CASE REPORT

Giant mediastinal parathyroid adenoma presenting as bilateral brown tumour of mandible: a rare presentation of primary hyperparathyroidism

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SUMMARY

Hyperparathyroidism (HPT) is becoming increasingly common endocrinopathy in clinical practice. Nowadays, it is mostly diagnosed in subclinical or early clinical stage. Bony involvement in HPT has seen significant fall in incidence. Brown tumour of bone is exceptionally rare as a first manifestation of primary HPT (PHPT). Its radiological and histopathological features may be mistaken for other bony pathologies. If possibility of underlying HPT is overlooked the disease is bound to recur after surgery adding to morbidity of the patient. Here we present a case of bilateral brown tumour of mandible which was mistakenly treated as giant cell granuloma by surgical curettage. That the patient was harbouring an ectopic parathyroid adenoma with hypercalcemia causing non-specific symptoms was missed by the referring physician. This led to recurrence of the lesion. On subsequent evaluation, a giant mediastinal parathyroid adenoma causing PHPT was detected at our centre and was removed via mini sternotomy approach.

BACKGROUND

Primary hyperparathyroidism (PHPT) is the third most common endocrinopathy with 0.1%–3% annual incidence.[1 2] Eighty to ninety per cent of PHPT cases are due to solitary adenoma.[3] The classical manifestation of hyperparathyroidism (HPT) was described as 'bones, stones, abdominal groans, psychic moans and fatigue over tones' by Frame and Jackson.[4] But in modern era majority are detected incidentally in asymptomatic or mild symptomatic phase, seldom reaching the morbid stage reported earlier.[5] Brown tumour of bone is seen in only 0.1% of all HPT and 4.5% of PHPT cases.[6] Brown tumour as first presentation of PHPT is extremely rare.[7 8] Inaccurate perioperative localisation of parathyroid adenoma especially in case of ectopia can result in failed surgical exploration. Scenario can be misleading if an ectopic adenoma presents in an unorthodox form like brown tumour in absence of classical features of hypercalcaemia.

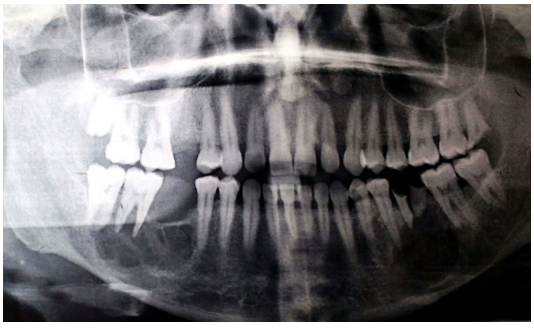

Figure 1 Orthopantomogram (OPG) showing bilateral lytic lesions in the body of mandible with cortical thinning and medullary lucency.

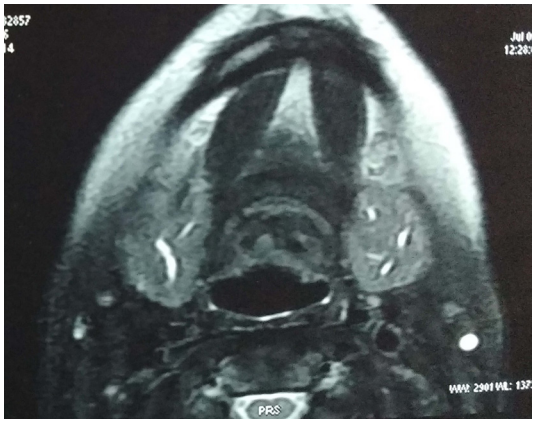

Figure 2 Contrast enhanced MRI (CEMRI) axial image showing poorly encapsulated soft tissue lytic lesion in both half of mandible.

CASE PRESENTATION

A 49-year-old woman was referred to us with history of recurrent painful jaw swelling and raised serum calcium level. Six months back, she consulted her dentist for rapidly increasing painful right-sided jaw swelling. Orthopantomogram (OPG) and contrast enhanced MRI showed bilateral radiolucent lytic soft lesions of the mandible (figures 1 and 2). An incision biopsy of the lesion suggested giant cell reparative granuloma. The patient underwent transoral curettage of both the lesions. Histopathology of the curettage specimen showed multiple randomly scattered multinucleate osteoclastic giant cells containing fewer nuclei in the background of sheets of spindle cells. Reactive bone formation was noted within the lesion (figure 3).

INVESTIGATIONS

Three months later, she again sought clinical attention for recurrent jaw swelling, new-onset headache and generalised body ache. In course of evaluation, blood biochemistry revealed abnormally

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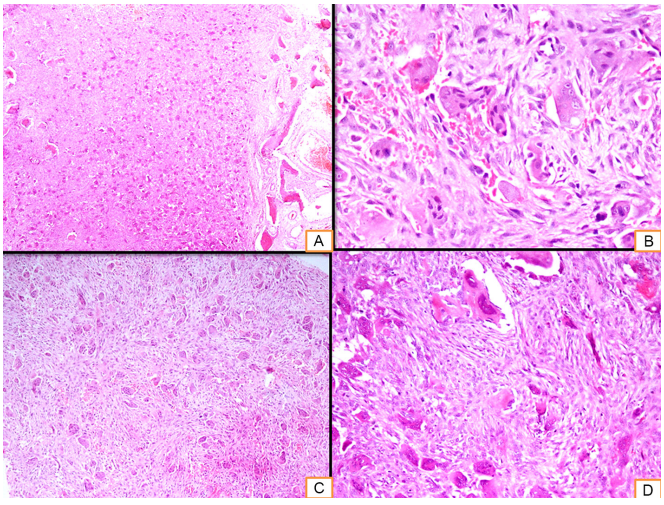

Figure 3 (A) Photomicrograph mandibular curettage specimen showing the lesion with scattered spatially distributed multinucleate giant cells with few reactive woven bony trabeculae in the left side of the photo and the native (lamellar) bony trabeculae in the right side (H&E; 40×). (B) The number of nuclei in the giant cells was much less than that of the giant cells of giant cell tumour (H&E; 400×). (C) The background spindle cells were arranged in sheets with short fascicles and vague whorling pattern (H&E; 100×); (D) The nuclear morphology of the giant cells and stromal spindle-shaped cells was different (H&E; 400×).

high serum calcium (14.07 mg/dL), relatively low phosphate (2.9 mg/dL) and normal vitamin D (37.7 ng/mL) levels. Serum intact parathyroid (iPTH) level was grossly elevated (1000 pg/dL; normal 15–65). Neck ultrasound scan did not pick any abnormal parathyroid gland. With this, physician referred her to our centre. Subsequent technetium (99 mTc) labelled sestamibi scan (figure 4) picked up 2.9×2.3 cm tracer avid lesion in anterior mediastinum. For further characterisation, radioactive fluorine (F18) labelled choline positron emission CT was done. This localised an ectopic parathyroid tissue (2.9×2.1 cm) in anterior mediastinum behind the manubrium sterni abutting the aortic arch (figure 5). It also picked up tracer avid lytic lesion in both mandibular rami and spine of right scapula. Dual-energy X-ray absorptiometry scan suggested osteopenia of lumbar vertebrae and femoral neck (figure 6).

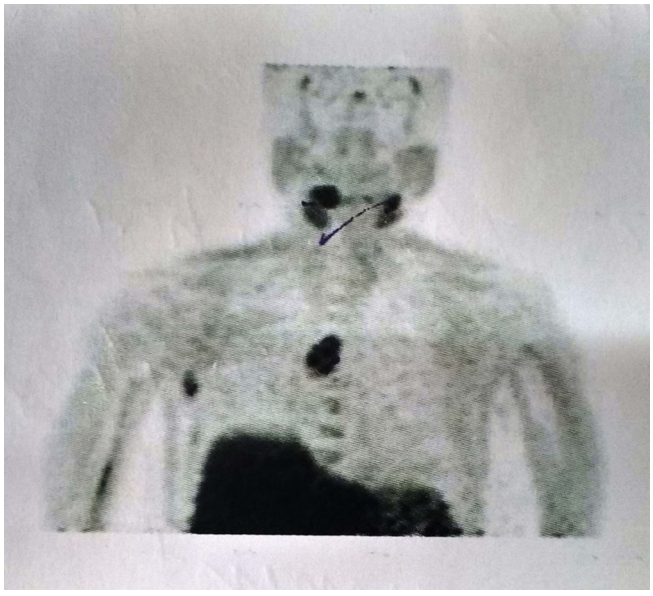

Figure 4 Whole body Tc99m sestamibi scan image showing tracer avid mediastinal lesion.

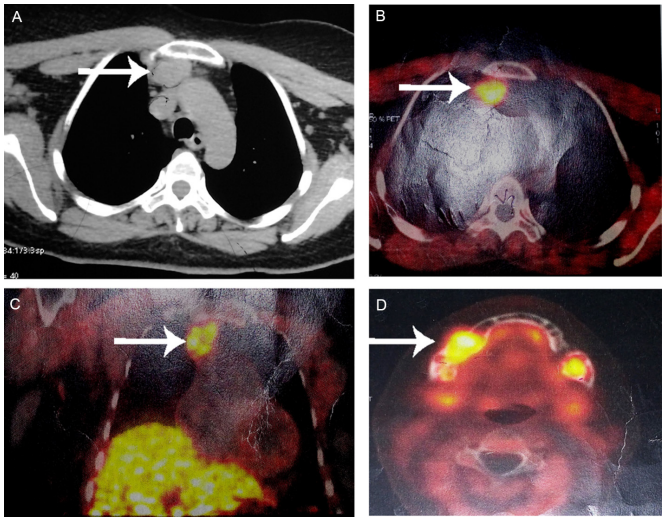

Figure 5 (A) Axial CT image showing superior mediastinal lesion abutting manubrium sterni (white arrow). (B) Axial view and (C) coronal view of choline positron emission CT (choline PECT) (maximum intensity projection) of the same showing intense tracer uptake in the lesion (white arrows). (D) Increased tracer uptake is noted in both half of the body of mandible (white arrow).

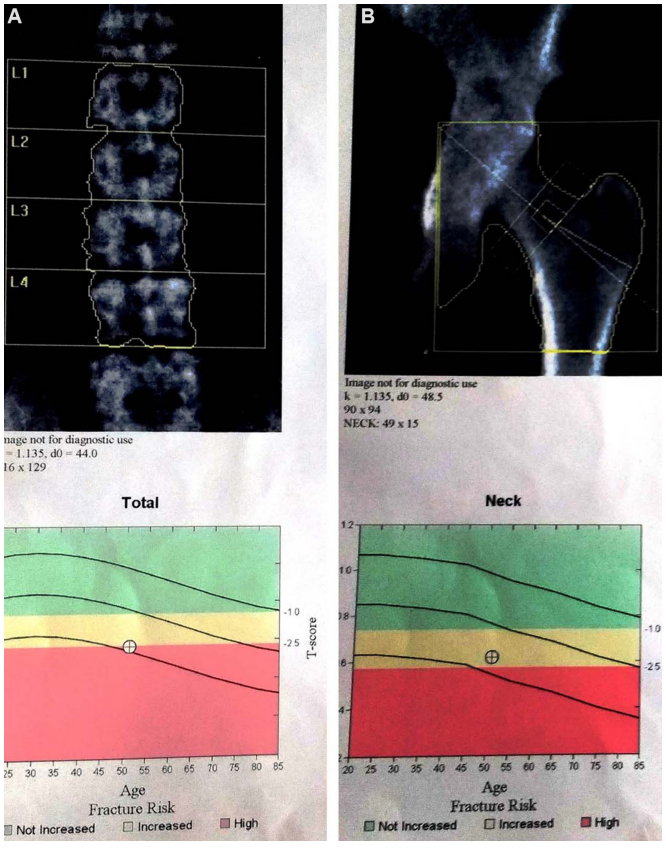

Figure 6 Dual-energy X-ray absorptiometry (DEXA) scan images of lumbar spine (A) and hip joint (B) showing osteopenic changes with reduced T-scores.

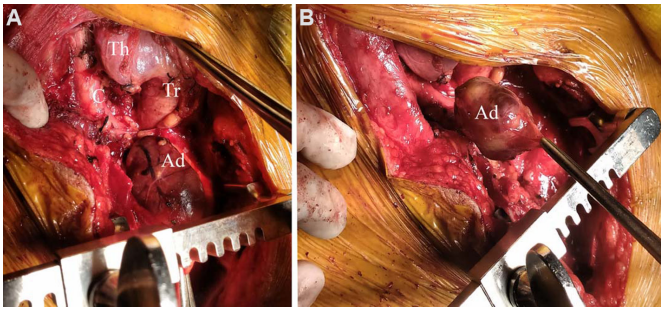

Figure 7 (A) Intraoperative photo of the giant parathyroid adenoma (GPTA) (Ad) in the superior mediastinum. Its relation to thyroid gland (Th), trachea (Tr) and right common carotid artery (C) is shown. (B) The well-encapsulated gland (Ad) is being dissected out from mediastinal fat.

DIFFERENTIAL DIAGNOSIS

A diagnosis of PHPT due to mediastinal parathyroid adenoma with bony involvement was made. However, given the size of lesion and high value of iPTH, parathyroid carcinoma could have been a rare possibility. The giant cell reparative granulomas of mandible which were the initial manifestation in this patient were actually brown tumours and they recurred due to uncorrected PHPT. Other differential diagnoses like giant cell tumour (GCT) of bone and giant cell reparative granuloma were ruled out in the background of PHPT.

TREATMENT

The patient's hypercalcaemia was controlled with hydration and forced diuresis before surgery. Under general incision, a cervical collar incision was made with a plan to explore the mediastinum via cervical root. But the adenoma was deep seated and we had to perform a hemisternotomy to access anterior mediastinum. A large brown red ovoid tumour was found lying within a pad of fat just above the carina anterior to left brachiocephalic vein (figure 7). The lesion measured 4×3×2 cm in size and weighed 12 g. It had a well-preserved capsule without infiltration to surrounding structures.

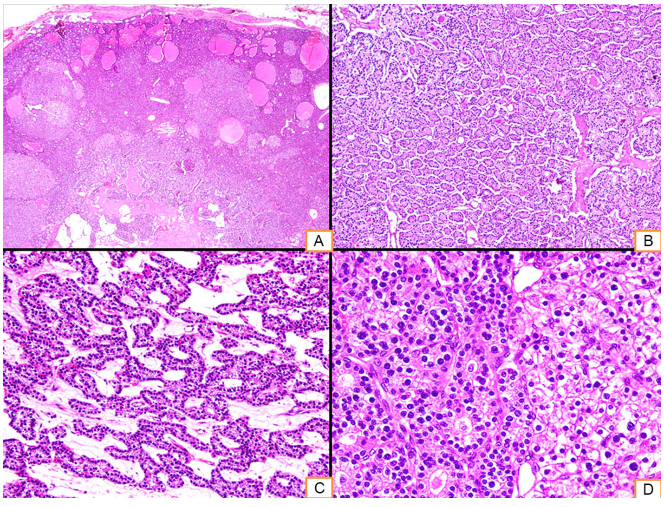

Figure 8 (A) The microphotograph of the resected tumour showing a well-circumscribed tumour with peripherally compressed normal parathyroid gland (upper part) (H&E; 40×). The tumour showed nesting (B) and trabecular (C) patterns (H&E; 100× (B) and 200× (C)). (D) The tumour cells were relatively monomorphic and had centrally placed round nuclei, stippled chromatin, inconspicuous nuclei and moderate amount of eosinophilic to clear cytoplasm (H&E; 400×).

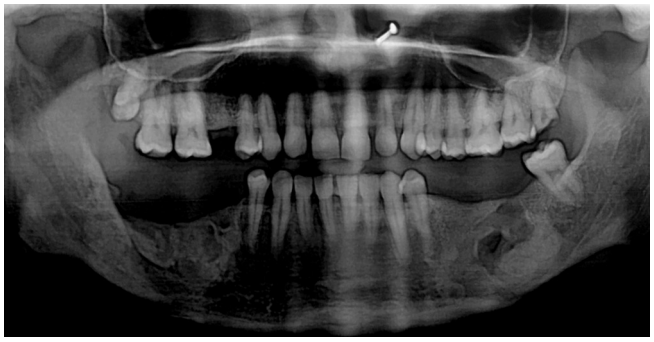

Figure 9 One-year follow-up orthopantomogram (OPG) showing healing of both the brown tumours with sclerosis.

OUTCOME AND FOLLOW-UP

The patient made uneventful recovery and her serum calcium, vitamin D and iPTH levels remained normal throughout the follow-up. Histopathology of the resected specimen showed a well-circumscribed tumour with peripherally compressed normal parathyroid gland (figure 8A). The tumour was all embedded and the whole of the tumour had been examined. The tumour cells were arranged in the forms of nests, islands, pseudoacini, trabeculae and cords (figure 8B,C). The tumour cells were monomorphic with classical cytomorphology of neuroendocrine cells (figure 8D). Ki67 index was <1%. No mitosis, atypia, necrosis, capsular or vascular invasion or permeation of the adjacent tissue was noted to suggest malignancy. Follow-up OPG (figure 9) at 1 year showed healing of both the mandibular lesions with sclerotic changes.

DISCUSSION

HPT is classified into primary, secondary and tertiary types depending on underlying cause of hypersecretion.[2 4] Majority of PHPT is due to hypersecretion of a single adenomatous gland (80%–90%). Polyglandular hyperplasia (10%–15%) and carcinoma (1%) comprise the rest. The disease shows a peak incidence (75%–78%) between third and sixth decades of life with strong predilection for women.[1] It produces manifestations due to hypercalcaemia and accelerated bone demineralisation. Acute hypercalcaemia can present with diuresis, diaphoresis, dehydration, abdominal cramps, cardiac arrhythmias and seizure. However, more protracted course characterised by chronic abdominal pain, constipation, peptic ulcer, recurrent renal stones and behavioural changes is more common. Renal damage, acute or recurrent pancreatitis and bony involvement are major causes of long-term morbidity in PHPT.[9]

Bony involvement in HPT can be in form of subperiosteal resorption, generalised demineralisation or focal lytic lesion.[4] Brown tumour or osteitis fibrosa cystica represents the end stage of bony remodelling in long-standing HPT.[10] It is seen in only about 4% of PHPT cases.[6 7] Pathologically, they represent giant cell reparative granuloma wherein osteoclastic demineralisation takes upper hand over mineralisation of trabecular bone.[11 12] Hypervascular demineralised stroma undergoes haemorrhagic degeneration and hemosiderin deposition gives it brown appearance.[2 6] The lesion involves ribs, clavicles,

pelvis, femur, vertebrae and craniofacial bones.[12 13] In the face, mandible is twice as commonly affected as maxilla.[14] Radiography shows cortical expansion and thinning with increased medullary lucency. Histologically, they are poorly encapsulated and rich in multinucleated giant cell in fibro vascular stroma. This makes it indistinguishable from central giant cell granuloma and GCT without given clinical background of HPT.[4 7] Majority are clinically asymptomatic. Focal bone pain, bony deformity, pathological fracture and compressive neuropathy develop occasionally. Aneurysmal bone cyst, metaphyseal fibrous defect and cherubism should be considered in its differential diagnosis.[4 15]

Less than two-thirds of parathyroid glands are found in orthotopic location posterior to thyroid gland.[16] Among the autopsied specimens, ectopia is seen in up to 42% of cases.[17] The inferior ones are more prone to migrate in close relation with thymus.[12] They can be found anywhere between the angle of mandible and pericardium and diaphragm.[8 16 17] About one-fifth of them are found in anterior mediastinum with majority (70%) being intrathymic.[16] They account for only 1%–3% of all PHPT cases encountered.[8] In 1932, Churchill reported the first case of mediastinal ectopic parathyroid adenoma (EPTA).[18] Pathological series report 6%–30% prevalence. Probability of encountering EPTA during re-exploration is almost two times higher (45% vs 16%) than in primary neck exploration.[13 19] Some large cervical adenomas may be sucked into the anterior mediastinum due to negative intrathoracic pressure or oesophageal peristalsis.[16] True mediastinal parathyroid lies completely below the level of clavicle as was in our case. EPTAs are associated with more severe forms of PHPT and have increased propensity for bony involvement.[17]

Most parathyroid adenomas are less than 70 mg in weight.[16] Giant parathyroid adenomas (GPTA) weighing more than 2–3 g are rare.[3 5 16] They have been sporadically reported in medical literature with majority being ectopic.[9 16 17 20] GPTAs usually give rise to severe biochemical and clinical derangement and are relatively common among men. Recent analysis by Sulaiman *et al* showed that they can harbour distinct genetic mutations and chromosomal recurrent copy abnormalities.[21]

Diagnostic algorithm of hypercalcaemia includes an assay of serum iPTH along with renal function test and serum phosphate assay. Once PHPT is confirmed, search is directed to localise the culprit gland(s). A battery of preoperative and intraoperative tests are available in clinical armamentarium including ultrasound, radionuclide scintigraphy, CT, positron emission tomography, intraoperative gamma probe and iPTH assay which allow precise localisation and successful surgical extirpation of the pathological glands.[9 12] Surgery offers definitive cure for PHPT and recurrence is unlikely if supernumerary pathology and multiple endocrine neoplasia syndrome are not missed. An intrathoracic EPTA can be extracted by cervical route in most instances. Formal thoracotomy or thoracoscopic or mediastinoscopic approach may be required in 1%–2% of cases.[17]

Addressing the underlying HPT forms the first step in brown tumour management.[8] Once PHPT has been taken care of, the small lesions may disappear spontaneously as with our case. In the event of persistence of pharmacological agents like calcitonin, intralesional steroids, bisphosphonates and subcutaneous interferons can be tried.[4 7] Large and severely symptomatic lesions or those growing after parathyroidectomy may require surgical interventions like curettage, excision with or without bone grafting.[8 12]

Learning points

- Though primary hyperparathyroidism is a common endocrinopathy, its primary presentation with brown tumour is rare.
- Underlying abnormality of calcium metabolism should be searched for whenever giant cell-containing bony lesions are encountered.
- EPTAs pose a unique clinical challenge in that they often require additional localisation and operative strategy over above the more common orthotopic adenomas.
- Precise preoperative localisation of all pathological parathyroid glands is key to permanent cure after surgical extirpation.

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Competing interests None declared.

Patient consent Obtained.

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