

# Maxillary hyperplasia and hyperostosis cranialis

## *A rare manifestation of renal osteodystrophy in a patient with hyperparathyroidism secondary to chronic renal failure.*

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### ABSTRACT

نستعرض في هذا التقرير حالة مريضة تبلغ من العمر 21 عاماً، مصابة بحالة مرضية معقدة من الفشل الكلوي المزمن وفُطِرَ نشاط مجاورات الدرق الثانوي، تظهر مع تاريخ تدريجي لتضخم عظام الوجه على مدى عام. يشمل التضخم الوجهي بشكل أساسي منطقة الفك العلوي مسبباً تشوه وجهي وسني غريب. بناءً على الفحوصات السريرية، الإشعاعية، والمخبرية تم تأكيد تشخيص تشوه الوجه على أنه حالة نادرة من الخلل العظمي الكلوي يظهر على شكل فرط تكون الفك العلوي وفرط عظمي جمجمي.

This case report describes a 21-year-old female patient with a complex medical condition of end-stage chronic renal failure and secondary hyperparathyroidism presenting with a history of gradual enlargement of the facial bones over a period of one year. The facial enlargement primarily involves the maxilla causing a bizarre facial and dental deformity. Based on the clinical, radiographic, and laboratory investigations the facial deformity was confirmed as a rare manifestation of renal osteodystrophy presenting as maxillary hyperplasia and hyperostosis cranialis.

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Secondary hyperparathyroidism as a consequence of end-stage chronic renal failure (CRF) induces a series of clinical and morphological manifestations known as renal osteodystrophy.<sup>1</sup> Renal osteodystrophy frequently affects the spine, ribs, long bones, and skull.<sup>1-3</sup> Findings of renal osteodystrophy in facial and cranial bones are not uncommon. However, the presentation of significant enlargement of facial and cranial bones in patients with secondary hyperparathyroidism defined as uremic leontiasis ossea (LO) is reported to be very rare.<sup>4-8</sup> In this paper, to highlight this rare presentation and to provide an updated review of the literature, we report a case of a 21-year-old female patient with a history of CRF and secondary hyperparathyroidism on hemodialysis who presented with gradual significant enlargement of the facial and skull bones.

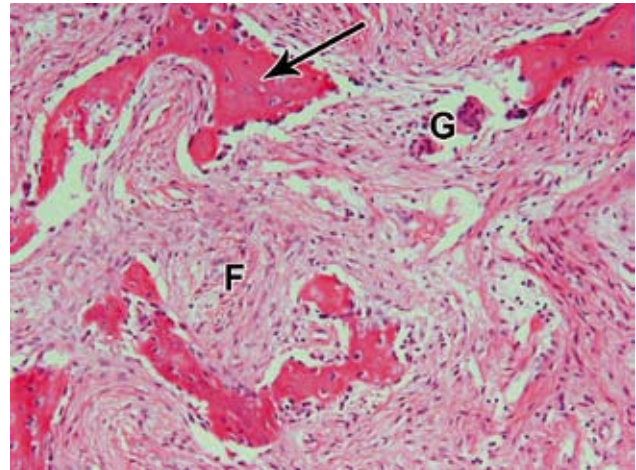
**Case Report.** A 21-year-old female patient was referred to our unit for opinion regarding the gradual enlargement of the facial bones, which had begun one year previously. There was no reported pain, visual or neurological deficiencies associated with the enlarged facial bones. The patient had a significant medical history of end-stage CRF, secondary hyperparathyroidism, and was on a regular renal dialysis programme for 4 years. Clinical examination showed that the patient is of short stature and was confined to a wheelchair due to fractured left femoral neck, and bone pain related to the severe osteoporosis status. There was a significant gross enlargement of the maxilla, and the hard palate with obliteration of the palatal vaults. Malocclusion, severe derangement with marked showing of upper labial gingivae and spacing of upper teeth resulted in an anterior open bite and gross incompetence of the lips (Figure 1). The visual acuity and visual fields were normal, and no facial neurological impairment was detected. Blood tests showed anemia, hypocalcemia, and significantly raised levels of serum creatinine, urea, phosphate, alkaline phosphatase. In addition, the parathyroid hormone level was grossly elevated (Table 1). Biopsy of the enlarged maxilla was performed, with the histopathology report suggestive



**Figure 1** - a) Front photograph of the patient showing severe enlargement of the maxilla with excessive showing of labial gingivae and spacing of the upper teeth. b) Lateral profile of the patient showing enlarged maxilla and severe lip incompetence.

**Table 1** - Laboratory data.

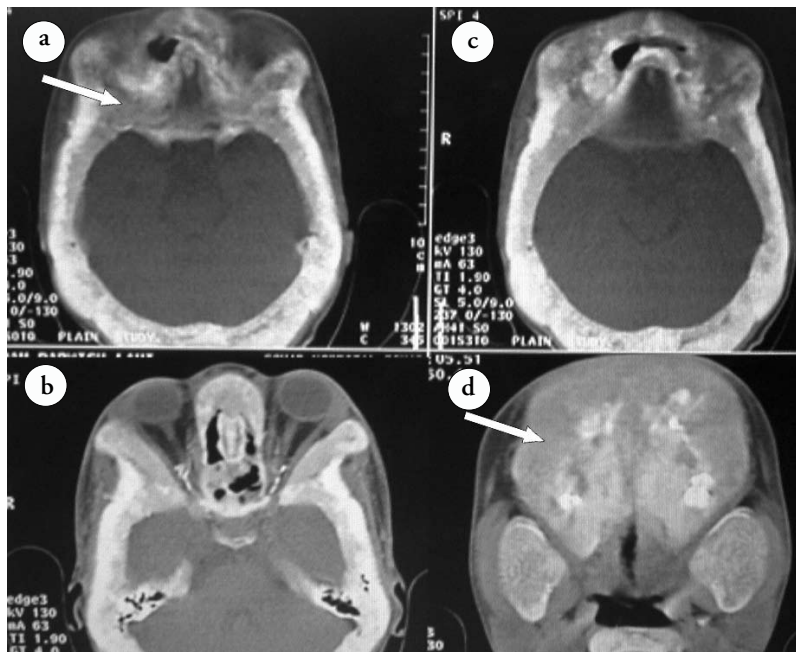
Investigation	Result
Hemoglobin (g/dl)	7.1
Parathyroid hormone (pmol/l)	350
Serum phosphate (mmol/l)	1.84
Serum alkaline phosphatase (IU/l)	1203
Serum urea (mmol/l)	26
Creatinine ( $\mu$ mol/l)	604
Calcium (mmol/l)	1.98



**Figure 2** - Photomicrograph of the maxilla showing curvilinear trabeculae of woven bone (arrow) rimmed by osteoblasts in some areas. The stroma is moderately hypercellular with immature fibroblasts (F) and few occasional giant cells (G). (Hematoxylin and eosin stain, original magnification x 200).

of fibrous dysplasia (Figure 2). Further comprehensive skeletal survey included bone densitometer, routine radiographs of different body sites and CT scan of skull and facial bones. The bone densitometer showed evidence of generalized severe osteoporosis. The CT of the skull and facial bones showed marked thickening of skull bones and gross enlargement of the maxilla. The radiographic and CT images showed typical ground glass appearance (Figure 3). Ultrasound of the neck showed enlarged parathyroid glands with features suggestively of parathyroid adenomata. Based on the collective findings of the clinical, radiographic, and laboratory investigations, the diagnosis of renal osteodystrophy presenting as maxillary hyperplasia and hyperostosis cranialis were established. Unfortunately, following the initial diagnosis and prior to the start of any treatment the patient died due to renal complications.

**Discussion.** Leontiasis ossea is a rare generalized homogenous swelling that implicates most facial bones leading to leonine appearance.<sup>9</sup> It can be encountered in patients with fibrous dysplasia, McCune-Albright syndrome, and rarely in Paget's disease, uremia with secondary hyperparathyroidism, or acromegaly.<sup>6,9-11</sup> The term LO was first used by Virchow in 1864 to describe the inflammatory hyperostotic bone disease.<sup>9</sup> Leontiasis ossea may lead to progressive visual disturbances, proptosis, nasal obstruction, sinusitis, facial asymmetry, hearing abnormalities, and airway obstruction.<sup>6,8,10-11</sup> In our presented case, the patient had no visual or nasal symptoms but significant cosmetic disfigurement due to the maxillary hyperplasia and hyperostosis cranialis. Leontiasis ossea secondary to CRF was not reported prior to 1953.<sup>8</sup> Uremic patients on regular dialysis treatment are often affected by a complex metabolic syndrome leading to renal osteodystrophy



**Figure 3** - Unenhanced computerized tomographic scan of the head; bone window a-c) axial at the level of orbits and d) axial at the level of maxilla and mandible. The selected images of facial bones reveal marked thickening of the maxilla and cranial bones with a "ground glass" appearance (arrow).

(ROD). Renal osteodystrophy describes the skeletal complications of end-stage chronic renal disease, with resultant fibro-osseous changes, which are primarily due to high bone turnover, and often combined with a mineralization defect leading to increased bone fractures and bone deformities.<sup>5,6,8,10</sup> Although rarely considered, the craniofacial skeleton represents one of the peculiar targets of this complex metabolic disease whose more dramatic pattern is a form of LO.<sup>10</sup> Only a few case articles reported the occurrence of LO in these patients presenting as gross structural bone deformities causing serious cosmetic and functional problems, as in our reported case.<sup>2,5,6,10</sup> Several published case reports in the literature reported the occurrence of mild forms of renal osteodystrophy in maxillofacial bones in patients with CRF who are on dialysis.<sup>8,10</sup> A recent published work by Ferrario et al<sup>12</sup> showed that facial structures of uremic patients are enlarged in comparison with matched normal subjects and that increased bone turnover could possibly be responsible for facial bone changes.

The etiology of renal osteodystrophy is incompletely understood. However, 2 mechanisms predominate: secondary hyperparathyroidism and abnormal vitamin D metabolism. The later results mainly from the loss of functioning renal parenchyma and subsequent decreased renal synthesis of active vitamin D. This leads to reduced gastrointestinal absorption of calcium, producing hypocalcemia. Reduced renal function also produces hypocalcemia by favoring phosphate retention. Low

serum calcium leads to a compensatory parathyroid hyperactivity, resulting in elevated phosphate excretion, decrease in calcium excretion, and increase removal of calcium from bones by osteoclast activation.<sup>1,4,8,10</sup> The osseous changes of renal osteodystrophy in renal dialysis patients have been reported to have a prevalence rate as high as 74%.<sup>10,13</sup> However, the clinical presentation is influenced by the patient's age at onset of renal failure, the etiology of renal disease, dietary content (protein, phosphate, and calcium), and treatment modalities.<sup>1,5,6</sup> Complete knowledge of the spectrum of the clinical, radiographic, and histopathological presentations of dialysis-related bone disease are lacking. Published reports in the last 2 decades have furthered our understanding by documentation of a small cohort of long-term dialysis patients exhibiting significant facial bones enlargement.<sup>10,13-15</sup> Damm et al<sup>10</sup> presented 9 cases of significant facial bone enlargement in renal dialysis patients with 7 involving both jaws and 2 involving only the mandible. In addition, all their cohort of patients demonstrated consistently normal-low calcium, high phosphate, high parathyroid hormone, and extreme elevation of serum alkaline phosphatase levels.<sup>10</sup> Histopathologically, the affected bones in ROD demonstrate immature trabecule of bone exhibiting osteoblastic riming, significant osteoclastic activity, and intertrabecule fibrosis; these changes represent the classic findings in high-turnover bone disease termed osteitis fibrosa.<sup>5,6-8</sup>

The radiographic alterations of the jaw bones in ROD include subperiosteal bone resorption, ground glass, or salt and paper appearance, and radiolucent brown tumors. These radiographic alterations may often mimic fibrous dysplasia, Paget's disease, and osteomalacia.<sup>4,5,10,13</sup> Damm et al<sup>10</sup> suggested that any fibro-osseous enlargement of the jaw in a dialysis patient must be considered as renal osteodystrophy until proven otherwise. The fact that the patient is being dialyzed often is the most important aspect in distinguishing among these 3 entities. The fibro-osseous changes occurring as ROD in craniofacial bones poses a difficult diagnostic dilemma as many lesions including fibrous dysplasia, giant cell tumor, and Paget's disease may all have similar radiographic and histopathological appearance, which can lead to inaccurate diagnosis.<sup>4,8,10</sup> In our reported case, 2 different pathologists reported the histopathology specimen as fibrous dysplasia. This finding is not surprising as many reported cases highlighted similar issues of errors leading to inaccurate diagnosis.<sup>10</sup> The present case clearly highlights the importance of evaluating the pathology specimens in the appropriate clinical context. If the final diagnosis were based only on pathology report, an erroneous diagnosis of fibrous dysplasia could have been accepted however, the clinical, radiographic, and biochemical findings of our case are more suggestive of renal osteodystrophy.

The management of significant facial bone enlargement in a renal dialysis patient should be initially directed towards increased patient compliance, as many published reports highlighted the common finding of poor therapeutic compliance.<sup>5,6,10</sup> Supplements of calcium and vitamin D combined with reduction of phosphate levels have been recommended to be effective.<sup>10</sup> In addition, patients should also be considered for possible need of surgical intervention of the hyperactive parathyroid glands. The surgical contouring of the enlarged facial bones is controversial with some reports recommending it, while others suggesting that it has limited or no benefits to the patients.<sup>2,8,10</sup> Damm et al<sup>10</sup> suggested that if the jaw enlargements stabilize but fail to return to normal after ensuring patient compliance and appropriate medical interventions, surgical re-contouring should then be considered necessary.

In conclusion, we present a rare case of gross facial bone enlargement occurring as ROD in a dialysis patient. Complete understanding of the disease process is required to establish an accurate diagnosis, which helps to start treatment and prevent the development of complications related to the disease process.

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