



Rare Association of Basal Ganglia Calcification and Primary Hyperparathyroidism: An Interesting Case Report with Review of Literature

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Abstract

Primary Hyperparathyroidism (PHPT) is an endocrine disorder which is caused by increased production of Parathyroid Hormone (PTH). Hypercalcemia leads to a number of symptoms and may cause patient's morbidity and even mortality if left untreated. In the present case, a 23 year old lady presenting with frequent attacks of urinary tract infection, seizures, diffuse bone pain and episodic pain abdomen since 15 months. On clinical, biochemical and radiological evaluation, the case was diagnosed as PHPT due to left superior parathyroid adenoma. CT scan of brain showed basal ganglia calcifications. She underwent uneventful surgical parathyroidectomy following preoperative optimization. She achieved normocalcemia without any surgical complications. This case is presented to highlight and discuss the rare association and causes of brain parenchymal calcifications associated with primary hyperparathyroidism.

Keywords: Hyperparathyroidism; Hypercalcemia; Adenoma; Calcifications; Parathyroidectomy

Introduction

Primary Hyperparathyroidism (PHPT) is an endocrine disorder which is caused by increased production of Parathyroid Hormone (PTH). Hypercalcemia leads to a number of symptoms and may cause patient's morbidity and even mortality if left untreated. The deranged calcium metabolism leads to impact on several end organs such as kidney, pancreas, bone and muscles in the form of decalcification or ectopic calcification. Mechanism of ectopic calcification is unknown. Rarely, it affects brain parenchyma and leads to Basal Ganglia Calcification (BGC) with its related neurological symptoms and sequelae. In this context, we report and discuss the relevant literature of a very rare interesting case of primary hyperparathyroidism leading to BGC.

Case Presentation

A 23-year-old lady presented with clinical history of recurrent burning micturition and frequency of urination for past 20 months. She also complained of episodic pain abdomen and diffuse bone pains for past 15 months. She also gave history of two attacks of seizures in past six months. She had multiple orthopedic, neuropsychiatric and urology consultations, but was only treated symptomatically. Later, a local physician detected hypocalcemia and referred her to our endocrine surgery department. The case was provisionally diagnosed as metabolic bone disease and was investigated for the cause. There was no family history suggestive of similar disease. Biochemistry was consistent with diagnosis of PHPT with serum parathyroid hormone of 369 pg/mL. Corresponding serum calcium, phosphorus, alkaline phosphatase, creatinine, 24 h urinary calcium, vitamin D as follows- 12.8 mg/dL, 2.4 mg/dL, 345 IU/L, 1.4 mg/dL 340 mg, 25 ng/dL and bone mineral density (T score) at hip, spine and radius of - 4.5, - 3.5 and - 5.0, respectively. Thorough clinical, biochemical and radiological evaluation confirmed the diagnosis of PHPT caused by single superior parathyroid gland enlargement as depicted in Contrast Enhanced Computed Tomography (CECT scan) of neck. The differential diagnosis of hypercalcemia such as multiple myeloma, tuberculosis, sarcoidosis, drug intake and co existing conditions like osteomalacia, steroid intake was excluded. Multiple Endocrine Neoplasia (MEN) syndromes, pseudohypoparathyroidism, pseudo-pseudohypoparathyroidism, secondary hyperparathyroidism and other familial syndromic associations were excluded. Plain CT scan of skull showed extensive osteoporosis and punched out osteopenia areas as shown in Figure

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Table 1: Comparison of Published literature with our case.

N	Authors	Age/ Sex	BGC	Type of HPT	Treatment for hyperparathyroidism	Effect of treatment
1	Margolin D et al. [3]	55/F	+	Primary	No treatment	No treatment
2	Margolin D et al. [3]	84/F	+	Primary	Parathyroidectomy	No improvement
3	Kisner et al. [4]	58/M	+	Secondary	No treatment	-
4	El Maghraoui et al. [5]	62/F	+	Secondary	Parathyroidectomy	Improvement in seizures
5	De la Plaza et al. [6]	49/F	+	Secondary	Parathyroidectomy	No neurological symptoms
6	Bhargav et al. (Our case)	20/F	+	Primary	Parathyroidectomy	Seizures improved

BGC: Basal Ganglia Calcification; HPT: Hyperparathyroidism

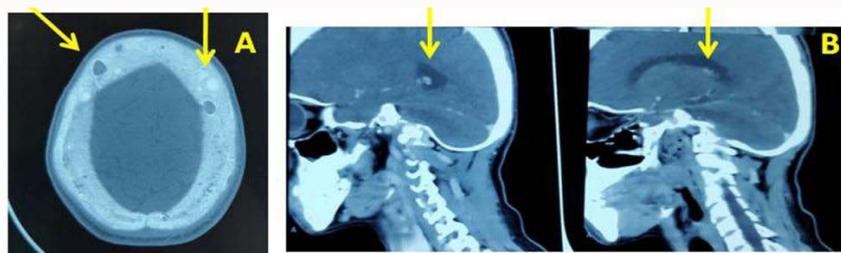


Figure 1: A) CT scan skull showing punched out lesions and islands of new born formation. B) CT brain showing calcifications in the region of basal ganglia, thalamus and around ventricle.

IA and CT scan of brain showed ectopic BGC (Figure 1B). CECT scan of abdomen shows extensive ductal and periductal calcifications in pancreas. Detailed neurological examination, ruled out any focal neurological deficits or extrapyramidal signs. With this diagnosis, we performed focused parathyroidectomy under general anesthesia and a 2.0 cm × 2.5 cm vascular right superior parathyroid adenoma was excised (Figure 2B), which was localized by CECT of neck (Figure 2A). Postoperatively, she had symptomatic hypocalcaemia from 3 to 6 days with least serum calcium level of 6.4 mg/dL. She was treated with parenteral calcium infusions and vitamin D supplements till normocalcemia was achieved and maintained. Normocalcemia was achieved at three months follow-up. Histopathology was reported as benign classical type Parathyroid adenoma. At 12 months follow-up, patient was normocalcemic, euglycemic with no attacks of urinary tract infection, pancreatitis or seizures or any neurological sequelae.

Discussion

Hyperparathyroidism associated with brain parenchymal calcification is very rare. Clinical presentation of nephrocalcinosis, pancreatic calcifications and BGC in a case of hyperparathyroidism with osteitis fibrosa cystica is indeed a rare phenomenon. Though, BGC are routinely reported with hyperparathyroidism, pseudohypoparathyroidism and Fahr’s syndrome, hyperparathyroidism has to be included in the differential diagnosis of symmetric intracerebral calcification with predilection for the basal ganglia. Parkinsonism and basal ganglia calcification are known sequelae of hypoparathyroidism [1,2], but they have been reported rarely in hyperparathyroidism. Hyperparathyroidism may result in depressed sensorium, behavioral changes mimicking psychiatric disease, generalized weakness, muscle hypertonicity, and hyperreflexia. These symptoms, especially the change in mentation, usually parallel the degree of hypercalcemia [3]. Focal neurologic signs, however, are rare. Hyperparathyroidism may result in a clinically significant neurologic dysfunction associated with intracerebral calcification as reported by Margolin et al. [3]. Convulsions have been reported with hyperparathyroidism by Kisner et al. [4] and Marghouzi et al. [5], though parathyroidectomy for the associated

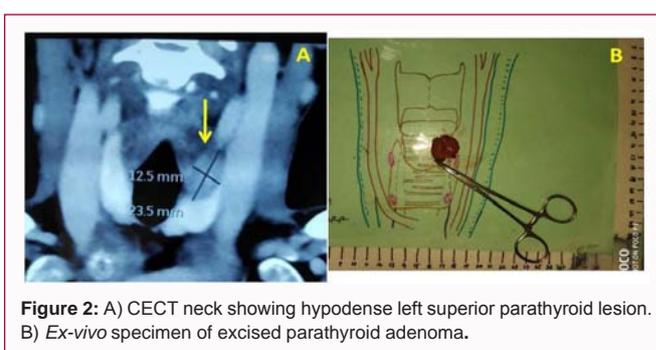


Figure 2: A) CECT neck showing hypodense left superior parathyroid lesion. B) Ex-vivo specimen of excised parathyroid adenoma.

illness was not contemplated. Exclusion of Fahr’s syndrome and any associated pseudo or pseudopseudohypoparathyroidism must be carried out diligently in such cases. We found no focal neurologic signs except seizures in our case, which never recurred at follow-up after parathyroidectomy. Hypocalcemic states including pancreatitis may be associated with cerebral calcifications. Anticonvulsant therapy has been linked with basal ganglia calcification [6,7]. Chronic hypocalcaemia states, such as renal failure (the most frequent), vitamin D deficiency, hypomagnesemia, pancreatitis and hypoparathyroidism, can be associated with intracranial calcifications [8]. As highlighted by the CT skull, our case showed the impact of deranged calcium metabolism on bone in the form of simultaneous decalcification (thin cortex and punched out lesions) and new bone formation (hyperechoic islands). In the above case scenario, parathyroid adenoma associated with seizures and predominant bone disease along with nephrocalcinosis and chronic pancreatitis coexisting with cerebral calcifications can be considered as sequelae of parathyroid disease. One article reported that secondary hyperparathyroidism related hypercalcemia could be associated with Parkinson disease without the presence of BGC [9]. Though, Parkinson symptoms were not found in our case, while they were reported in other reports [3]. Failure to cure hyperparathyroidism in our case might have resulted in Parkinson disease subsequently. There was very scanty literature on this association of BGC in primary hyperparathyroidism. We found only five published articles matching our case report [3-6]. Detailed

comparison of published literature is detailed in Table 1. But, detailed analysis of those articles suggested that those reported cases [4-6] were secondary hyperparathyroidism and associated BGC. Only one report matched our case of PHPT associated with BGC. In this report, they reported two cases of PHPT, but we are unsure about the authenticity of their PHPT diagnosis, as it was a four decade old report at which time the assays were first generation making the accuracy and diagnostic precision dubious. Thus, we opine that our case is only the third case of PHPT with associated BGC in World literature. However, we hypothesize that the cause of BGC in our case, could be intermittent hypocalcemia caused by pancreatic calcifications might have precipitated parenchymal calcification in brain leading to BGC. Further, as cross sectional imaging of brain is not routinely performed in PHPT cases, might have resulted in extreme rarity of this case scenario (PHPT+BGC). Etiopathogenesis, clinical impact, natural history and management of BGC in hyperparathyroid states needs further research.

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