

# Multiple myeloma with presentation in the oral cavity

Pooja Kamath, Cathy Babu, Avinash Tamgadge, Treville Pereira

Department of Oral and Maxillofacial Pathology, D Y Patil University School of Dentistry, Navi Mumbai, Maharashtra, India

## Abstract

Plasma cell neoplasms may present in the bone as monoclonal gammopathy of undetermined significance, solitary plasmacytoma of bone, multifocal plasma cell neoplasm of bones known as multiple myeloma (MM) and in soft tissues as extramedullary plasmacytoma. MM is a malignant disease of atypical plasma cells characterized by their multifocal proliferation and production of monoclonal immunoglobulins. Often, the initial clinical feature of this disease is subtle and requires trained primary health-care providers to identify this illness and put together a suitable treatment plan. This case report describes a patient with a swelling in the buccal vestibule which on clinical and pathologic investigation turned out to be MM.

**Keywords:** Bence-Jones proteins, CRAB criteria, monoclonal immunoglobulins, multiple myeloma, oral plasmacytoma, plasma cells

**Address for correspondence:** Dr. Pooja Kamath, Department of Oral and Maxillofacial Pathology, D Y Patil University School of Dentistry, Sector 7, Nerul, Navi Mumbai - 400 0706, Maharashtra, India.  
E-mail: drpoojak1@gmail.com

**Submitted:** 16-Oct-2021, **Revised:** 25-Nov-2021, **Accepted:** 21-Jan-2022, **Published:** 31-Mar-2022

## INTRODUCTION

Multiple myeloma (MM) is a malignant proliferation of monoclonal plasma cells in the bone marrow, leading to the production of nonfunctional intact immunoglobulins (Igs) or Ig chains.

It accounts for 15% of all hematologic malignancies and ranks as the second-most common in this category after Non-Hodgkin lymphoma. It is the most important plasma cell dyscrasias and differs from other variants such as monoclonal gammopathy of undetermined significance, solitary plasmacytoma of bone, and extramedullary plasmacytoma by factors such as plasma cell load and site of involvement.<sup>[1,2]</sup>

This report describes a case of swelling in the buccal vestibule which on investigation was diagnosed as MM.

## CASE REPORT

A 65-year-old female presented to the department with a chief complaint of pain and swelling in the lower right back region of the jaw which was of 3-month duration. The pain was persistent and dull in nature. She also complained of mobility of teeth in the affected area. She gave a medical history of diabetes for 3 years and hypertension for 8–9 years and was under medication for the same.

On intraoral examination, a swelling measuring about 5 cm × 3 cm was seen over the right mandibular buccal sulcus extending from 46 to 47 regions which obliterated the vestibular depth. Forty-six and 47 were missing. The swelling was soft in consistency and tender on palpation. Regional lymphadenopathy was absent. There was no sign of anesthesia or paresthesia. Radiographic examination revealed

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Kamath P, Babu C, Tamgadge A, Pereira T. Multiple myeloma with presentation in the oral cavity. J Oral Maxillofac Pathol 2022;26:104-7.

### Access this article online

#### Quick Response Code:



#### Website:

www.jomfp.in

#### DOI:

10.4103/jomfp.jomfp\_377\_21

a bone loss in relation to 43–47. A large lytic lesion was observed in the adjacent quadrant as well albeit the absence of any clinically evident lesion there. Cone-beam computed tomography of the mandible revealed large radiolytic lesions on either side, involving the inferior border [Figures 1a and b].

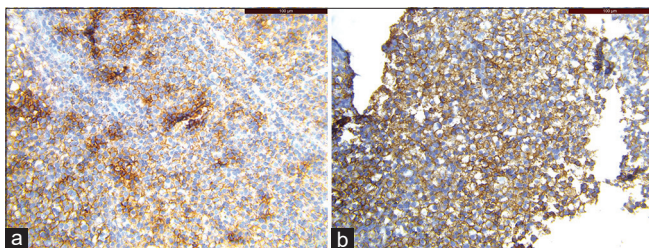
Incisional biopsy was performed on the right and left side of the lower jaw and histopathological examination revealed sheets of neoplastic cell proliferation with plasmacytic differentiation [Figure 2]. Cells showed abundant eosinophilic cytoplasm, eccentrically placed hyperchromatic nucleus with granulated radial chromatin. Overall features were suggestive of plasmacytoma. Immunohistochemical investigation was performed using CD138, kappa and lambda. CD138 showed diffuse positivity [Figures 3a and b]. The tissue showed negative staining for kappa light chain and lambda light chain staining showed a prevalence of lambda positivity in the neoplastic cells evaluated, confirming the final diagnosis of plasmacytoma [Figures 4 and 5a, b].

Further investigations were carried out as a part of screening for MM. The evaluation of Bence-Jones protein gave a negative result. Positron emission tomography scan revealed lytic lesions involving multiple bones of axial and appendicular skeletons showing low-grade metabolic activity. The lytic lesion in the sphenoid bone and right horizontal ramus of the mandible showed soft tissue component. Diffuse osteopenia was also noted. Metabolically active disease was not observed elsewhere in the body. The above findings favored the diagnosis of MM.

The patient expired in a month's time.



**Figure 1:** (a) Orthopantomogram of the mandible showing multiple radiolucent areas, (b) Cone-beam computed tomography of the mandible showing multiple osteolytic lesions with ragged borders

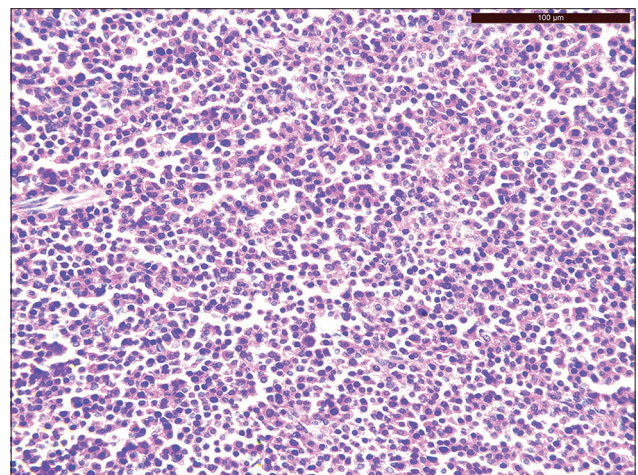


**Figure 3:** (a and b) Immunohistochemical staining with CD138 showing diffuse positivity (IHC - CD138, x400)

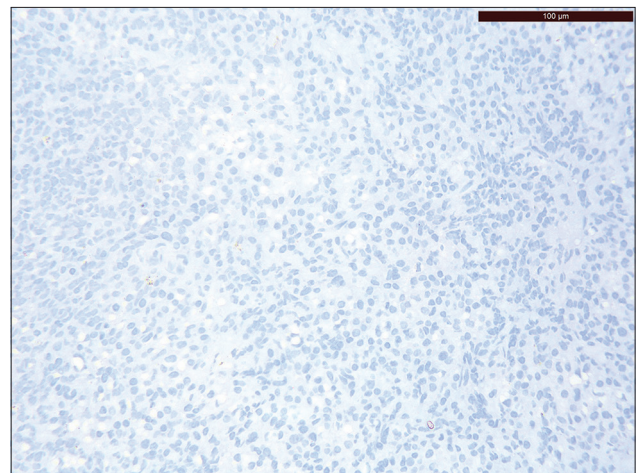
## DISCUSSION

MM, according to the World Health Organization, is a lymphoproliferative systemic malignant disease of the blood, characterized by the uncontrolled proliferation of monoclonal plasma cells in the bone marrow.<sup>[2-4]</sup> Plasma cells are usually found in the spleen, tonsils, lymph nodes, nasal mucosa, upper airway, lamina propria of the gastrointestinal tracts and inflammation sites and their major function is to produce Igs (also called antibodies)<sup>[5,6]</sup> [Figure 6].

When B-cells develop into abnormal plasma cells (myeloma cells), they make large amounts of one type of abnormal Ig (monoclonal Ig), also called an M-protein or paraprotein and can be measured in the blood and urine.<sup>[7]</sup> Sometimes, the myeloma cells do not make whole Igs and only release the free light chains into the blood. These are called Bence-Jones proteins, which have a characteristic property of coagulating when heated to 50°C but redissolve at 70°C.<sup>[7]</sup>



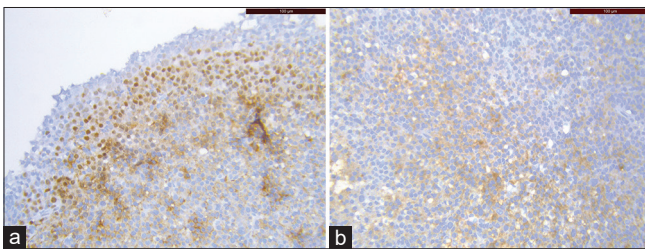
**Figure 2:** Histopathological image shows sheets of neoplastic cell proliferation with plasmacytic differentiation (H&E, x400)



**Figure 4:** Immunohistochemistry showed negative staining with kappa light chain (IHC - kappa light chain, x400)

Some of the molecular alterations associated with progression and unfavorable prognosis of disease are activation of one of the three cyclin D genes, translocations that nonrandomly involve the Ig heavy chain locus on chromosome 14q32 and one of five well-defined chromosomal partners: 11q13 (cyclin D1), 6p21 (cyclin D3), 4p16 (fibroblast growth factor receptor 3 and MM SET domain), 16q23 (c-maf) and 20q11 (mafB)<sup>[2,3]</sup> and deletions of chromosomes 13 and 17 (17p13; the p53 locus).<sup>[3,8]</sup>

The complex changes in MM involve the transformation of malignant cells and bone marrow microenvironment disturbances. Interactions between the myeloma cell and the stromal and hematopoietic stem cells in the marrow microenvironment, and also the extracellular matrix activate multiple signaling pathways, resulting in proliferation/antiapoptosis of the myeloma cell. Myeloma cells are thought to increase the production of proosteoclastogenic cytokines such as macrophage inflammatory protein-1, parathyroid hormone-related protein, vascular endothelial growth factor and interleukin-6. An increase in expression of receptor activator of NF- $\kappa$ B ligand by osteoblasts and a decrease in the level of its decoy receptor osteoprotegerin result in activation of osteoclasts.<sup>[8]</sup>

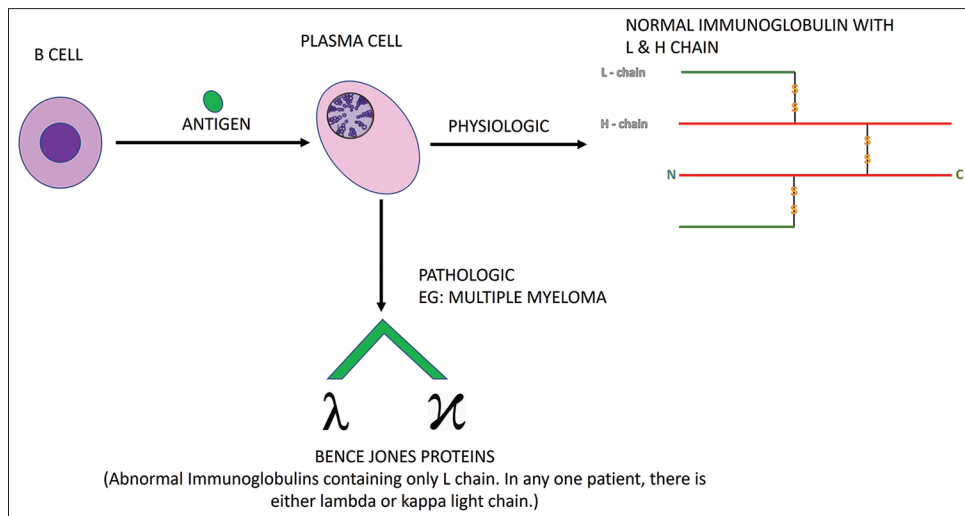


**Figure 5:** (a and b) Immunohistochemical staining with showing diffuse positivity (IHC - lambda light chain,  $\times 400$ )

Various classifications in the past have categorized plasmacytomas based on the tumor burden (Durie-Salmon staging system), and laboratory and radiologic parameters.<sup>[9]</sup> As per the diagnostic criteria published by the International Myeloma Working Group in 2014, symptomatic MM can be determined if the proportion of plasma cells in bone marrow is more than or equal to 10%, M-protein detectable in serum as well as urine and if the patient fits the CRAB criteria which includes hypercalcemia (serum calcium above normal), renal insufficiency (serum creatinine  $> 2$  mg/dl), anemia (hemoglobin  $< 10$  g/dl) and bone lesions (lytic lesions and osteoporosis). Anemia is usually a normocytic, normochromic variant related to overproduction of abnormal plasma cells or high monoclonal protein (M-protein) level.<sup>[2]</sup> Without intervention, excessive calcium or overproduction of M-proteins can lead to kidney impairment which can progress to kidney failure.<sup>[2]</sup>

Newly defined biomarkers are the presence of clonal plasma cells in bone marrow  $\geq 60\%$ , ratio of involved/uninvolved free light chains  $\geq 100$  and more than one focal lesion of 5 mm size or more on magnetic resonance imaging.<sup>[2,10]</sup> Hyperviscosity syndrome, cryoglobulinemia and amyloidosis are also often associated with MM.<sup>[11]</sup>

Oral presentation is considered to be a sign of disease progression and its incidence varies from  $< 2\%$  to 70%. It can manifest as swelling, pain, numbness, bleeding, mobile teeth, xerostomia, amyloid deposits, root resorption and mobility, labial anesthesia, jaw radiolucencies and fractures.<sup>[12,13]</sup> Oral manifestations of myelomatous lesions can mimic common dental pathologies, for instance, periapical or periodontal abscess, severe gingivitis or periodontitis. When patients with a history of myeloma present with an oral lesion,



**Figure 6:** Diagrammatic illustration showing the formation of normal and abnormal (Bence-Jones proteins) immunoglobulins

oral plasmacytoma must be part of the differential diagnosis.<sup>[14]</sup>

Treatment for MM is majorly influenced by the age, general health of the patient, previous therapy and the presence of complications of the disease. Disease-specific therapy includes initial consolidation with high-dose chemotherapy and autologous hematopoietic stem cell transplantation, maintenance therapy, salvage therapy and supportive care includes management of hypercalcemia, skeletal complications, anemia, infections and pain.<sup>[8]</sup> Oral manifestations of MM must be promptly recognized, as a short survival time after discovery of an oral lesion has been observed in a series of cases,<sup>[14]</sup> as was the fate of our patient. With the introduction of chemotherapy, the 10-year survival rate has improved to about 3%. Greater improvement in prognosis has been achieved with advent of therapies such as pulse corticosteroids, thalidomide, lenalidomide, bortezomib and autologous and allogeneic stem cell transplantations.<sup>[1,3,15]</sup>

## CONCLUSION

An aggressive approach with novel therapeutics is seemingly justified in patients with oral plasmacytoma.

## Declaration of patient consent

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

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Board PA. Plasma cell neoplasms (Including Multiple Myeloma) Treatment (PDQ®). In: PDQ cancer information summaries. Bethesda (MD): National cancer institute (US);2021.
2. Gerecke C, Fuhrmann S, Striffler S, Schmidt-Hieber M, Einsele H, Knop S. The diagnosis and treatment of multiple myeloma. *Dtsch Arztebl Int* 2016;113:470-6.
3. Fairfield H, Falank C, Avery L, Reagan MR. Multiple myeloma in the marrow: Pathogenesis and treatments. *Ann N Y Acad Sci* 2016;1364:32-51.
4. San-Miguel JF, Mateos MV. Can multiple myeloma become a curable disease? *Haematologica* 2011;96:1246-8.
5. Sabarinath B, Sivapathasundharam B, Vasanthakumar V. Plasma cell granuloma of lip. *Indian J Dent Res* 2012;23:101-3.
6. Namboodiripad PC, Namboodiripad PC, Jaganath M, Sunitha B, Sumathi A. Plasma cell granuloma in the oral cavity. *Oral Surg* 2008;1:206-12.
7. The Plasma Cells – Canadian Cancer Society. Available from: <https://www.cancer.ca/en/cancer-information/cancer-type/multiple-myeloma/multiple-myeloma/the-plasma-cells/?region=on>. [Last accessed on 2021 Aug 17].
8. Singhal S, Mehta J. Multiple myeloma. *Clin J Am Soc Nephrol* 2006;1:1322-30.
9. Durie BG, Kyle RA, Belch A, Bensinger W, Blade J, Boccadoro M, et al. Myeloma management guidelines: A consensus report from the Scientific Advisors of the International Myeloma Foundation. *Hematol J* 2003;4:379-98.
10. International Myeloma Foundation. International Myeloma Working Group (IMWG) Criteria for the Diagnosis of Multiple Myeloma. International Myeloma Foundation. Available from: <https://www.myeloma.org/international-myeloma-working-group-imwg-criteria-diagnosis-multiple-myeloma>. [Last accessed on 2021 Aug 17].
11. Sandoval CL, Acosta BJ, Contreras Ó, Vargas J. Multiple myeloma and light-chain amyloidosis: A rare presentation. *Case Rep* 2018;4:99-110. Available from: [http://www.scielo.org.co/scielo.php?script=sci\\_arttext&pid=S2462-85222018000200099](http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S2462-85222018000200099). [Last accessed on 2021 Aug 17].
12. Romano A, Marescalco MS, Liardo C, Villari L, Vetro C, Conticello C, et al. Oral lesion as unusual first manifestation of multiple myeloma: Case reports and review of the literature. *Case Rep Hematol* 2014;2014:529452.
13. Pinto LS, Campagnoli EB, Leon JE, Lopes MA, Jorge J. Maxillary lesion presenting as a first sign of multiple myeloma: Case report. *Med Oral Patol Oral Cir Bucal* 2007;12:E344-7.
14. Cardoso RC, Gerngross PJ, Hofstede TM, Weber DM, Chambers MS. The multiple oral presentations of multiple myeloma. *Support Care Cancer* 2014;22:259-67.
15. Cömert M, Güneş AE, Sahin F, Saydam G. Quality of life and supportive care in multiple myeloma. *Turk J Haematol* 2013;30:234-46.