INTRODUCTION

Medullary plasmacytoma (MP) or osseous or solitary bone plasmacytoma is a specializing hematopathology lesion typically present with local symptoms, such as pain, paresthesia and pathologic bone fractures as a result of proliferation of plasma cells. The most often involved sites are active hematopoietic long bones and the vertebrae. The clinical course of disease is identical to spectrum of other plasma cell dyscrasias. The diagnostic criteria include punched-out radioluencies, monoclonal plasma cells and M protein. This lesion should be considered for the differential diagnosis of bone tumors. It is highly radiosensitive although combination modalities of radiation, surgery and chemotherapy have been used in the treatment. The long-term follow-up is essential. We report two rare cases of oral MP with unusual clinical presentation.

Keywords: Calcium levels, renal insufficiency, anemia and bone lesions’ criteria, immunohistochemistry, monoclonal serum protein, positron emission tomography

CASE REPORTS

Case 1
A 60-year-old female patient came with complaints of pain and paresthesia of lower lip for 1 month. The patient had undergone extraction of healing socket-38 one week ago. Intraoral examination revealed the presence of a healing socket-38, and no other intraoral lesions were evident. Tenderness on palpation in relation to the left lower labial vestibule was elicited. An orthopantomogram revealed a well-defined unicocular radiolucent lesion involving the
body of the mandible [Figure 1a]. Three-dimensional computed tomography (CT) scan revealed an osteolytic lesion measuring about 3 mm × 4 mm × 2 mm in the left posterior mandible [Figure 1b]. With provisional diagnosis of aneurysmal bone cyst, an incisional biopsy revealed solid proliferation of atypical plasmacytoid cells with eccentric nuclei and basophilic cytoplasm [Figure 1c1 and c2]. An Immunohistochemical analysis revealed membrane immunopositivity for kappa chain [Figure 1d1] and immunonegative with faint background staining for lambda [Figure 1d1]. Hematological examination revealed a red blood cell (RBC) count of 4.0 × 10^6/mm^3, hemoglobin (Hb) – 11.02 g/dl, white blood cell (WBC) count – 8800/mm^3, platelets – 3.15 × 10^5/mm^3, serum protein – 6.0 g/dl, serum calcium – 4.7 mg/dl and gamma globulin – 31.6, all of which were within normal limits, and other serum electrolytes were also found to be normal. A urine test, which was done for Bence Jones protein, was positive. An electrophoresis revealed abnormal free light chain ratio [Figure 1e].

**Case 2**

A 48-year-old male reported with complaint of a painful swelling in the left back jaw region over the past 2 months. The pain was dull and nonradiating in nature, and the swelling had gradually increased over the past 2 months. On extraoral examination, a firm mass measuring approximately 5 cm was noted, from the left preauricular region to the mandibular angle. Intraoral examination revealed a diffused mass on the retromolar pad area, covered with normal oral mucosa. Orthopantomograph revealed an ill-defined radiolucent mass in the left mandibular angle and ramus [Figure 2a]. CT scan showed a 4.8 cm × 3.7 cm × 3.7 cm destructive mass involving the body, angle and ramus of mandible [Figure 2b]. Based on the clinical and radiological findings, a provisional diagnosis of ameloblastoma or giant cell lesion was given. An incisional biopsy was done under local anesthesia. The microscopic examination showed monotonous sheets of

---

Figure 1: (a and b) Orthopantomograph shows osteolytic lesion (unilocular) in the posterior aspect of the left side of the mandible, and threedimensional computed tomography scan revealed an osteolytic lesion in the left posterior mandible. (c1 and c2) H&E staining ×20 shows sheets of closely packed cells resembling plasma cells and ×40 shows the presence of two nuclei within a single cell. (d1 and d2) Immunohistochemistry staining ×40 shows tumor cells’ strong Kappa positivity and negative lambda staining ×40 with faint background staining. (e) Electrophoresis shows the altered the serum free light chain ratio

Figure 2: (a) OPG shows radiolucency involving the left ramus of the mandible. (b) Three-dimensional facial scan shows massive osteolytic lesion eroding ramus of mandible. (c1 and c2) H&E staining (×20) shows sheets of monotonous population of cells with eosinophilic cytoplasm and ×40 shows richly cellular areas with eccentric nucleus. (d1-d3) CD138, kappa chain immunostaining (×40) shows tumor cells showing strong positivity and immunonegative with faint background staining for lambda. (e) Serum protein assay shows altered the free light chain ratio
dense proliferation of neoplastic cells with highly vascular stroma and inflammatory cells. The cell population varied from small, well-differentiated cells with an eccentric nucleus and basophilic cytoplasm to less differentiated atypical cells resembling immunoblast [Figure 2c and e]. An immunohistochemical analysis revealed positivity with Vimentin, CD45, CD138, kappa chain and negative expression for lambda chain [Figure 2d and d]. Hematological examination revealed a RBC count of $4.73 \times 10^6$/mm$^3$, Hb – 14.9 g/dl, WBC count – 8600/mm$^3$, platelets – $1.5 \times 10^5$/mm$^3$, total serum protein – 7.8 g/dl, globulin – 2.2 g/dl and serum calcium – 9.7 mg/dl and gamma globulin – 23.4, all of which were within normal limits, and other serum electrolytes were also found to be normal. A urine test performed for Bence Jones protein was negative. The free light chain ratio was altered [Figure 2e].

DISCUSSION

Plasma cell neoplasm usually affects the bone and bone marrow in the older age groups. The most common clinical presentation is bone pain, pathologic fractures, hypercalcemia and neurological symptoms. The roentgenographic findings vary from well-defined radiolucency or punched-out appearance to ill-defined destructive radiolucencies with ragged border. Clinical and radiologic variants of plasmacytoma can be identified by genetic loss and genetic gains in chromosome – 13, 1p, 1q, 14q, 19p, 9q and 1q. Many authors have considered solitary plasmacytoma as a primary manifestation of further devastating disease – multiple myeloma (MM). MP progressed to MM due to high-grade angiogenesis. A few authors proposed that MP could be a middle plane between monoclonal gammopathy and MM.

Microscopically, the lesions are composed of sheets or aggregates of atypical plasma cells and eccentrically placed nucleus with pink cytoplasm and perinuclear halo. Amyloid deposition may be seen in some cases. It is indeed a challenging task to the pathologists to disentangle potential differences in disease pattern of MP and MM. Some authors stated that role of chemokine receptors and CAM in the tumor microenvironment contributes to the disease presentation. A well-differentiated plasmacytoma is difficult to distinguish from reactive proliferation. Differential diagnosis of moderate and poorly differentiated plasmacytoma is metastatic melanoma and malignant lymphoma. A complete blood picture, biochemical analysis of serum protein and marrow aspiration/biopsy are required for the diagnosis of this disease. A positron emission tomography (PET) scan or CT is required for evaluation of metastasis. The diagnostic CRAB criteria are calcium levels, renal insufficiency, anemia and bone lesions. Serum electrophoresis and immunohistochemistry attributed to rule out its disseminated form. The final diagnosis of the present cases were done based on radiological, histopathological findings, immunohistochemical and supportive investigative modalities.

The primary treatment for patients with solitary lesion is localized radiation therapy. Surgical therapy is recommended for structural unstable bony lesions.

Bisphosphonates is advised for patients with osteopenia. Two concurrent distinct plasmacytomas with no bone marrow involvement, radiation to both sites followed by systemic therapy is recommended. A follow-up is essential after completion of radiotherapy, complete laboratory tests every 4–6 months for 1 year and annually thereafter.

CONCLUSION

MP of the oral cavity is a distinct plasma cell neoplasm that requires clinical, radiological, and histopathological and immunohistochemical correlation to arrive at the right diagnosis. New modalities such as PET, electrophoresis will have a prognostic value of disease status and the survival analyses, especially in the highrisk category of patients.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol 2014;15:e538.
2. Dayisoylu EH, Ceneli O, Coskunoglu. Solitary Plasmacytoma of the mandible: an uncommon entity. I rundown Med J 2016;18:e22932.
3. Caballero BR, Santolino SS, Perea BGM, et al. Mandibular solitary plasmacytoma of the jaw: A case report. Med Oral Patol Oral Cir Buccal 2011;16:e47-50.
4. Salogub G, Lokhmatova E, Sozin S. Solitary Bone and Extramedullary Plasmacytoma, Multiple Myeloma – A Overview, Dr. Ajay Gupta (Ed.), 2012 ISBN: 978-953-307-768-0, InTech. Available from: http://www.intechopen.com/books/multiple-myeloma-an-overview/
plasmacytoma. [Last accessed on 2017 Oct 23].
5. Kilciksiz S, Celik OK, Aqaoglu FY, Haydaroglu A. A Review for Solitary Plasmacytoma of Bone and Extramedullary Plasmacytoma. The Scientific World Journal 2012;2012:895765.
6. Romano A, Marescalco MS, Liardo C, Villari L, et al. Oral Lesion as Unusual First Manifestation of Multiple Myeloma: Case Reports and Review of the Literature. Case Reports in Hematology 2014;2014:529452.
7. Hughes M, Doig A, Soutar R. Solitary Plasmacytoma and multiple myeloma: adhesion molecule and chemokine receptor expression patterns. Br J Haematol 2007;137:486.
8. Dimopoulos MA, Hillengass J, Usmani S, et al. Role of magnetic resonance imaging in the management of patients with multiple myeloma: A consensus statement. J Clin Oncol 2015;33:657.
9. Paiva B, Chandra M, Vidriales MB, et al. Multiparameter flow cytometry for staging of solitary bone plasmacytoma: New criteria for risk of progression to myeloma. Blood 2014;124:1300.
10. Hill QA, Rawstron AC, de Tute RM, Owen RG. Outcome prediction in plasmacytoma of bone: A risk model utilizing bone marrow flow cytometry and light-chain analysis. Blood 2014;124:1296.