Oral manifestations of secondary hyperparathyroidism: A case report

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Abstract

There are a number of systemic diseases causing bony lesions throughout the body. Secondary hyperparathyroidism (HPT) which is associated with chronic renal failure is one such disorder resulting in a variety of bony changes. Secondary HPT develops when the parathyroid hormone is continuously produced in response to chronic low levels of serum calcium, a situation usually associated with the chronic renal disease. Here we present a case of secondary HPT causing bony changes in maxilla and mandible.

Keywords: Bony changes, chronic renal failure, mandible, maxilla, parathyroid hormone, secondary hyperparathyroidism

Introduction

Hyperparathyroidism (HPT) is an excessive production of parathyroid hormone (PTH) by parathyroid glands. HPT can be of primary, secondary, tertiary, or quaternary types.[1,2] Secondary HPT is a frequent complication of chronic renal failure as a consequence of renal osteodystrophy as in such cases active Vitamin D is not formed which results in low serum calcium ultimately leading to increased PTH levels.

HPT can affect various bones and jaws are no exceptions to it. It can result in generalized loss of lamina dura, changes in trabecular pattern, etc. In the severest form, it can cause enlargement of both jaws and such cases are known as osteitis fibrosa cystica.

In secondary HPT, the jaw bone changes are very rarely seen. Jaw bone changes are a generalized loss of lamina dura, osteopenia, and blurring of normal trabecular pattern causing ground glass appearance. Loss of lamina dura is seen in only 10% of cases. In his study of 42 patients, Silverman found only five cases with partial loss of lamina dura and not a single case with a complete loss.[3] Lamina dura was completely absent in present case. Bicortical expansion was also seen in this case, which is a rare manifestation of metabolic bone diseases.

In this article, a case of secondary HPT associated with gross jaw bone changes is presented and discussed.

Case Report

A 40-year-old female patient reported to our institution with a chief complaint of gradually enlarging, painless swelling of both the jaws of 1-year duration with difficulty in speech. The patient was apparently alright 1 year back when she noticed a swelling in the right mandibular region which was painless and caused no discomfort, except for unesthetic appearance. Subsequently, the patient had consulted an oral health care center and underwent radiological examination followed by excisional biopsy along with the extraction of 47. The mass was diagnosed histopathologically as a peripheral ossifying fibroma. However, 1 month after the mass was excised; patient had developed a swelling in the same region again.

The patient suffered from hypertension since past 12 years and was taking beta blockers ad aspirin 75 mg regularly for the same. In addition, she was suffering from chronic kidney disease and was undergoing regular dialysis since past 4 years. She also had a history of tuberculosis 7 years back for which she had taken dots therapy for 6 months. She had no habits, and her family history was unremarkable. On general examination, the patient had a small built and normal gait. On extra-oral examination, there was a gross

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expansion of the midface. The expansion in the maxilla was more pronounced than that in the mandibular region giving the impression of a cherubic face [Figure 1].

On intraoral examination, a generalized bony hard, nontender expansion of maxilla and mandible arches was observed. No pulsations or fluctuant areas were noted. In the mandibular arch, severe buccolingual expansion was seen which was more pronounced in the lower right posterior segment in the 46, 47, and 48 region [Figure 2]. The maxilla revealed buccopalatal expansion which was more pronounced in the anterior part of hard palate [Figure 3].

The mucosal coverage of maxilla, as well as mandible, was smooth, shiny and normal; except on the right side mandibular region where the opposing teeth had caused indentations [Figures 2 and 3].

On examination of the teeth, 46, 47, 48, 18, and 28 were found to be missing, and there was generalized Grade I mobility with increased interdental spacing in the remaining teeth.

After clinical examination the following list of differential diagnosis was considered:
- Cherubism
- Fibrous dysplasia
- Pagets disease
- Osteopetrosis.

The orthopantomogram (OPG) was taken 1 year back and on OPG, it was noted as the generalized loss of lamina dura with thinning of cortical outlines of maxilla and mandible [Figure 4].

On histopathological diagnosis (H and E stained slide), proliferative stratified squamous epithelium with underlying fibrous connective tissue was observed. Lesional zones having multiple irregularly shaped bony spicules of woven bone in a fibrocellular stroma, as well as plump fibroblasts and occasional giant cells, were present in the surrounding fibrocellular connective tissue [Figure 5].

On biopsy of parathyroid gland, hyperplasia of right and left inferior parathyroid glands was noted. Left inferior parathyroid gland was associated with focal metaphasic ossification and hyperplasia of right and left superior parathyroid gland was also seen. The radiological examination was performed again subsequently. On Maxillary occlusal radiograph, the loss of lamina dura with a displacement of anterior teeth was noted. Decreased trabecular density and blurring of bony trabeculae with multiple foci of radiolucencies in between were noted [Figure 6].

On mandibular occlusal radiograph, similar findings with bone expansion being evident as a prominent feature was noted [Figure 7].

On OPG, it were noted as the generalized loss of lamina dura, decreased trabecular density, and blurring of normal trabecular pattern causing ground glass appearance. Loss of
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cortication of superior and inferior border of the mandible was noted along with demineralization and thinning of cortical boundary of mandibular canal [Figure 8].

OPG also shows the generalized haziness of maxillary and mandibular arches and superio-inferior expansion of the mandible on right side. Cortication of lower border of mandible, inferior alveolar canal, and posterior wall of maxilla and floor of the maxillary sinus were not seen. A dome shaped radiopaque shadow was encroaching upon the left maxillary sinus was appreciated. On closer scrutiny, the cortices of the anterior border of the ramus and posterior border of the maxilla were not traceable on the right side and hence could not be delineated radiographically. On hand, wrist radiographs, signs of subperiostal erosion, or any other bony changes were not seen [Figure 9]. Cone-beam computed tomography (CBCT) examination was performed [Figures 10-13] and on CBCT, it was seen as the generalized osteoporosis involving maxilla, mandible, and visualized skull bones. Maxilla and mandible showed bicortical expansion; however the cortical outlines were hypocalcified.

Internal of the lesion showed both the radiopacities and radiolucencies. Multilocular radiolucencies were seen in the posterior mandible. There was an expansile mass involving the floor and posterior wall of left maxillary sinus, and the mass was found to protrude into the antrum as dome shaped radiopacity in coronal and sagittal sections.

After clinical and radiographic examination and correlating it with the history of patient (chronic kidney disease and dialysis), a provisional diagnosis of secondary HPT was made.

Osteoporotic changes were noted in the long bones, spines, and chest radiograph [Figure 14a-c]. In Figure 15a and b it was noted as:

### Early static images

Both lobes of thyroid show uniform tracer uptake. Both lobes appear slightly elongated with left lobe extended slightly inferomedially.
There are foci of retention is seen in inferior pole region of both lobes of thyroid with normal washout of tracers from rest of the gland.

**Figure 8:** Expanded mandible appears to be continuous with maxilla in posterior region, as distinction is difficult to make out

**Figure 9:** On hand wrist radiograph bony changes cannot be appreciated

**Figure 10:** Cone beam computed tomography coronal view showing bicortical expansion of maxilla and mandible. Dome shaped expansion of maxilla into antrum can be seen bilaterally

**Figure 11:** Axial cone beam computed tomography view showing expansion of maxilla bucally and lingually. Decrease in trabecular density can be appreciated

**Figure 12:** Axial cone beam computed tomography view showing multiple radiolucent areas in body of mandible in posterior regions

**Figure 13:** Sagittal cone beam computed tomography showing ground glass appearance and loss of lamina dura

**Delayed static images**

There are foci of retention is seen in inferior pole region of both lobes of thyroid with normal washout of tracers from rest of the gland.
Single-photon emission computerized tomography-computed tomography
The foci of tracer retention in both lobes of thyroid localize to its anterio-inferior aspect with soft tissue nodularity on fused single-photon emission CT-CT images.

Tc04 thyroid scan
- Both the lobes of thyroid appear normal in size and shape
- There is normal uptake of tracer in both lobes of the thyroid gland
- The salivary uptake is normal.

The following differential diagnosis was considered:
- Cherubism: At the first impression, diagnosis of cherubism was considered but later ruled out as cherubism is more common in younger age, is familial, regresses after certain age and has no relation to kidney disease
- Fibrous dysplasia: Fibrous dysplasia will appear as localized radiopacity after maturation. Features such as generalized loss of lamina dura and cortical thinning are not seen. No association with systemic condition is seen
- Pagets disease: Pagets’ disease is a disease of elderly normally seen after 60 years. Radiographically it will appear as areas of increased radiopacity. Generalized loss of lamina dura is not seen.

The patient was subjected to following blood investigations [Table 1].

Thus, the laboratory investigations confirmed the changes in blood chemistry, which could be attributed to secondary HPT. The patient was referred to Endocrinology Department of a Government Institute for further management and follow-up was carried out after 1 month.

Patient was prescribed a combination of sodium alendronate (bisphosphonate) 35 mg 1 tablet once a week, calcitriol 0.25 mcg once a day (OD), cinacalcet 30 mg OD, and sevelamer (phosphate binder) 400 mg three times a day by the endocrinologist and her alkaline phosphatase levels were reduced to 637 IU/L from 1047 IU/L after 1 month of starting the medications.

Figure 14: (a-c) Osteoporosis of long bones, spine and rib cages are appreciable

Figure 15: (a and b) Nuclear and positron emission tomography-computed tomography of parathyroid and thyroid section (SESTAMIBI) shows tracer uptake by hyperplastic parathyroid gland
Discussion

The first case of HPT was described and treated by Fuller Albright in 1930. The oldest known case was found in a cadaver from an early neolithic cemetery.\(^4\)

HPT can be classified as:

- **Primary** – parathyroid adenoma (80–90% of cases), parathyroid hyperplasia, parathyroid carcinoma. Secondary HPT – Vitamin D deficiency, chronic kidney diseases, rickets, and some forms of osteomalacia [Flow Chart 1].

- **Tertiary** – secondary HPT causing parathyroid hyperplasia are tertiary variants.

Clinical features

Age/sex - HPT is generally seen in middle-aged patients (30–60 years) with women affected three times more than men.\(^5\) In the present case, the patient was a 40-year-old woman.

Signs and symptoms - classically described as abdominal groans, stones, tender bones, psychic moans, and fatigue overtones.

Jaw bone changes are a generalized loss of lamina dura, osteopenia, and blurring of normal trabecular pattern causing ground glass appearance. Loss of lamina dura is seen in only 10% of cases. In his study of 42 patients with HPT Silverman found only five cases with partial loss of lamina dura and not a single case with a complete loss.\(^6\) Lamina dura was completely absent in present case. Gradual loosening, drifting, and loss of teeth may occur. Our patient showed these features.

In persistent disease, well-demarcated, unilocular or multilocular radiolucencies develop known as brown tumors. They may be solitary but are often multiple, and longstanding lesions may produce significant cortical expansion. The frequency of brown tumors in secondary HPT is 1.5–1.75.\(^7,8\) Present case showed multilocular lesions in posterior mandibular body regions along with bicortical expansion of both the jaws.

Osteitis fibrosa generalisata (cystica) is a condition that develops from the central degeneration and fibrosis of longstanding brown tumors. It is seen in approximately 13% cases of (renal osteodystrophy) secondary HPT caused by end-stage renal disease.\(^9\) Significant enlargement of jaws is seen. Similar features are seen in the present case.

Dental considerations – clinicians must be careful to avoid iatrogenic jaw fractures during oral surgical procedures due to the presence of lytic bone lesions and cortical bone loss. Surgical intervention of giant cell tumors is not necessary except for the large deformities.

The need for prophylactic antibiotic therapy to prevent local or distant infection, patient’s ability to tolerate dental treatment, coagulation profile, and severity of cardiac arrhythmias should also be assessed.\(^3\) Patients undergoing dialysis are exposed to a large number of blood transfusions and are therefore at a higher risk of contracting hepatitis B and C.\(^10,11\)

In addition, bacterial endocarditis is an uncommon but serious complication in the dental management of patients undertaking hemodialysis.

The hematological conditions that most commonly affect patients with uremia and renal failure are excessive bleeding and anemia, which are attributed to a combination of factors, including the anticoagulants used for hemodialysis and vascular access maintenance.\(^9\)

Diagnosis

Diagnosis of secondary HPT can be made by correlating the clinical findings and classical radiographic features with the history of chronic kidney disease.

Blood investigations showing elevated PTH and Alkaline phosphatase with normal or low serum calcium levels confirm the diagnosis and also help in differentiating it from primary variant.

Treatment

The treatment remains a challenge for patients and their clinicians. Active Vitamin D compounds such as calcitriol and latest generations Vitamin D analogs such as paricalcitol are very useful. A combination of dietary phosphorus restriction, phosphate binders, calcimimetics, and Vitamin D analogs can be used.\(^12\)

Cinacalcet lowers PTH levels and improves calcium-phosphorus homeostasis.\(^13\)

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**Table 1: Blood investigation reports of patient**

| Tests                        | Patient values | Normal values | Interpretation |
|-----------------------------|----------------|---------------|----------------|
| Serum calcium (mg/dL)       | 9.2            | 8.4-11        | Normal         |
| Serum phosphorus (mg/dL)    | 6.1            | 2.5-4.8       | Increased      |
| Alkaline phosphatase (IU/L) | 1047           | 60-170        | Significantly increased |
| Parathormone levels (pg/mL) | >1900          | 14-72         | Significantly increased |

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**Flow Chart 1: Pathogenesis of secondary hyperparathyroidism**

**Flow Chart 1:** LACK OF VIT D/CHRONIC KIDNEY DISEASE → REDUCED CALCIUM ABSORPTION FROM INTESTINES (HYPOCALCAEMIA) → SECONDARY HYPERPARATHYROIDISM
Patient took the above medication for 3 months but there was no reduction in the PTH level, so she underwent parathyroidectomy and then her PTH level were reduced to 257 pg/ml from 1900 pg/ml [Figure 16a-c].

**Conclusion**

An unusual case of secondary HPT associated with chronic renal disease presenting with classical oral and radiologic features is presented.

**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.

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**Conflicts of interest**

There are no conflicts of interest.

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