Multiple osteosclerotic lesions of skull in two cases with co-existing hyperparathyroidism and vitamin D deficiency

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Abstract
Osteosclerotic lesions have rarely been reported among patients with hyperparathyroidism. Usually, osteosclerotic changes manifest as patchy or diffuse increase in bone density in the spine, skull, and pelvis. There have been anecdotal reports of discrete localised osteosclerotic lesions in these patients. Here, we describe two adolescent females with co-existing hyperparathyroidism and vitamin D deficiency with multiple well-defined osteosclerotic lesions in the skull.

Key words: Hyperparathyroidism, vitamin D, osteosclerotic lesions

Introduction
The classic triad of hyperparathyroidism includes skeletal changes, nephrolithiasis, and neuromuscular dysfunction. The characteristic bony lesions described in patients with hyperparathyroidism include diffuse osteopenia, bone cysts (brown tumours), subperiosteal bone resorption, pathological frature, ‘salt and pepper’ motting of the skull, and terminal tuft erosion. Among patients with co-existing vitamin D deficiency, osteoporosis, pseudofractures, multiple collapsed vertebrae, and a deformed chest or pelvis have also been reported. While diffuse or patchy osteosclerosis has been described rarely among these patients, localised well-defined osteosclerotic lesions have anecdotally been reported. Here, we describe two rare cases of hyperparathyroidism with vitamin D deficiency who had multiple localised osteosclerotic lesions in the skull.

Cases
The first patient – A 12-year-old bed ridden female with history of bony aches and pains, repeated lower limb fractures, and progressive proximal muscular weakness since the last 2 years. There had been no history of vitamin D intake in the past. Investigations revealed hypercalcaemia (12.1 mg/dl), hypophosphataemia (2.5 mg/dl) with raised ALP levels (12,589 U/litre). Renal parameters were normal. Serum intact parathyroid hormone was high (PTH: 2,200 pg/ml), and 25-dihydroxyvitamin D was low (44 pg/ml). The radiological skeletal survey showed generalised osteopenia and multiple pathological fractures. Multiple osteosclerotic foci, which were well-defined and not expansile, were found superimposed on a heterogeneous ground glass-like appearance on skull roentgenograms (Fig.1). Skull computerised tomography revealed multiple high-density foci clearly demarcated from the surrounding bone (Fig.2). Ultrasound and magnetic resonance imaging of the neck revealed parathyroid adenoma. A diagnosis of tertiary hyperparathyroidism due to long-standing nutritional osteomalacia was made.

Another similar case was of a 20-year-old female, who presented primarily with a progressive swelling in the right maxillary region. Investigations revealed normal serum calcium levels (9.6 mg/dl), hypophosphataemia (2.3 mg/dl), raised alkaline phosphatase (1,363 U/l) and parathyroid hormone (632 pg/ml), and low 25-dihydroxyvitamin D (22 pg/ml) levels. The radiological survey was essentially normal except for multiple localised osteosclerotic lesions

Fig. 1: Lateral skull radiograph of case 1 shows multiple well-defined round-to-oval sclerotic lesions. The ‘salt and pepper’ granular appearance of the skull is also well seen.

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in the skull roentgenograms (Fig. 3). Parathyroid scan and ultrasound of the neck did not reveal parathyroid adenoma. Computerised tomography paranasal sinuses of the right maxilla revealed a large soft tissue.

Discussion

The classic description of hyperparathyroidism – “stones, bones, abdominal moans, and psychiatric overtones” – refers to renal calculi, bone pain, peptic ulcers, pancreatitis, and CNS symptoms. When associated with co-existing vitamin D deficiency, bone disease is marked, though serum calcium levels may be normal. With the improvement of vitamin D status in the Western countries, there has been a marked decline of bone disease in these patients. However, in developing countries like India, we continue to see a significant number of cases with co-existing hyperparathyroidism and vitamin D deficiency with marked skeletal manifestations.

The process of bone resorption and fibrous replacement results in the characteristic radiologic features of generalised bone demineralisation, resorption, cysts, brown tumours, erosion of the dental lamina dura, and pathologic fractures. Excess parathyroid hormone results in an increase in bone breakdown by means of osteoclastic resorption with subsequent fibrous replacement and reactive osteoblastic activity. A roentgenogram showing osteosclerotic changes is an uncommon feature of hyperparathyroidism. It has been described in secondary hyperparathyroidism associated with renal osteodystrophy, but osteosclerosis unrelated to renal failure has occasionally been reported. The osteosclerosis may be generalised or localised. Patchy increase in bone density is usually seen in skull, pelvis, and spine (rugger jersey spine). It has been postulated that there is an increase in osteoblastic response after
prolonged osteoclastic activity seen in hyperparathyroidism. This disproportionate osteoblastic activity is responsible for the radiologic manifestation of osteosclerosis.

While there are reports of diffuse or patchy osteosclerotic lesions in patients with hyperparathyroidism, discrete osteosclerotic lesions in skull are only anecdotally reported in these patients. The occasional and exaggerated response of osteoblasts to compensate for the bone loss induced by hyperparathyroidism has been attributed for discrete osteosclerosis in these patients. Fujino et al reported multiple osteosclerotic lesions of skull similar in appearance to the present case in a 26-year-old Japanese man with primary hyperparathyroidism. The vitamin D levels in this patient were elevated. These lesions appeared as hot spots in the 99Tc-MDP bone scan. Histomorphometry revealed increased osteoblastic activity and extremely high bone turnover rates in the osteosclerotic foci. The authors postulated that the younger age of the patient, when the bone mass is still being gained and bone turnover high, may have caused osteosclerosis. Boechat et al reported two children with primary hyperparathyroidism who radiologically manifested with prominent osteosclerosis in the tibia, although they did not undergo bone biopsy at the osteosclerotic sites. The two patients in the present report were also adolescent females when the bone accrual is at its peak. Both the patients had hyperparathyroidism—in the first patient it appeared to be a tertiary hyperparathyroidism due to long-standing vitamin D deficiency. The second patient had vitamin D deficiency with secondary hyperparathyroidism.

Vitamin D deficiency has commonly been described among patients with primary hyperparathyroidism in India. Harinarayan et al described 20 patients with primary hyperparathyroidism, half of them were normocalcaemic, but all were hypercalcuiic. Vitamin D levels were low in all the patients. Radiologically, subperiosteal resorption was present in 90% of the total group of patients, brown tumours in 60%, and pathological fractures in 40%. A high incidence of bone disease as compared to the West has been attributed to hypovitaminosis D. Our patients also had diffuse osteopenia, subperiosteal resorption, and bony cysts. However, discrete osteosclerotic lesions in the skull were also observed in these two patients, a finding previously not described among patients with co-existing vitamin D deficiency and hyperparathyroidism.

In conclusion, the present two cases with multiple localised osteosclerotic foci in the calvarium are extremely rare features of co-existing hyperparathyroidism with vitamin D deficiency.

References