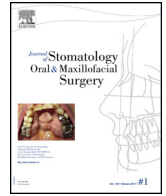




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Case Report

Uremic leontiasis ossea, a rare presentation of severe renal osteodystrophy secondary to hyperparathyroidism



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ABSTRACT

Renal osteodystrophy is a common complication of end-stage renal failure patients. Its most severe osseous complication is characterized by massive thickening of the cranial vault and facial bones, called uremic leontiasis ossea (ULO), with only few cases reported in the literature. A case of a 47-year-old female patient with ULO is presented. Physical examination showed enlargement of the jaws, which hinders proper ventilation and feeding. The computed tomography examination showed marked osseous proliferation in the jaws causing severe bony expansion and loss of normal bony architecture in the skull and the skull base. The most relevant clinical, histopathological and laboratory findings are discussed. The uremic leontiasis ossea causes significant aesthetic and functional changes. Correct diagnosis and management of the factors responsible for the development of bone lesions due to altered bone metabolism are key factors. The maxillofacial surgeon must have the proper knowledge of patient's medical condition and bone maturation status to address an adequate surgical strategy.

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1. Introduction

Chronic renal failure (CRF) is a multifactorial syndrome characterised by progressive and irreversible loss of renal mass and function [1]. CRF is associated with several complications influenced by aetiology, residual renal function, response to treatment, and individual variation [2]. In patients with end-stage renal failure, a common complication is renal osteodystrophy (RO), which is a descriptive term for the skeletal complications that results from pathologic alterations in calcium, phosphate, and bone metabolism [3]. Findings of RO caused by secondary hyperparathyroidism (SH) in cranial bones are frequent and include osteomalacia, osteosclerosis, and erosion of the cortical bone, brown tumours, and resorption of the lamina dura [4].

The most severe osseous complication is characterized by massive thickening of the cranial vault and facial bones, called uremic leontiasis ossea (ULO), with only few cases reported in the literature [4,5]. The term leontiasis ossea is a descriptive term applied to such hyperostotic changes in the facial bones that can lead to bilateral expansion of the malar processes, thus reducing the nasomaxillary angle [4,5].

The progressive enlargement of the facial bones and the facial deformation can lead to encroachment upon the orbital, oral and nasal cavity with its accessory sinuses, exophthalmos, optic nerve compression and potential airway obstruction [4,5].

The differential diagnosis between leontiasis ossea and other conditions with similar clinical appearances is made by clinical and laboratory findings [4]. Management of this condition includes reduction of phosphate levels, treatment of hyperparathyroidism and surgical contouring of the enlarged facial bones [4].

In the current article, a rare case of uremic leontiasis ossea with previous history of end-stage CRF in haemodialysis who developed secondary hyperparathyroidism is reported. The most relevant clinical features and laboratory findings are discussed, highlighting the complex and interdisciplinary manage these patients must have.

2. Case presentation

A 47-year-old female with CRF on hemodialysis for 6 years is referred from the endocrinology service to Maxillofacial Surgery Department with a chief complaint of severe maxillary and mandibular enlargement.

In the clinical history, evaluation by Nephrology and Endocrinology Department recorded three years ago reported that the patient had hyperparathyroidism (PTH 2500 pg/mL, normal range 12–88 pg/mL), hyperphosphatemia (5.5 mg/dL, normal

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range 2.3–4.7 mg/dL) and was normocalcemic (8.4 mg/dL, normal range 8.6–10.2). Parathyroid ultrasound showed increased thyroid size, presenting a complex node in the right thyroid lobule, and complex cysts and calcified nodule with benign appearance in the left thyroid nodule. Bone scintigraphy showed abnormalities with craniofacial predominance, compatible with bone changes.

Patient did not attend to follow-up and the parathyroidectomy surgery was postponed. Two years later, the patient reappeared. At that time, a soft and mobile 1 centimetre size nodule was found in the right thyroid lobule during physical examination. Laboratory screening was made, showing PTH levels over normal range values (3825 pg/mL, normal range 12–88 pg/mL). Hyperthyroidism was diagnosed.

Parathyroid scintigraphy was requested and suggested a parathyroid hyperplasia and showed a nodule in the right thyroid gland with radioisotope hyper-uptake. A total thyroidectomy and 3½ parathyroidectomy was performed, plus auto transplantation of half of the left superior parathyroid gland.

When the patient was admitted at the maxillofacial service, she complaint about significant enlargement of both, maxillary and mandibular bones, with subsequent dyspnea, malocclusion and dysarthria. The physical examination revealed maxillary and mandibular bone tumors, loss of nasal commissure, tooth mobility, and a tumor of the hard palate that compromised proper swallowing and adequate ventilation (Figs. 1 and 2).

The craniofacial computer tomography (CT) showed extensive bone involvement that compromised the frontal bone, skull base, craniofacial bones, and specially the jaws, the zygomatic and the nasal bones. In the jaws, the most affected portion was the hard palate, characterized by bone expansion with thinning and loss of cortical, with an alternated pattern of osteolysis and osteosclerosis, resembling a tabby appearance. Osteolysis of the right mandibular condyle was also present (Figs. 3 and 4).

An incisional biopsy of palatal bone tissue was performed, showing multiple immature bone trabeculae with multinucleated giant cells and augmented vascularity. Histopathological diagnosis is consistent with a hyperparathyroidism brown tumor (Fig. 5).

Despite the parathyroidectomy, PTH levels remained high (1907 pg/mL, normal range 12–88 pg/mL). Subsequently a scintigraphy was performed revealing an ectopic gland located at the posterior portion of sternum-manubrium.

Four months later, a new parathyroidectomy was performed to remove the residual parathyroid glandular tissue. PTH values 5 days after surgery decreased to normal ranges (63.8 pg/mL, normal range 12–88 pg/mL). After successful surgical treatment, administration of calcium, vitamin D, folic acid and iron supplementation is indicated.

During the follow-up, the maxillary bone continues to change. A second incisional biopsy would be required to assess the bone maturation and schedule the facial bones remodelling.

3. Discussion

When the glomerular filtration rate decreases below 25% of normal, phosphate excretion is impaired [3]. Hyperphosphatemia leads to hypocalcemia, because phosphate renal retention decreases renal synthesis of calcitriol (1,25-dihydroxyvitamin D3), the active form of vitamin D3 [3]. This inadequate activation of vitamin D leads to a decreased intestinal absorption of calcium [2].

Parathyroid hormone (PTH) is produced and secreted by the parathyroid glands, whose activities are controlled by free (ionized) serum calcium levels [6]. Hyperphosphatemia and hypocalcemia increased parathyroid activity (secondary hyperparathyroidism), with subsequent hypercalcemia [5]. Hypocalcemia and hyperphosphatemia mark the beginning of the biochemical sequence that culminates in renal bone disease [3,5].



Fig. 1. Lion-like expression caused by maxillary and mandible deformation.

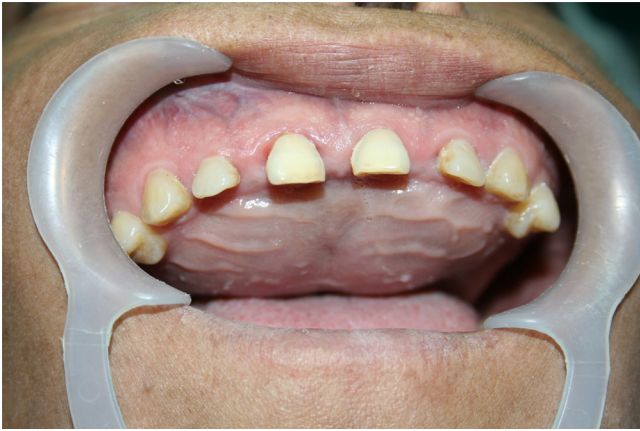


Fig. 2. Deformation of the hard palate hinders proper ventilation and feeding.

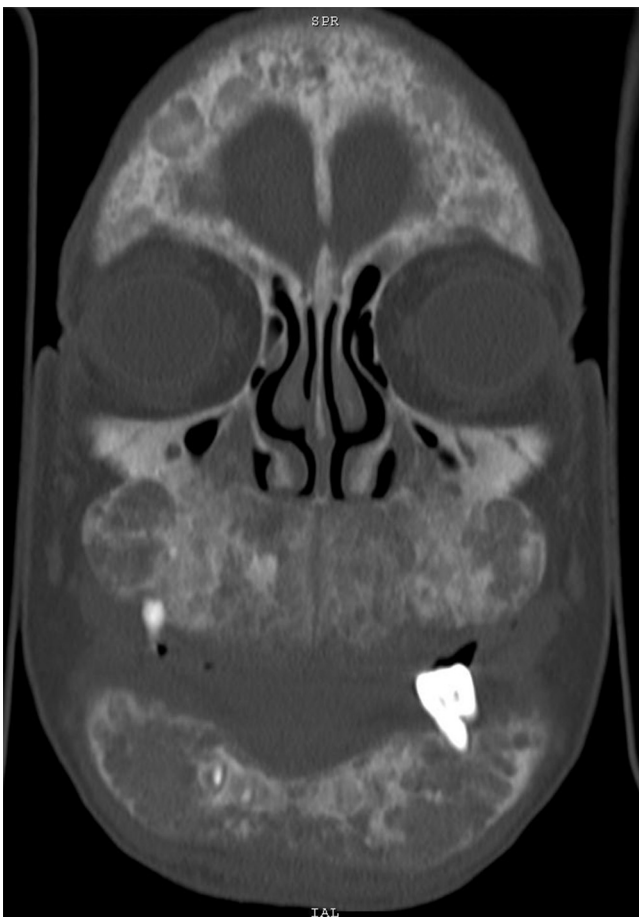


Fig. 3. Coronal computer tomography (CT) of the face showing expansive osteoporotic bone growth with demineralization of the mandible and maxilla.

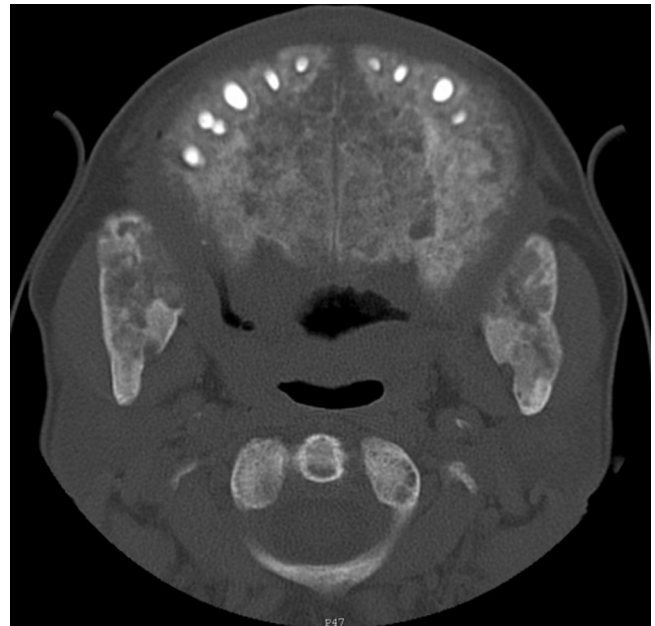


Fig. 4. Axial computer tomography (CT) of the face with characteristic appearance of diffuse bone tunnels.

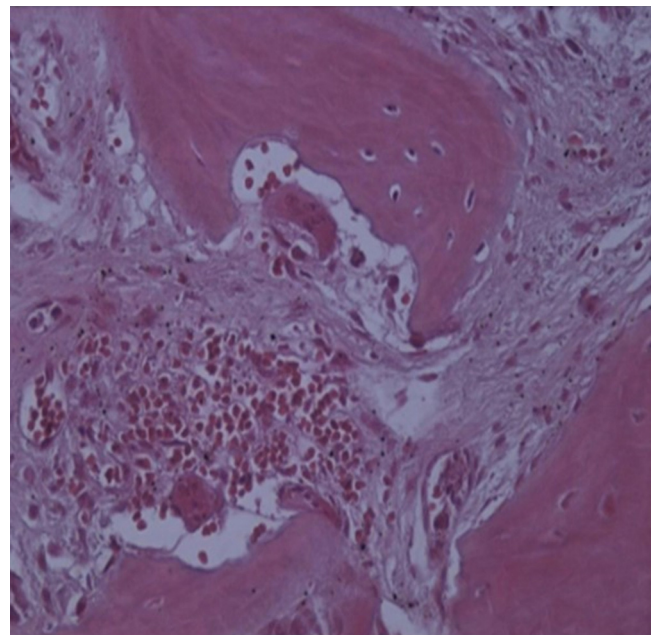


Fig. 5. EH 40 \times . Multiple trabecula of immature bone surrounded by fibrous connective tissue cell.

Hypocalcemia and hyperphosphatemia directly stimulate PTH production by the parathyroid glands. Hyperphosphatemia, which becomes significant when the glomerular filtration rate decreases to lower than 40 mL/min [5], can also increase the PTH production indirectly by decreasing renal synthesis of calcitriol [3], serum ionized calcium, vitamin D receptors and calcium sensor in the parathyroid glands, and produces skeletal resistance to the calcemic action of PTH [7].

The excessive secretion of PTH after long-standing secondary hyperparathyroidism leads to tertiary hyperparathyroidism that is

characterized by the development of autonomous hypersecretion of PTH, and subsequently hypercalcemia [8] (Fig. 6).

The management of tertiary hyperparathyroidism is surgery, with total parathyroidectomy plus auto transplantation or subtotal parathyroidectomy [5].

The bone metabolic disorder is the responsible for renal osteodystrophy and uremic leontiasis ossea is an uncommon clinical presentation of the disease. The term was originally introduced by Virchow about an inflammatory hyperostotic bone disease [9], and it is characterized by craniofacial overgrowth that produces the appearance of lion facies in variety of diseases such as Paget's disease, fibrous dysplasia and uremic leontiasis ossea.

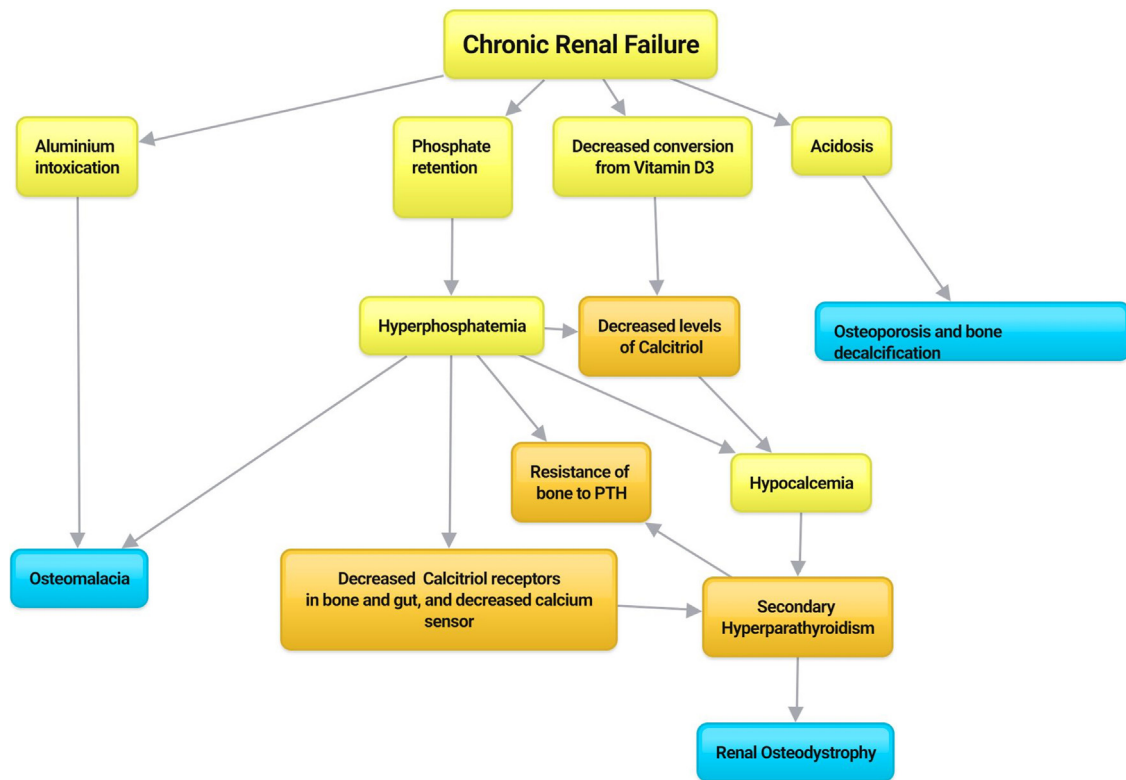


Fig. 6. Diagrammatic presentation of renal osteodystrophy physiopathology.

Uremic leontiasis ossea refers to the massive thickening of craniofacial bones as a result of CRF [4]. Its clinical presentation includes progressive painless massive enlargement of the jaws, widening of the nares, flattening of the nasal bridge, and increased interdental spacing. In addition to the cosmetic impairment, patients suffer functional impairment, including cranial nerve compromise and potential airway obstruction [4,5]. These clinical changes can be stabilized or improve mildly after parathyroidectomy [4].

In the present case, the patient showed the pathognomonic facial enlargement due to long-standing CRF in treatment with haemodialysis. At the moment of diagnosis, the blood screening showed altered levels of PTH secretion with hyperphosphatemia and normocalcemia. The increase in the secretion of PTH was in response to hypocalcemia and hyperphosphatemia due to CRF.

It's important to note that increased levels of PTH can be detected in blood test analysis prior to clinical features of calcium impaired metabolism, thus it is important to emphasize on patients preventive screening during haemodialysis [10].

Despite of parathyroidectomy, the PTH levels in the patient were over its normal range, which could be explained by residual parathyroid gland that was not removed during surgery or ectopic parathyroid gland tissue. After scintigraphy scan with Tc-99m, one foci of radioisotope accumulation was found in the posterior portion of sternum-manubrium. The patient was reoperated and residual glandular tissue was removed. After this second intervention, the patients showed a decrease of PTH levels to its normal range.

Changes in the facial skeleton due to hyperparathyroidism assume 3 known radiographic patterns [5]. The classic form is termed cystic osteitis fibrosa and presents with a combination of peritrabecular fibrosis, osteoblastic activity and cystic brown tumours. Radiographically, the osteolytic lesions have a "salt-and-pepper" appearance, which is the result of mixed osteolytic and sclerotic osseous involvement. The second form resembles fibrous dysplasia, with a classic ground-glass pattern on both conventional

films and CT. Unlike true fibrous dysplasia, these findings can be diffuse and generalized, with poor corticomedullary distinction, an imaging not present in fibrous dysplasia. The third pattern is the most uncommon form, and it is present in uremic leontiasis ossea, characterized by significant hypertrophy of the jaws with serpiginous "tunnelling" or channelling within the bone and poor visualization of the cortical bone [11].

In our case, the noncontrast CT scan showed bony thickening of the hard palate with low-attenuation serpentine "tunnelling" extending through the maxilla and mandible. The affected area lacked clearly defined cortical bone and, thus, had no corticomedullary distinction.

Biopsy of the palatal mass revealed a fibro-osseous lesion composed of irregular curved individual spicules of bone intermixed with fibrous tissue, with no normal bone identification, and with the presence of multinucleated giant cells. Bone biopsy is not particularly helpful in distinguishing uremic leontiasis ossea from fibrous dysplasia and Paget's disease, since both conditions can have very similar histological findings [6,11]. The differential diagnosis can be assessed based on the combination of clinical, laboratory, and diagnostic imaging findings.

Despite of the differential diagnosis the most relevant histopathological feature is the presence of immature bone, which therefore implies the presence of giant cells. This kind of cells are known for their rapid proliferation and multiplication under a proper molecular stimulus such as inflammatory mediators [12].

The rapid cellular proliferation can even lead to a greater bone tumor, in a critical anatomical space such as the hard palate and may cause airway compromise. It is essential to achieve a correct balance between improving the patient's quality of life by performing a surgical bone remodeling and waiting for the right timing in the tumor bone maturation to avoid causing harmful cellular changes.

Early recognition of incipient uremic leontiasis ossea is essential to prevent progression to severe disfigurement that

can result from prolonged untreated secondary hyperparathyroidism [10].

The presentation of this condition is rare. Since 1988, only a few cases of leontiasis ossea have been published in the literature, and it is difficult to know the exact number because there is a spectrum of skeletal sequel from hyperparathyroidism under different names [5]. Most of cases reported have been published in dental and oral and maxillofacial surgical literature [13].

With therapeutic developments in CRF management and the more frequent occurrence of renal transplantation, the longevity of CRF patients have increased and in the same way the prevalence of renal osteodystrophy with jaw involvement [1]. Correct diagnosis, prevention and management of the factors responsible for the development of bone lesions due to altered bone metabolism are important issues for health professionals who face these patients [14].

Because of the lack of cases published so far in the literature, a proper surgical management is not developed. The maxillofacial surgeon must have an accurate knowledge of patient's medical condition and bone maturation status to decide the adequate surgical strategy before it may result in complications such as life-threatening upper airway obstruction and compressive cranial neuropathy [15]. This kind of large osseous lesions could be treated by remodelling the bone in a similar way such as the fibrous dysplasia, but only in these cases where there is a significant percentage of mature bone in the lesion.

Disclosure of interest

The authors declare that they have no competing interest.

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