Primary hyperparathyroidism: A report of two unusual cases

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Abstract Primary hyperparathyroidism (PHPT) has a variable clinical expression. Majority of the patients are asymptomatic. Symptomatic PHPT with classical skeletal, renal, abdominal and neuro-psychiatric manifestations have become exceedingly rare. Asymptomatic maternal PHPT manifesting as neonatal hypocalcaemic convulsions is another rare entity. The commonest cause of PHPT are solitary parathyroid adenomas. These benign tumors are extremely small being difficult to identify even at surgical exploration. Very large tumors known as giant adenomas are uncommon. Double parathyroid adenomas account for only a small percentage of the lesions associated with PHPT. Considerable debate exists as to whether double adenomas are a distinct entity or represent early stages of four gland hyperplasia. We report two interesting cases of PHPT with classical features, that have become rare today such as nephrolithiasis, nephrocalcinosis, and X-ray findings of bone disease, caused by unusual pathological lesions like double and giant adenomas and discuss rare presentations like neonatal convulsions.

Keywords Primary hyperparathyroidism · Neonatal convulsions · Double adenoma

Introduction

Classical symptoms of PHPT popularly summed up as bones, stones, abdominal groans and psychic moans are rarely encountered today [1]. Another extremely rare but well known entity is asymptomatic maternal hyperparathyroidism presenting as neonatal hypocalcaemic convulsions [2]. We report a case of a symptomatic giant parathyroid adenoma (Fig 1A). Our search of world literature on Medline and Pubmed revealed only 9 reports of symptomatic giant parathyroid adenomas. To the best of our knowledge, this is the only case in literature where double parathyroid adenomas are responsible for maternal hyperparathyroidism manifesting as neonatal convulsions (case 1).

Case 1

A 29-year-old-female, was diagnosed to have PHPT after her infant developed generalized seizures on the 8th postnatal day. She was operated for an obstructing vesico ureteric junction calculus, 3 years ago and had open cholecystectomy for acute calculus cholecystitis, one and a half years ago following which she was asymptomatic. Investigations of the neonate revealed hypocalcaemia (4.9 mg/dl); hyperphosphataemia (8.7 mg/dl); and low parathyroid hormone levels (7.8 pg/ml). This prompted evaluation of the mother which revealed hypercalcaemia (11.3 mg/dl; normal range 8.1–10.7 mg/dl), hypophosphataemia (2.0 mg/dl; normal range 3.5–5.5 mg/dl), elevated serum alkaline phosphatase (270 IU/L), and elevated serum parathyroid hormone levels of 678 pg/ml (normal range 10–53 pg/ml). Abdominal ultrasound revealed multiple bilateral renal calculi. Ultrasonography of the neck and technetium 99 sestamibi scan confirmed the presence of double parathyroid adenomas. On surgical exploration of the neck bilateral inferior adenomas were easily found and other two

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Fig. 1 Operative specimens. (A) Showing the giant parathyroid adenoma (white arrow) and thyroid (black arrow). Compare the size. (B) Excised double parathyroid adenomas.

glands appeared normal. Selective gland excision (two adenomas) (Fig. 1B) and biopsies from the normal glands were taken. Histopathology report confirmed only two abnormal glands (double adenomas). Postoperatively she developed hypocalcaemic tetany (serum calcium 8.2 mg/dl), which required intravenous calcium supplementation. Parathyroid hormone levels reverted to normal (12 pg/dl) following surgery.

Case 2

A 45-year-old-male, a known hypertensive presented with haematuria. Abdominal ultrasonography revealed cholelithiasis, multiple bilateral renal calculi, right ureteric calculi and medullary nephrocalcinosis. With a clinical suspicion of hyperparathyroidism, investigations revealed hypercalcemia (13.4 mg/dl), hypophosphataemia (2.1 mg/dl), elevated parathormone levels (> 1000 pg/ml: Normal range 10–53 pg/dl), elevated serum alkaline phosphate (371 U/l). Ultrasonography and CT scan of the neck revealed a multi-nodular goitre with a large right inferior solitary adenoma (4×2 cm). At bilateral neck exploration a large right inferior parathyroid adenoma measuring $5 \times 2.6 \times 1.6$ cm and weighing 20 gm was excised (Fig. 1A). The remaining three parathyroid glands appeared normal. Sub-total thyroidectomy with excision of the adenoma was performed. Histopathology report confirmed the diagnosis of parathyroid adenoma and a multinodular goitre. Postoperatively the patient developed hypocalcaemia which required parenteral calcium supplementation. Parathyroid hormone levels reverted to normal (14 pg/dl) following surgery.

Discussion

PHPT is the third most common endocrine disorder after diabetes and thyroid disease [2]. The incidence is 25 per

100,000 of the general population and in women of child bearing age it is 8 per 100,000 population per year. PHPT commonly presents in the fifth and sixth decades of life. The male to female ratio is 1:3. Pathological lesions responsible for PHPT include solitary adenomas ($>80\%$); double adenomas (2–3%) multigland hyperplasia (15%) and carcinoma (2%). Adenomas are usually small ranging from 0.5 g to 5 g. Tumors weighing more than 5 g are termed giant adenomas [3]. Vitamin D deficiency has been postulated as a cause for large adenomas in developing countries.

Controversy still exists as to whether double adenomas are a distinct entity or four gland hyperplasia presenting metachronously. There is no absolutely reliable method to distinguish adenoma from hyperplasia. Some authors feel that the most reliable clinical criteria to document double adenomas, is the absence of recurrent hyperparathyroidism on follow up of at least 5 years following selective gland excision [4].

The biochemical results in both our patients were typical of PHPT, namely hypercalcemia, hypophosphatemia elevated serum parathyroid hormone levels and elevated serum alkaline phosphatase levels [5].

Neonatal hypocalcemia due to maternal hyperparathyroidism first described by Friedrichsen in 1938, is classified into early onset (<48 hours of life) and late onset (1st week of life). Since maternal hypercalcemia due to hyperparathyroidism suppresses the fetal parathyroid glands leading to late onset neonatal hypocalcemia. The neonate may present with seizures, poor feeding, apnea and cyanosis. If calcium status is not assessed in the antenatal period asymptomatic hyperparathyroidism can be easily missed [2] as seen in our patient.

In both our patients the X-ray findings were pathognomonic of PHPT [5] (Figs. 2, 3). Increased bone resorption is thought to be brought about by stimulation of osteoclast-activating factors such as interleukin-6 from osteoblasts [6, 7].

Fig. 2 X-ray skull lateral view showing 'salt and pepper skull' or 'ground glass' appearance due to diffuse punctuate osteopenia and microerosions, typical of PHPT. Clearly seen in area between the arrows.

Fig. 3 Radiograph of the hands demonstrating classical findings in PHPT such as generalized demineralization, subperiosteal bone resorption over the radial aspects of middle phalanges (white arrow) and sub cortical tunneling (black arrow).

Fig. 4 (A) Ultrasonograph of the right kidney showing multiple renal calculi and medullary nephrocalcinosis. (B) CT scan of neck showing the giant parathyroid adenoma (black arrows) posterior to the inferior pole of the right lobe of the thyroid.

Multiple bilateral renal calculi were found in both patients. Another rare finding in our patient was the presence

of nephrocalcinosis (Fig. 4A) which is found only in 5–10% of the cases [5] and can be detected by ultrasonography before they become demonstrable on radiographs (Fig 4B). Both our patients had gallstone disease, probably due to high calcium content in bile.

Parathyroid adenomas are rarely palpable. Various methods of preoperative tumor localization are available [5, 6, 8]. Parathyroidectomy is the definitive treatment for PHPT. We performed the standard surgical approach of bilateral neck exploration with identification of all four glands. Minimally invasive unilateral approaches are becoming increasingly popular nowadays.

Conclusion

Routine antenatal serum calcium estimation and abdominal ultrasonography may help pick up asymptomatic hyperparathyroidism, especially if there is a past history of renal calculi and gall stone disease. Radiographs complement the diagnosis and should always be ordered for in suspected cases of PHPT. A long recurrence free interval might be necessary to confirm diagnosis of double parathyroid adenomas following selective gland excision.

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