MULTIPLE MYELOMA PRESENTING AS PERiapICAL PATHOLOGY

ABSTRACT
Multiple myeloma is a relatively rare malignant haematological disease; characteristic of it are multicentric proliferation of plasma cells in the bone marrow, osteolytic bone lesions and detectable presence of monoclonal immunoglobulins in serum and/or urine. Diagnosis of multiple myeloma can sometimes be challenging because of the abundance of its clinical signs and symptoms and because of the different types of unusual clinical manifestations of the malignant plasma cells. The first sign of the disease in the case of a 55 years old female was periapical swelling in the anterior maxilla in relation to 11.

KEY WORDS
Multiple myeloma, osteolytic lesion in maxilla, periapical radiolucencies, plasmacytoma.

INTRODUCTION
Multiple myeloma is a relatively rare neoplastic proliferation of monoclonal plasma cells. The disease was first described in 1844 as a disease characterised by proliferation of malignant plasma cells and subsequent overabundant production of monoclonal paraprotein. An intriguing feature of multiple myeloma is that the plasma cells are neoplastic and, therefore, may cause unusual manifestations.

Jaw lesions are rarely the first sign of the disease and their incidence varies from 8-15\%. In the given case the initial and first sign of it presentation was as a periapical lesion in the anterior maxilla of a 55 year old female. Multiple myeloma represents 1\% of all cancers and 10\% of all haematological neoplasms.

Case Report
A 55 year old female patient reported to the craniofacial surgery unit of Annasawmy Mudaliar General Hospital, Bangalore with a complaint of swelling in the right side of the face near the nostril lasting for a period of six months which was slow growing and not painful. Earlier she consulted an endodontist with a complaint of pain and tenderness in relation to 11. She was diagnosed as having a non vital 11 with periapical radiolucency. Endodontic therapy in 11, along with an attempted incision and drainage was performed by the attending Endodontist. Later she was referred for apicoectomy in relation to 11.

On examination the patient was well built; had no history of any systemic disease. Extraorally, the patient had a diffuse swelling in the right ala region measuring 1.0 cm x 1.5 cm. The colour of the skin was normal and there was no pain on palpation. Intraorally, the patient had a restored 11 tooth and periapical swelling in relation to it. The lesion measured 2.5x3.0 cm, firm in consistency; the overlying mucosa was reddish in colour with break in the continuity of the mucosa (Fig. 1).

Intra oral periapical radiograph revealed ill defined periapical radiolucency in relation to 11 (Fig. 2). The orthopantomograph was non contributory.

Routine blood examination was carried out and all values were within normal limits. Under local anaesthesia the lesion was surgically enucleated in toto with intravenous sedation. The enucleated mass was soft and fleshy in consistency, creamish brown in colour and had an irregular surface. The specimen was sent for histological examination with a clinical provisional diagnosis of periapical granuloma.

HISTOLOGICAL FINDINGS
The haematoxylin and eosin stained sections of the lesion showed an extremely cellular lesional tissue showing diffuse sheets of neoplastic variably differentiated plasmacytoid cells in the connective tissue stroma. The nucleus of these cells appeared round and eccentric with fine granular chromatin and evident nucleolus. Mitotic activity was evident. These features are characteristic of solid malignant hemopoietic neoplasm and hence the lesional tissue in the stained section was suggestive of plasmacytoma (Fig. 3).

The patient was advised to have, her urine analysed for the presence of Bence Jones protein, serum electrophoresis, a computerised axial tomograph (CT) of the head and neck and a full body positron emission tomograph (PET) scan.

Blood examination revealed increase of free kappa light chains (392 mg/L). In the urine sample free kappa light chain was seen (146mg/L) and urine kappa lambda ratio was elevated (130.4). CT Scan (paranasal with Axial and Coronal) was performed which showed a small destructive lesion in the maxillary alveolar process in the right paramedian region extending to the hard palate; associated small soft tissue mass was also seen. Small destructive lesions were seen in the frontal bone (Fig 5), left frontal
sinus in midline and left paramedian extending to the left ethmoidal sinus (Fig.6). Associated mild enhancing soft tissue mass was seen extending intracranially in the epidural plane. Small soft tissue mass was seen in the right frontal sinus. A PET CT revealed bone defects in the anterior hard palate and multiple lytic expansile lesions in the sternum and calvaria.

Detailed immunohistochemistry (IHC) work up was done for the following markers; and the following were observed on the lesional tissue.
1. CD138 - strongly positive (+++)
2. Kappa light chain- strongly positive (+++)
3. Lambda light chain- negative
4. Ki67-70% proliferation (Fig 4)

The patient was referred to the regional oncology unit and was treated with chemotherapy and is awaiting a bone marrow transplant.

**DISCUSSION**

Multiple myeloma is a debilitating malignancy and it is part of a spectrum of diseases ranging from monoclonal gammopathy of unknown significance to plasma cell leukaemia. Plasma cell tumours are lymphoid neoplastic proliferations grouped among B-cell peripheral lymphomas, according to the classification of the European-American International Lymphoma Study Group. They may affect a single bone,
which is a condition called solitary plasmacytoma or may involve only soft tissues - an extramembranous plasmacytoma. However, in approximately 95% of the cases, it involves several bones, and hence is called multiple myeloma. The signs and symptoms of the disease were first documented by Samuel Solley in 1844, though the name multiple myeloma was given only in 1873 by Jvon Rustzky. It is also known as Kahler's disease and medullary plasmacytoma. The disease occurs frequently in individuals of 50-80 years of age with a mean age of 60 years. The lesion is rarely seen in patients younger than 40 years of age. It is more frequently seen in men, of all races, but more commonly in African-Americans and less commonly in the Asian population. Bone involvement secondary to bone marrow infiltration is most common. Frequently affected sites are vertebrae, ribs, skull, femur, clavicle, pelvis and scapula. Jaw lesions in multiple myeloma may vary from 5-39% of cases and are the first sign of disease in approximately 17% of patients. Though its occurrence in the maxilla and mandible is very common oral lesions rarely appear as primary manifestation of the disease. More than 30% of patients with multiple myeloma develop osteolytic lesions in the posterior mandible. Oral manifestations such as gingival haemorrhage, odontalgia, paraesthesia, dental mobility, ulcerations may be the first or early presenting symptom.

Multiple myeloma lesions are more common in the mandibular posterior region but in this case it presented itself as anterior maxillary swelling. Hence when single or widespread involvement is seen in jaw bones it is prudent to include multiple myeloma in the differential diagnosis. A plain radiograph remains the golden standard for imaging procedure for diagnosis and staging of multiple myeloma. Soap bubble appearance of the osteolytic lesion can be frequently seen. PET scanning and MRI can add great value in diagnosis/prognosis and prediction. MRI has higher sensitivity and specificity in diagnosis and treatment.

Fine needle aspiration of jaw swellings can yield useful results. Aspiration of bone/bone marrow can also be resorted to. Microscopic appearance of the biopsy of the lesion and the bone marrow of multiple myeloma, characteristically show a monoclonal population of proliferating plasma cells with variable maturity. Differential diagnosis of jaw swellings can be exhaustive clinically but main histopathological differential diagnostic features are lymphomas (lympho-plasmacytotic), Granulomatosis (Langerhans cell) and metastatic tumours.

Immunohistochemistry proves a useful tool to differentiate lymphomas and multiple myelomas and gives an insight into the molecular basis of the disease. Myeloma cells express Syndecan–1 (CD 138) surface antigen that is limited to terminally differentiated plasma cells of B cell lineage.

Light chain restriction for Kappa or Lambda is usually observed, and nearly 70% of plasma cell neoplasms are Kappa positive. AE1/AE3, HMB45 and S100 immunoreactivity in plasmacytomas is generally considered rare but are done to exclude other pathologies.

Monoclonal precursors of myeloma cells in bone marrow originate in lymph nodes. Not very well understood are the mechanisms that enable these precursor cells to selectively lodge in the bone marrow where the microenvironment is conducive to their differentiation, proliferation and survival. However, it is probable that bone marrow microenvironment provides specific chemotactic signals, and monoclonal myeloma precursors express necessary cell surface receptors for bone marrow lodgement. There is adhesion to and transmigration of the endothelium that lines the bone marrow sinuses by monoclonal precursors, which contribute to preferential trafficking of these cells in the bone marrow. The interaction between tumour cells and bone marrow stromal cells promotes neoangiogenesis essential for the growth of myeloma and facilitates lodging of new tumour cells in the bone marrow and their subsequent uncontrolled proliferation. This leads to osteolytic activity responsible for the development of bone lesions characteristic of myeloma.

What clinched the diagnosis in the case presented was the histological picture followed by subsequent immunohistochemical diagnosis and diagnostic workup.

Conclusion

Multiple myeloma is a disseminated plasma cell neoplasm. It is a systemic B cell lymphoproliferative disease with varied head and neck and systemic manifestations. Diagnosis of multiple myeloma can be established by haematologic and biochemical findings, urine analysis and skeletal radiographic survey. Cystic and radiolytic lesions of the jaw bones reinforce the fundamental role of the dentist in the recognition and early diagnosis of many a systemic condition including multiple myeloma. It should be noted the disease has an unfavourable or poor prognosis. Ongoing research in the field of molecular biology and phenotyping can improve diagnosis, classification, management and prognostic protocols of multiple myeloma.

REFERENCES