Aswathi Krishnan, Arjun Mahajan, Ravina Rajpoot

Department of Oral and Maxillofacial Surgery, Faculty of Dental Sciences, IMS, BHU, Varanasi, Uttar Pradesh, India

Abstract

Rationale: Radiolucent lesions over the angle–body region of the mandible are frequently difficult to diagnose but crucial to provide patient-centred care. **Patient Concerns:** An elderly female presented with a painless slow-growing swelling over her left lower face for one year, radiographically appearing as a well-defined unilocular radiolucency over the left body of the mandible. **Diagnosis:** Aspiration was negative, and biopsy was inconclusive. Further imaging, bone marrow biopsy, immune profile and serum electrophoresis confirmed the diagnosis of multiple myeloma. **Treatment:** She was referred to Medical Oncology for chemotherapy of lenalidomide, bortezomib and dexamethasone regimen cycle that was repeated every 21 days. **Outcomes:** There was no increase in swelling, and radiographically 'punched-out' lesions were reduced significantly. **Take-Away Lessons:** Maxillofacial clinicians should be attentive to the oral manifestations of underlying disease, have a high index of suspicion and start the treatment promptly to increase chances of a favourable outcome.

Keywords: Mandible, multiple myeloma, radiolucent lesion

Introduction

The diagnosis of radiolucent lesions in the body region of the mandible is frequently perplexing.

The presence of nonvital teeth[1] becomes the distinguishing factor for radicular cyst, the most common[2,3] punched-out radiolucent lesion, succeeded by dentigerous cysts and periodontal cysts when associated with impacted teeth and mobile teeth respectively. Odontogenic keratocyst (OKC) occurring in the second and third decades[1] grows anteroposteriorly within the confines of the bone and seldom shows cortical expansion. Residual cyst and giant cell granuloma were the closest differential diagnosis for this case.

Multiple myeloma (MM) in the maxillofacial region is challenging to diagnose solely based on the primary manifestation of underlying quiescent bony pathology, that may manifest as bone pain, exhaustion, anaemia and vulnerability to infectious diseases, all of which are prominent clinical symptoms in general.

MM is a malignancy characterised by multifocal proliferation of atypical plasma cells as well as the presence of monoclonal gamma globulins and/or their subunits in the serum, referred as myeloma (M) proteins.[4] Review of literature states that primary manifestations of oral lesions are rare.[4,5] The classic 'punched-out' osteolytic lesions are frequently seen on radiography.[6]

This case unfolds the diagnostic journey commencing from a solitary mandibular lesion without adjoining mobility of teeth, which was traced back to a rare case of MM that was primarily manifesting intraorally. Hence, rather than settling for a most probable diagnosis, any solitary corticated radiolucency in jaw bones should be comprehensively investigated.

Case Report

A 61-year-old female presented with a history of a slow growing, non-resolving swelling over the left lower face region for one year. She was relatively asymptomatic for one year

Access this article online

Quick Response Code:

Website: https://journals.lww.com/aoms

DOI: 10.4103/ams.ams_75_22

Address for correspondence: Dr. Mehul Shashikant Hirani, Department of Oral and Maxillofacial Surgery, Faculty of Dental Sciences, IMS, BHU, Varanasi, Uttar Pradesh, India.
E-mail: mehul1795@gmail.com

Received: 25-03-2022 **Last Revised:** 11-01-2023
Accepted: 23-02-2023 **Published:** 02-06-2023

How to cite this article: Sharma NK, Singh AK, Hirani MS, Krishnan A, Mahajan A, Rajpoot R. Oral manifestations of malignant immunoglobinopathy hidden in plain sight - A rare case report. Ann Maxillofac Surg 2023;13:101-4.

when she noticed the swelling, which slowly increased to present size causing obvious facial asymmetry [Figure 1]. There was no history of pain, pus discharge, overlying growth or ulceration. Left submandibular lymph nodes were palpable, firm, non-tender and mobile. She had a history of chronic back pain for approximately 18 months. There was no associated neurosensory impairment.

Intraoral examination revealed the obliteration of vestibule and normal overlying mucosa [Figure 2]. Mandibular first molars were missing as a result of previous extractions owing to caries.

Panoramic radiograph showed a well-defined oval radiolucent lesion in the left body of the mandible [Figure 3a]. Multiple punched-out radiolucencies on the contralateral side of the mandible were also evident. Further aspiration of the lesion with a 16-gauge needle was negative. Incisional biopsy yielded bright red, soft fragile tissue, with microscopy revealing moderately intense hypercellular connective tissue stroma with abundant plasma cells; endothelium lined vascular spaces of varying sizes, interspersed with extravasated blood, and a focal area of ossification. The oral pathologist diagnosed the lesion as a chronic inflammatory lesion [Figure 4a].

Radiographs of the skull were then advised, which showed multiple punched-out lesions in the cranial vault [Figure 5a]. A subsequent computed tomography scan [Figure 6] revealed a hypoattenuated lytic lesion extending from the left body to the angle of the mandible, as well as many minor lytic lesions over the ramus, zygoma and cranial vault indicating an unknown underlying pathogenic aetiology.

Blood profile showed normal bleeding and clotting times, low haemoglobin, elevated erythrocyte sedimentation rate (ESR), increased total serum proteins, normal serum parathormone and elevated serum calcium levels. In peripheral blood smear, normochromic, normocytic anaemia with mild rouleaux was observed. Few circulating plasma cells (3%) were observed with the absence of haemoparasites in blood. Bence-Jones protein was absent in urine samples.

The patient was advised for serum electrophoresis that showed a characteristic spike of M band [Figure 4b]. Bone marrow aspirate revealed normocellular-appearing marrow with increased number of plasma cells and proportionally reduced

Figure 1: (a and b) Extra-oral clinical picture

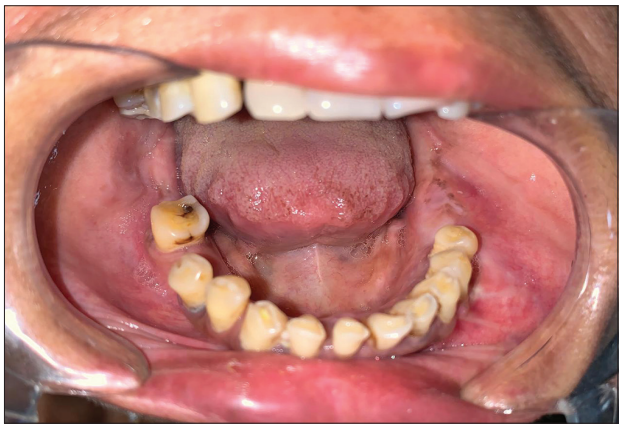

Figure 2: Intraoral clinical picture

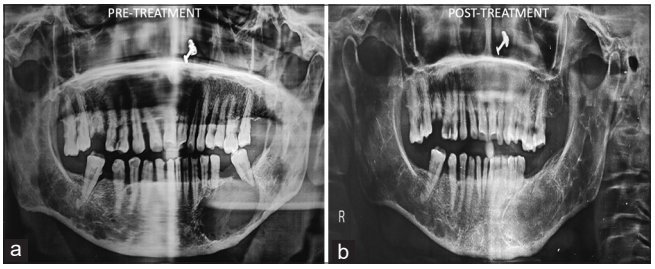

Figure 3: (a) Pre- and (b) Post-treatment Orthopantomographs

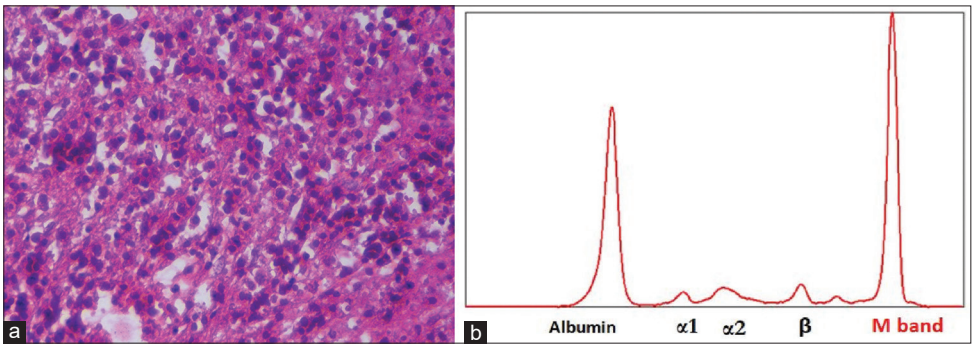

Figure 4: (a) Microscopic image, (b) 'M' spike on graph after protein electrophoresis and immunofixation

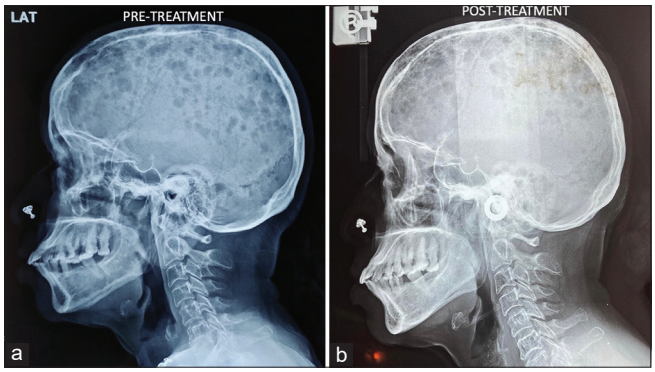

Figure 5: (a) Pre- and (b) Post-treatment Lateral skull radiograph

trilineage haematopoiesis. There was 81% plasma cell infiltrate in bone marrow aspirate smear.

Hence, based on immunological profile, the presence of M band on serum electrophoresis, bone marrow biopsy and imaging findings of extensive bone lesions, the diagnosis of MM was made. After referral to Medical Oncology, the patient was advised for chemotherapeutic lenalidomide, bortezomib and dexamethasone regimen[7] cycle that was repeated every 21 days, without any side effects. At one year follow up, resolution of 'punched out lesions' can be observed on plain radiographs i.e. orthopantomograph [Figure 3b] and lateral skull x-ray [Figure 5b] respectively.

Discussion

Radicular cyst, periodontal cyst, and dentigerous cyst were all ruled out as probable diagnoses due to the lack of carious tooth involvement, lack of mobility of associated teeth and absence of impacted teeth respectively. Given the patient's age, associated swelling, and fine-needle aspiration cytology report with plasma cell infiltration, the differential diagnosis of OKC and residual cyst were ruled out.

MM is the most aggressive plasma cell neoplasia characterised by growth of malignant plasma cells and consequent overproduction of monoclonal paraprotein. MM is about 1% of all malignancies and 10-15% of all haematologic malignancies.[6,7]

MM, solitary plasmacytoma of bone and extra-medullary plasmacytoma are the three chief clinical entities of plasma cell myeloma/plasmacytoma.[7] Calvarium, mandible, pelvic girdle, sternum, clavicle and proximal sections of the humerus and femur are all common sites for myeloma infiltrates. It is common in patients older than 50 years of age, with a peak incidence rate of 60–70 years.[8]

The diagnosis of MM requires 10% or more clonal plasma cells on bone marrow examination or a biopsy-proven plasmacytoma plus the presence of one or more myeloma-defining events that include the presence of one or more (hypercalcaemia, renal failure, anaemia and bone disease) features and/or biomarkers of malignancy.[9]

Oral manifestations are the initial presenting signs in 12-15% of MM cases,[5,6] manifesting as swelling, orofacial pain, tooth mobility, lip paraesthesia, haemorrhage, jaw fracture, and root resorption. The mandible is more commonly involved than the maxilla.[7-9]

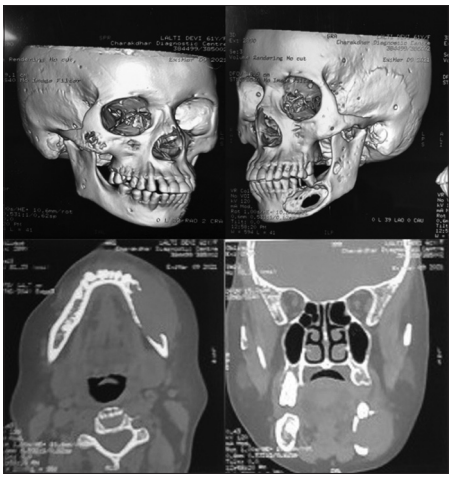

Figure 6: Pre-treatment CT scan. CT = Computed tomography

Monoclonal gammopathy of unknown significance, multiple metastatic lesions, systemic amyloidosis and Langerhans cell disease are amongst the differential diagnoses for small, multiple, independent, well-defined radiolucencies. When various bones in the skeleton are involved in adults, MM and metastatic carcinoma are quite likely. The diagnosis of MM needs a multidisciplinary approach, requiring complete blood evaluation, renal function tests, calcium status, serum immunoelectrophoresis, bone marrow biopsy and aspiration, urinalysis and a radiographic skeleton survey.[7,8,10]

MM is an incurable disease; treatment can only prolong lifespan and provide symptom relief. Corticosteroids, either alone or in combination with thalidomide, have been the mainstay of MM therapy.[7,10] This can be combined with autologous stem cell transplantation as a part of the standard initial treatment. Factors such as stage of MM, advanced age (>65 years), poor activity performance and poor response to therapy may determine a worse prognosis.[7]

This case report highlights the early identification of MM that requires an understanding of manifestations with primary intraoral involvement. The patient was relatively asymptomatic and was only concerned about the lesion in the jaw. Surgeons should pay meticulous attention to diagnosis; otherwise, surgical misadventure to treat the lesion without considering the underlying pathophysiology would lead to undesirable outcomes. Atypical disease presentation complicates diagnosis, potentially leading to misdiagnosis or delay in diagnosis, which could jeopardise the final treatment plan.

Conclusion

This case report emphasises the role of oral clinicians to thoroughly examine the oral cavity for suspicious lesions that could indicate serious underlying disease.

Myeloma can present in a variety of ways and its oral manifestation, although infrequent, may be the only symptom or one of the several indicators of disease progression. Clinicians must be attentive to the oral manifestations of underlying disease, have a high index of suspicion and refer promptly to start the early treatment for increasing the chances of a favourable outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Avril L, Lombardi T, Ailianou A, Burkhardt K, Varoquaux A, Scolozzi P, *et al.* Radiolucent lesions of the mandible: A pattern-based approach to diagnosis. Insights Imaging 2014;5:85-101.
2. Dunfee BL, Sakai O, Pistey R, Gohel A. Radiologic and pathologic characteristics of benign and malignant lesions of the mandible. Radiographics 2006;26:1751-68.
3. Devenney-Cakir B, Subramaniam RM, Reddy SM, Imsande H, Gohel A, Sakai O. Cystic and cystic-appearing lesions of the mandible: Review. AJR Am J Roentgenol 2011;196:S66-77.
4. Misra S, Singh A, Kumar V. Plasma-cell myeloma with double M-bands on serum protein electrophoresis: A diagnostic conundrum? MAMC J Med Sci 2021;7:265-8.
5. Feitosa ÉF, Magalhães RJ, Barbosa CA, Guedes FR, Maiolino A, Torres SR. Oral health status of patients with multiple myeloma. Hematol Transfus Cell Ther 2020;42:166-72.
6. Albagoush SA, Shumway C, Azevedo AM. Multiple myeloma. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534764/. [Last updated on 2022 Feb 08].
7. Punke AP, Waddell JA, Solimando DA Jr. Lenalidomide, bortezomib, and dexamethasone (RVD) regimen for multiple myeloma. Hosp Pharm 2017;52:27-32.
8. Healy CF, Murray JG, Eustace SJ, Madewell J, O'Gorman PJ, O'Sullivan P. Multiple myeloma: A review of imaging features and radiological techniques. Bone Marrow Res 2011;2011:583439.
9. Rajkumar SV. Updated diagnostic criteria and staging system for multiple myeloma. Am Soc Clin Oncol Educ Book 2016;35:e418-23.
10. Legarda MA, Cejalvo MJ, de la Rubia J. Recent advances in the treatment of patients with multiple myeloma. Cancers (Basel) 2020;12:3576.