CASE REPORT

Metastatic calcification of floor of the mouth secondary to chronic renal failure—report of a rare case with atypical presentation

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Soft-tissue calcification is always pathological. Metastatic calcification is calcification of soft tissues owing to hyperphosphataemia with or without hypercalcaemia. Metastatic calcification of oral cavity is extremely rare. A case report of metastatic calcification of the floor of the mouth with atypical radiologic and clinical picture is presented here along with a review of earlier reports. A chance finding of the granular oral mucosa on palpation led to a radiographic examination revealing granular calcifications of the floor of the mouth. Blood chemistry and hormone analysis revealed chronic renal failure and hyperparathyroidism. A diagnosis of metastatic calcification secondary to renal failure was made and the treatment was aimed at correcting the renal failure without any intervention for the asymptomatic calcifications. Key differences between the present case and other cases reported in the literature are outlined.

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Introduction

Metastatic calcification (MC) is a pathological condition characterized by the deposition of calcified products in otherwise normal tissues because of hyperphosphataemia with or without concurrent hypercalcaemia. MC may be seen in patients with chronic renal failure (CRF), hyperparathyroidism, extensive bone malignancy, hypervitaminosis D, diffuse myelomatosis and milk-alkali syndrome.¹ MCs have been reported in various tissues such as the lungs, under skin, blood vessels, kidneys, central nervous system and breasts, among others.² MC presenting clinically as an oral lesion is extremely rare. To date, only five cases of MC involving the oral soft tissues have been described, and to the best of our knowledge, no case has been reported

involving the floor of the mouth till now in the English literature. This is a report of a case of MC of the floor of the mouth. The present case differed from other reports of oral MC in many aspects.

Case report

A 65-year-old asymptomatic, edentulous female patient was referred by the Department of Prosthodontics, Surendera Dental College and Research Institute, Rajasthan, India, for investigating a chance finding of multiple small granular radio-opacities in the right premolar residual alveolar ridge region on orthopantomograph (Figure 1). She had undergone extraction of all her teeth over a period of 5 years owing to chronic generalized periodontitis. She did not have any significant medical or personal history. On

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Figure 1 Orthopantomograph showing granular calcifications in the mandibular right premolar residual alveolar ridge region.

examination, the oral mucosa appeared normal on inspection including the site in question. However, on palpation, the mucosa in the right premolar region felt granular. The mucosa was otherwise asymptomatic and non-tender. The floor of the mouth also felt the same anteriorly and on the left side. Salivary flow appeared normal from submandibular ducts bilaterally. A mandibular occlusal view revealed clusters of multiple small granular radio-opacities (Figure 2). On the right floor of the mouth, the clusters were arranged in a linear fashion medially and in a ring laterally. Anteriorly on the floor of the mouth, they formed a linear pattern ending in an irregular arrangement. On the left side of the floor of the mouth, the clusters had an irregular arrangement with a single speck posteriorly.

Blood chemistry revealed normal serum calcium, 9.0 mg dl^{-1} and elevated phosphate, 8.4 mg dl^{-1} ; serum creatinine, 13 mg dl^{-1} ; blood urea nitrogen, 118 mg dl^{-1} ; uric acid, 10.6 mg dl^{-1} ; total plasma protein, 7.0 g dl^{-1} ; serum albumin, 4.2 g dl^{-1} ; alkaline phosphatase, 200 IU ; and parathyroid hormone, 70 pg ml^{-1} . A CT scan of the neck was advised, which revealed mild hyperplasia of the parathyroid glands. Radiographic survey of the chest, abdomen, pelvis and limbs did not reveal any soft tissue calcifications. There was no radiographic evidence of resorption of phalangeal bones. The patient refused to undergo biopsy. The case was diagnosed as MC of the floor of the mouth secondary to renal failure. As the calcifications were asymptomatic, the patient was advised against any surgical intervention for the calcifications. The patient was referred to a nephrologist for further management of CRF where dietary changes, renal dialysis and parathyroidectomy were advised. A subtotal parathyroidectomy was performed. Post-operatively, there was significant clinical improvement with serum calcium (9.7 mg dl^{-1}), phosphate (6.1 mg dl^{-1}) and parathormone (0.16 ng ml^{-1}) in normal range. At 1-year follow-up, the clinical and radiological picture was essentially unchanged.

Discussion

The aetiopathogenesis of MC is complex and is not clearly understood. It is generally agreed that hyperphosphataemia

with or without hypercalcaemia along with alteration in local pH plays a significant role in the pathogenesis of MC. It has been suggested that a high calcium-phosphate product is associated with soft tissue MC.³ Hyperphosphataemia has also been implicated in the pathogenesis of secondary hyperparathyroidism. Conditions associated with hyperphosphataemia and hypercalcaemia are CRF, hyperparathyroidism, sarcoidosis, disseminated malignancy, multiple myeloma and metastatic carcinoma.

CRF is commonly associated with calcium and phosphorous imbalance along with hyperparathyroidism. As the renal tubular function progressively decreases in CRF, the ability to reabsorb calcium and excrete phosphorous is significantly affected leading to hyperphosphataemia. Low serum calcium and raised serum phosphate stimulates the synthesis and release of parathyroid hormone that in turn stimulates osteoclastic activity, reabsorption of calcium, urinary excretion of phosphorous along and stimulation of renal synthesis of calcitriol. Calcitriol promotes absorption of dietary calcium and phosphorous. With progressive deterioration of renal function, the calcium-phosphorous homeostasis is lost, ultimately leading to hyperphosphataemia in most of the patients of end-stage renal disease. Decreased synthesis of renal calcitriol in CRF also contributes to hypocalcaemia by decreased absorption of calcium from the intestine.

Secondary hyperparathyroidism, adynamic bone disease, hypermagnesemia, vitamin D and K overload, aluminium intoxication, metabolic alkalosis and tissue injury may also play a role in the aetiopathogenesis of MC.¹

Based on their crystallographic properties, the deposits in MC have been divided into two groups. Type I has an X-ray diffraction pattern of hydroxyapatite identical to that found in the bone, and Type II has a diffraction pattern of an amorphous compound with

Figure 2 Occlusal view of the mandible showing calcifications of the floor of the mouth.

thermochemical properties of whitlockite. Dystrophic calcification is similar to hydroxyapatite.⁴

Dystrophic calcification, when compared with MC, is more common and results from precipitation of calcium salts in injured, degenerating or necrotic tissue. It generally involves visceral organs, corneas and vascular structures. Calciphylaxis is a life-threatening form of extraskeletal calcification, characterized by systemic medial calcification of the arterioles leading to ischaemia and subcutaneous necrosis. Based on history and biochemical findings of hyperphosphataemia, deranged renal function and secondary hyperparathyroidism, the present case was diagnosed as MC. Advanced imaging techniques such as ultrasonography and CBCT might have revealed more details about the nature of calcification and the tissues surrounding it; however, these investigations were not advised in the present case owing to the poor financial status of the patient.

Intraoral MC is extremely rare to come across, and, to the best of our knowledge, there are no reported cases of MC of the floor of the mouth. The present case differed from other reported cases of intraoral MC in some key aspects. While all the previous reports of MC involving oral cavity were associated with multiple sites of calcifications,⁵⁻⁸ the present case had MC of only the floor of the mouth. Also, contrary to the most common aetiologic factors cited for intraoral MCs as chronic occlusal and denture trauma,^{5,6,8,9} no such correlation could be made in the present case. All the cases of intraoral MC reported so far have presented as a painful or painless nodule with or without ulceration,^{5,6,8,9} unlike the present case that was asymptomatic and granular on palpation. The radio-opacities in the present case were multiple, small and spread over a wide area of the floor of the mouth in contrast to others where it presented

as a solitary radio-opaque mass. Hyperphosphataemia was a consistent finding in all the reports, including the present one. All the cases reported in the literature, including the present case, have occurred in adults, probably related to the fact that CRF is primarily a disease of adults.

The microscopic picture of MC has been described as a mass of fibrous connective tissue containing extensive, amorphous, variably sized and irregularly shaped calcified deposits surrounded by large, foreign-body giant cells and epithelioid histiocytes with a variable chronic inflammatory cell infiltrate.^{5,6,8} The diagnosis of MC could not be verified histopathologically in the present case, as the patient refused biopsy because of asymptomatic nature of the calcifications.

The differential diagnosis should include calcifying cysts and tumours of soft tissues, sialoliths, lymph node calcifications, phleboliths and dystrophic calcifications. All cases of soft-tissue calcification should undergo investigations to rule out calcium-phosphorous imbalance, renal insufficiency and hyperparathyroidism, as renal insufficiency is usually the starting point. The management of intraoral MC involves managing CRF, hyperparathyroidism, calcium-phosphorus imbalance and local excision of calcified lesion if it interferes with function. The treatment in the present case was aimed at restoring her renal function, controlling hyperphosphataemia and parathyroid hormone levels. Since the calcifications were asymptomatic and did not interfere with function, surgical intervention for the calcifications was not recommended for the patient.

An early diagnosis of MC may be lifesaving, as it usually is a manifestation of underlying severe systemic disorder.

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