Clinical Case Report

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Idiopathic hypoparathyroidism with extensive intracranial calcification in children

First report from Saudi Arabia

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Abstract

Rationale: Pediatric idiopathic hypoparathyroidism with extensive intracranial calcifications outside the basal ganglia (BG) is extremely rare with less than 10 cases worldwide.

Patient concerns: An 11-year-old Saudi male child presented with tetany with otherwise normal neurological and other body system examination diagnoses severe hypocalcemia for differential diagnosis.

Interventions: Further investigations revealed hyperphosphatemia and undetectable serum intact parathyroid hormone. Brain computed tomography revealed BG and extensive brain calcifications. He has no dysmorphic features, vitiligo, mucocuataneous manifestations, or hair loss. He had normal hemoglobin, electroencephalogram, and skeletal survey, with negative autoantibodies to alpha and omega interferons and negative genetic testing for Glial Cell Missing 2 (GCM2) and calcium-sensing receptors (CaSRs) excluding known causes of hypoparathyroidism.

Outcomes: This case presents a rare entity of idiopathic hypoparathyroidism with extensive intracranial calcification, not only in BG but also outside the extrapyramidal system with normal mentality, development, pubertal achievement, and neurological examination. To our knowledge, this is the first report from Saudi Arabia in pediatrics.

Lessons: Idiopathic hypoparathyroidism is a diagnosis of exclusion after ruling out all known causes of hypoparathyroidism. It is associated with BG calcifications, but extensive intracranial calcifications outside the BG are extremely rare.

Abbreviations: BG = Basal ganglia, CaSR = Calcium-sensing receptors, CT = Computed tomography, GCM2 = Glial Cell Missing 2, PTH = Parathyroid hormone.

Keywords: basal ganglia calcification, extensive brain calcifications, hypocalcemia, idiopathic hypoparathyroidism

1. Introduction

Hypoparathyroidism is an endocrine disorder caused as a result of congenital disorders, iatrogenic causes, infiltration of the parathyroid glands, suppression of parathyroid function, or idiopathic mechanisms.[1] Idiopathic hypoparathyroidism is an uncommon condition of unknown etiology diagnosed by exclusion of different possible etiologies.[2] Radiologically, hypoparathyroidism causes calcification most often in bilateral basal ganglia (BG).[3] The most common site is often globus pallidus,[4] but extensive intracranial calcification beyond the extrapyramidal system is rare.[5] We present case of idiopathic hypoparathyroidism with extensive intracranial calcification, without features of extrapyramidal system symptom or previous history of neurological manifestation, and presented with tetany.

2. Case report

An 11-year-old Saudi male child with negative past medical history for seizures, abnormal movements, hematological or other chronic diseases, hemochromatosis, radiation or other abnormal environmental exposures, and no history of previous thyroid surgery or other surgeries presented to the Pediatric Emergency Department with sustained tetanic contraction of both hands for 2 hours with positive Chvostek and Trousseau signs.

He was vitally stable with no fever or history of fever before presentation. Meticulous history revealed history of tingling and numbness sensations and sometimes facial twitches used to occur with exercise or hyperventilation started few years; roughly 4 years as the child remembers; before current presentation.

Further examination revealed average anthropometric measurements; lying on the 50th centile; with good nutritional status. The patient was fully conscious, cooperative, well oriented to

Editor: Anser Azim.

Funding/support: This research did not receive any grant from any funding agency.

The authors declare no conflicts of interest.

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Medicine (2017) 96:16(e6347)

Received: 23 September 2016 / Received in final form: 8 February 2017 / Accepted: 16 February 2017

http://dx.doi.org/10.1097/MD.0000000000006347

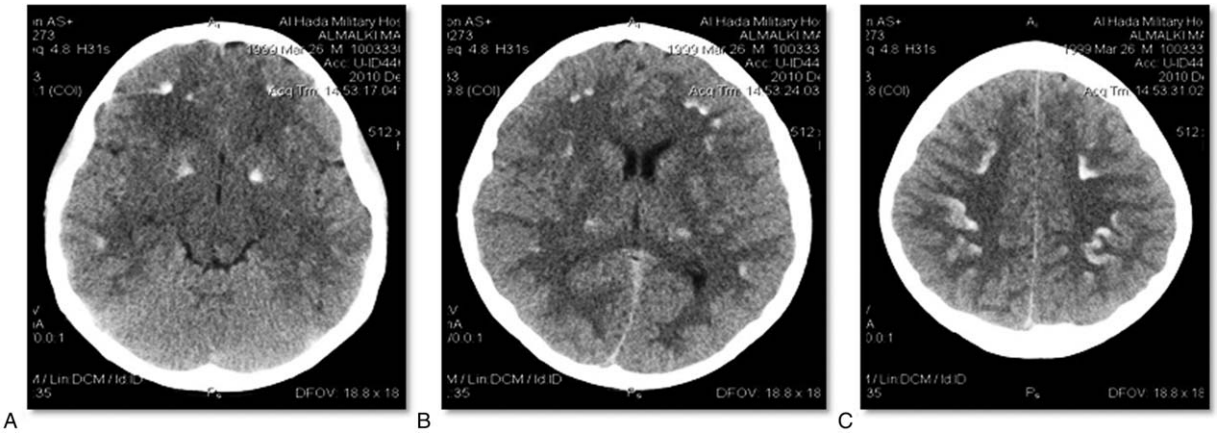

Figure 1. CT brain showing dense calcification in the head of caudate nucleus, basal ganglia, and the subcortical white matter region bilaterally in the cerebral cortex.

time, person and place, with average mood, memory, and intelligence along with normal gait and speech. Examination showed no gross dysmorphism with normal teeth. He had no signs suggestive of cerebellar, extrapyramidal, or any other neurological affection. No skin or mucus membrane abnormalities were noted, including normal hair with no hair loss, no vitiligo, or mucucutaneous candidiasis. Other thorough body systems examination revealed no detectable abnormalities.

The patient was immediately admitted to the Pediatric Intensive Care Unit and connected to cardiac monitor. Electrocardiogram showed prolonged QT interval. Intravenous calcium gluconate treatment was immediately started.

His initial investigations before calcium supplementation revealed severe hypocalcaemia (0.6 μmol/L) and hyperphosphatemia with normal magnesium level. One-alpha-hydroxy-cholecalciferol was then started. The patient condition improved within 24 hours and the patient was transferred to the pediatric ward.

Ophthalmological assessment including slit lamp and fundus examinations was normal with no cataract and no any fundus abnormalities.

No evidence of heterotrophic calcium deposition in the skin, no brachydactylies, and no evidence of spondyloarthropathy was noted.

Further investigations looking for the cause of severe hypocalcemia revealed undetectable serum parathyroid hormone (PTH) with normal blood picture, erythrocyte sedimentation rate, C-reactive protein, serum glucose level, serum total proteins, serum albumin, liver functions, renal functions, thyroid functions, serum iron-ferritin-total iron binding capacity, morning adrenocorticotropin, and cortisol tests. Tuberculosis was also ruled out. Urinary calcium was mildly elevated.

Anti-calcium sensing receptors antibodies (Anti-CaSR) were negative. No signs suggestive of other autoimmune diseases with negative anti-alpha and anti-omega interferons antibodies excluding autoimmune polyglandular syndrome I were noted. Anti-thyroglobulin, anti-thyroid peroxidase, anti-21-hydroxylase, anti-insulin, anti-parietal cell, anti-liver-kidney-microsomal, and anti-tissue-transglutaminase antibodies were all negative. 1,25-di-hydroxy-vitamin-D3 level was normal. Abdominal ultrasound revealed no nephrocalcinosis. Parathyroid scan was normal. Karyotyping excluded any structural or numerical chromosomal aberrations. Electroencephalogram was normal.

Skeletal survey of the patient was normal with no calvarial thickening, no soft tissue calcification, no premature closure of epiphysis, and no osteosclerosis; computed tomography (CT) of brain showed bilateral extensive nonenhancing-hyperdense lesions (calcifications) involving the thalamus, dentate nuclei, putamen, globus pallidus, caudate nucleus, and subcortical white matter with Hu of 40 to 70 (Fig. 1).

Screening of other family members for bone profile and PTH levels was normal.

Genetic testing for Glial Cell Missing 2 (GCM2) and CaSR genetic mutations was sent for the patient and came out to be negative.

On the basis of the clinical, hormonal, radiological, and genetic findings, known causes of hypoparathyroidism were excluded. Pseudohypoparathyroidism and pseudopseudohypoparathyroidism were also excluded on the basis of the undetectable PTH level. FAHR syndrome was ruled out, as the patient had normal mentality and development.

Accordingly, idiopathic hypoparathyroidism was diagnosed in our patient.

The patient was discharged on regular oral Calcium gluconate 2 g/day and one-alpha-hydroxy-Vitamin-D3 of 1 μg/day with regular follow-up to adjust doses based on serum calcium and phosphorus levels.

The patient is being followed up for 5 years now with good serum calcium levels with no recurrence of tetany, and frequent adjustments of medication doses were required. The patient is growing well, achieving normal development without any neurological sequels with normal pubertal development and intelligence.

Follow-up CT brain revealed increased density of the calcifications (Hu of 160). Skeletal survey and renal ultrasound remained normal.

We report this case after approval of the research and ethical committees of Alhada Armed Forces Hospital, Taif, KSA. Written informed consent was signed by the father for reporting and publishing the patient's clinical data.

3. Discussion

Pediatric idiopathic hypoparathyroidism has been associated with BG calcifications in a considerable number of patients, but extensive intracranial calcifications outside the BG are extremely rare with only few reports in pediatrics (Table 1).[6–9] Our patient is the first report from Saudi Arabia. Although most of BG calcifications are a-symptomatic, but this patient is unique in

Table 1

Clinical characteristics of reported pediatric patients with idiopathic hypoparathyroidism who have extensive intracranial calcifications.

Case	Age/Sex	Etiology	Neurological findings		Basal ganglai calcification	Cerebral cortex calcifications (Outside the BG)	Reference
			Extrapyramidal	Others			
1	12/M	Idiopathic	+ (parkinsonism)	–	+	+	6
2	12/M	Idiopathic	+ (choreoathetosis)	–	+	–	7
3	17/M	Idiopathic	+	–	+	+	8
4	18/M	Idiopathic	+ (choreoathetosis, hemiballismus)	–	+	Also in the cerebellum + Also in the cerebellum	9
Our patient	11/M	Idiopathic	–	–	+	+	

having no neurological affection with normal intelligence in spite of the extensive bilateral cerebral cortex and intracranial calcifications added to the BG calcification. He is also unique in having normal growth and in achieving normal puberty.

We did not include the report of Soffer et al[10] in Table 1, as no intracranial calcifications were detected in their patients with idiopathic hypothyroidism and extrapyramidal manifestations.

Thorough history, physical examination, and investigations excluded most known causes of hypoparthyroidism. In addition, anti-alpha and anti-omega interferons antibodies that have a high sensitivity and specificity in detecting autoimmune polyglandular syndrome I[11,12] were negative; also, anti-CaSR was negative, excluding autoimmune hypoparathyroidism.

Our report is the first to study both CASR and GCM2 genetic mutations as compared with the previous 5 reports that made the diagnosis of idiopathic hypoparthyroidism in our patient on solid basis.

Multidisciplinary long-term follow-up by endocrinologist, neurologist, mental health consultant, nephrologist, and general pediatrician is planned to achieve excellent care of the patient and for better characterization of disease progression.

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