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CASE REPORT

Adult onset recurrent seizures as the first presentation of primary hypoparathyroidism [version 1; peer review: 2 approved with reservations]

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Abstract

Introduction: Hypoparathyroidism leading to hypocalcemia is an important treatable cause of recurrent seizures. Primary hypoparathyroidism presenting for the first time as seizures in adulthood is quite infrequent. Patients may present with hypocalcemic seizures even in the absence of subtle hypocalcemic signs.

Case report: A 30 year old male, was presented to the emergency facility in an unconscious condition. He was intubated on the way to the hospital as he had suffered from two episodes of ventricular tachycardia. He had previous history of recurrent seizures for 6 years inspite of multiple anticonvulsants including phenytoin sodium, sodium valproate, and levetiracetam. The seizure frequency increased in the last year and he would have 5-6 episodes/ month. A MRI brain scan and EEG at the onset were both normal, as was the general examination but he had history of bilateral cataracts. There were no signs of tetany. Investigations revealed a normal hemoglobin and glucose level with normal electrolytes and both TLC and DLC levels were also normal. He had a serum calcium level of 3.3 mg% with a serum parathyroid hormone level of 1pg/ml, serum 25(OH) vitamin D levels of 6.6ng/ml and hypomagnesemia. NCCT head scan showed bilateral basal ganglia, and deep white matter calcification.

Conclusions: 1) Ironically, increasing reliance on high end investigations such as a MRI brain scan could lead to certain conditions being missed; conditions that could be easily identifiable by the humble CT scan. 2) All treatable metabolic conditions should be excluded at first before commencing with anticonvulsants; this will restrict patients from burdensome polytherapy and related side effects.

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Approval Status ? ?

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1. **Gordon Klein**, University of Texas Medical Branch at Galveston, Galveston, TX, USA
2. **Michael A Levine**, The Childrens Hospital of Philadelphia, Philadelphia, PA, USA

Any reports and responses or comments on the article can be found at the end of the article.

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Editorial note:

Please note that the refereeing status of this article was changed from "indexed" to "[v1; ref status: approved with reservations 2]".

When this article was first published, *F1000Research* was still in its beta phase; during this period articles that received any two of "Approved" or "Approved with Reservations" statuses from the reviewers were labelled as "indexed". When the journal was formally launched in January 2013, the requirements for indexing were tightened, and only articles that are given either two "Approved" or one "Approved" plus two "Approved with Reservations" statuses by the reviewers are labelled "indexed". The new criteria for "indexing" can still be met in the future if a new revised version receives the necessary approval status from the reviewers.

Introduction

Hypoparathyroidism leading to hypocalcemia is an important treatable cause of recurrent seizures. Even though it is not an uncommon condition, primary hypoparathyroidism presenting for the first time as seizures in adulthood is quite infrequent. Patients may present with hypocalcemic seizures even in the absence of subtle hypocalcemic signs inclusive of tetany, Chvostek's sign or carpopedal spasms. As this is an entirely treatable condition, a high index of suspicion for primary hypoparathyroidism with hypocalcemic seizures should be maintained even in otherwise asymptomatic adults.

Case report

A 30 year old male, was presented to the emergency facility in an unconscious condition. He had been intubated on the way to the hospital as he had suffered from two episodes of ventricular tachycardia in the cardiac ambulance. He was being transported from a local hospital where he had been admitted for profuse diarrhea with dehydration.

He recovered during the hospital stay and on further inquiry it was discovered that he had a past history of recurrent seizures for the last 6 years inspite of being on multiple antiepileptic medications including phenytoin sodium, sodium valproate and levetiracetam. The seizure frequency had increased considerably in the last year, and he would have at least 5–6 episodes in a month, thereby creating a considerable toll on his personal and professional life. He had been evaluated with an MRI brain scan and an EEG at the onset of symptoms 6 years earlier and both were reported to be normal.

General physical examination was relatively normal, though he had a past history of being operated for bilateral cataracts six months ago. Also fundoscopic examination showed bilateral acute papilloedema. There was no carpopedal spasm or any other signs of tetany like Chvostek's or Trousseau's sign.

Investigations revealed normal hemoglobin and glucose level with normal sodium and potassium levels. TLC and DLC levels were also normal. He was found to have a serum calcium level of 3.3 mg% with a serum parathyroid hormone level of 1pg/ml, serum 25(OH) vitamin D levels of 6.6 ng/ml and hypomagnesemia. NCCT head scan was done which showed bilateral basal ganglia calcification and deep white matter calcification. A 2D ECHO study was performed, and showed normal results (Figures 1 and 2).

Figures 1 and 2. NCCT head scan showing bilateral basal ganglia calcification and deep white matter calcification.

A diagnosis of primary hypoparathyroidism was made. He was treated with anticonvulsants, oral calcium, magnesium and vitamin D supplementation. During his hospital stay he did not have any other seizure events.

Discussion

Intracranial calcifications can be classified mainly into 6 groups based on their etiopathogenesis: age-related and physiologic, congenital, infectious, endocrine and metabolic, vascular, and neoplastic¹ (Table 1). The function of the parathyroid hormone is primarily maintaining the plasma calcium levels. Hormonal disturbance of

Table 1. Causes of intracranial calcifications¹.

Classification	Cause
Age-related and physiologic	Pineal gland, habenula, choroid plexus, falx cerebri, tentorium cerebelli, dura mater, petroclinoid ligament, sagittal sinus
Congenital	Sturge-Weber syndrome, tuberous sclerosis, neurofibromatosis, lipoma, Cockayne syndrome, Gorlin syndrome
Infectious	TORCH diseases, granulomatous infections, chronic viral encephalitis
Endocrine & Metabolic	Fahr disease, hypothyroidism, hypoparathyroidism, hyperparathyroidism, pseudohypoparathyroidism, postthyroidectomy
Vascular	Primary atherosclerosis, cavernous malformation, arteriovenous malformation, aneurysms, dystrophic in chronic infarction and chronic vasculitis
Neoplastic	Oligodendroglioma, craniopharyngioma, germ cell neoplasms, neurocytoma, primitive neuroectodermal tumor (PNET), ependymoma, ganglioglioma, dysembryonic neuroectodermal tumor (DNET), meningioma, choroid plexus papilloma, medulloblastoma, low grade astrocytoma, pilocytic astrocytoma, pinealoma, pinealoblastoma, schwannoma, dermoid, epidermoid, calcified metastases (osteogenic sarcoma, mucinous adenocarcinoma)

the parathyroid glands including hypoparathyroidism, hyperparathyroidism and pseudohypoparathyroidism may lead to intracranial calcifications. Calcium accumulation is demonstrated primarily in the bilateral basal ganglia, dentate nuclei, and peripheral subcortical white matter sites².

The principal function of the parathyroid hormone (PTH) is the maintenance of calcium plasmatic levels, withdrawing the calcium from bone tissue, reabsorbing it from the glomerular filtrate, and indirectly increasing its intestinal absorption by stimulating active vitamin D (calcitriol) production. There are two mechanisms that may alter its function, limiting its control on calcium: 1) insufficient PTH production by the parathyroids (hypoparathyroidism), or 2) a resistance against its action in target tissues (pseudohypoparathyroidism). In both cases, there are significantly reduced levels of plasmatic calcium associated with hyperphosphatemia³.

In acute and/or severe symptomatic hypocalcemia there is a predominance of neuromuscular, neuropsychiatric, and cardiovascular abnormalities. There is an increase in neuromuscular excitability, latent or evident, with sensory and motor disruption. Perioral or extremity paresthesia, cramps, myalgia, and muscular weakness are mild to moderate symptoms. Neuropsychiatric manifestations include irritability, anxiety, psychosis, hallucinations, dementia, depression, mental confusion, and extrapyramidal abnormalities. Increased intracranial pressure, papilledema, and convulsions can also be present, and must be differentiated from severe tetany muscular spasms^{4,5}. Typical clinical signs of neuromuscular irritability

associated with latent tetany include hyperreflexia and Chvostek's and Trousseau's signs, respectively. Severe hypocalcemia may result in bradycardia or ventricular arrhythmias, cardiovascular collapse, and hypotension that is non-responsive to fluids and vasopressors³.

A decrease in myocardial contractility occurs, as well as a typical electrocardiographic abnormality, which is the rate-corrected QT interval (QTc) prolongation. Patients with chronic hypocalcemia may or may not have symptoms of discreet neuromuscular irritation, even with markedly low calcium levels. Asymptomatic cases may be detected by chance, by the dosage of calcium in routine exams, during periods of greater calcium demand (i.e. gestation, lactation, menstrual cycle and states of alkalosis), or during the use of hypocalcemic drugs (i.e. bisphosphonates)⁶.

Significant cognitive deficits, neuropsychiatric abnormalities, and extrapyramidal symptoms that resemble Parkinson's disease or chorea are associated with the calcification of basal ganglia, which occurs in all forms of chronic hypocalcemia and may be detected with greater sensibility using computerized tomography⁷. Other findings of chronic hypocalcemia include sub-capsular cataracts, an increase in bone mineral density (BMD), and greater susceptibility to dystonic reactions induced by phenothiazines⁴.

Differential diagnosis of hypocalcemia will depend largely upon PTH and phosphorus levels, evaluated along with other clinical and laboratory data (Table 1). Cases presenting hypophosphatemia should include differential diagnosis of vitamin D, while cases associated with hyperphosphatemia are determined according to PTH levels. Hypoparathyroidism is an abnormality caused by a parathyroid hormone (PTH) secretion deficiency, and encompasses heterogeneous conditions (Table 2), which makes etiological differentiation crucial to the detection of abnormalities associated with some of these diseases beforehand, thereby preventing complications⁴. Signs and symptoms are caused by hypocalcemia.

Laboratory measurements present hypocalcemia, hyperphosphatemia, and inappropriately low or undetectable PTH. Generally, levels of 1.25(OH) 2D are low and the alkaline phosphatase level

Table 2. Causes of hypoparathyroidism³.

Classification	Cause
Parathyroid Destruction	Surgery Auto-immune (isolated or polyglandular) Cervical irradiation Infiltration by metastasis or systemic diseases (Sarcoidosis, amyloidosis, hemochromatosis, Wilson's disease, thalassemia)
Reduced parathyroid function	Hypomagnesemia PTH gene defects Calcium sensing receptor mutations
Parathyroid agenesis	DiGeorge Syndrome Isolated x-linked hypoparathyroidism Kenny-Caffey syndrome Mitochondrial neuropathies

is normal. In the majority of cases, hypoparathyroidism is sporadic, but there are familial cases in which transmission may be autosomal recessive, dominant, or X-linked.

Management of acute or severe symptomatic hypocalcemia must be made with intravenous calcium, with the goal of interrupting symptoms, preventing laryngeal spasm, and maintain total calcium levels above 7.0–7.5 mg/dL (ionized calcium greater than 0.7mmol/L). Long-term treatment of patients with chronic hypocalcemia is done with 1 to 3 grams of elementary calcium per day in the various forms of salts available³.

All patients with hypoparathyroidism or pseudohypoparathyroidism who become hypocalcemic must use vitamin D or analogues in addition to calcium. The vast majority of patients obtain control with calcitriol in dosages of 0.25 µg, taken twice daily, up to 0.5 µg four times daily. Hypoparathyroidism causes increased excretion of urinary calcium in relation to serum calcium and predisposes hypercalciuria, nephrolithiasis, and nephrocalcinosis. The product of *calcium × phosphate* must be kept below 55. Patients must have their kidneys radiologically evaluated regularly in order to rule out nephrocalcinosis⁴.

Conclusion

1. Ironically, increasing reliance on high end investigations such as a MRI brain scan could lead to certain conditions being missed; conditions that could be easily identifiable by the humble CT scan.

2. All treatable metabolic conditions should be excluded at first before commencing with anticonvulsants; this will restrict patients from burdensome polytherapy and related side effects.

Consent

Written consent was obtained for publication of the patient's clinical details and images obtained from the patient.

Author contributions

PC compiled the entire dataset and wrote the entire report. RR was a treating neurophysician for the work and overlooked the writing of the report and CSA contributed to the data collection and report writing.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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References

- Kiroğlu Y, Çallı C, Karabulut N, *et al.*: **Intracranial calcifications on CT.** *Diagn Interv Radiol.* 2010; **16**(4): 263–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
- You JS, Kim HJ, Chung SP, *et al.*: **Intracranial bilateral symmetric calcification in hypoparathyroidism.** *Emerg Med J.* 2008; **25**(3): 162.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Maeda SS, Fortes EM, Oliveira UM, *et al.*: **Hypoparathyroidism and Pseudohypoparathyroidism.** *Arq Bras Endocrinol Metabol.* 2006; **50**(4): 664–73.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Levine M: **Hypoparathyroidism and pseudohypoparathyroidism.** In: DeGroot LJ, Jameson JL. *Endocrinology*, 4th ed. Philadelphia: WB Saunders, 2001; 1133–53.
[Reference Source](#)
- Weiss-Guillet EM, Takala J, Jakob SM: **Diagnosis and management of electrolyte emergencies.** *Best Pract Res Clin Endocrinol Metab.* 2003; **17**(4): 623–51.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Abugassa S, Nordenstrom J, Eriksson S, *et al.*: **Bone mineral density in patients with chronic hypoparathyroidism.** *J Clin Endocrinol Metab.* 1993; **76**(6): 1617–21.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Kowdley KV, Coull BM, Orwoll ES: **Cognitive impairment and intracranial calcification in chronic hypoparathyroidism.** *Am J Med Sci.* 1999; **317**(5): 273–7.
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Michael A Levine

Division of Endocrinology and Diabetes, Center for Bone Health, The Childrens Hospital of Philadelphia, Philadelphia, PA, USA

I do not believe that this case report advances this field as such findings are quite trivial. The tables are incorrect or incomplete and omits GCM2 mutations as a cause of hypoparathyroidism.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 21 November 2012

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Gordon Klein

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A few comments should be made about this case report. The first is that the authors note low serum levels of 25 hydroxyvitamin D. This is **not** parathyroid hormone (PTH) dependent and an etiology should be sought, i.e. inadequate sun exposure or failure of adequate vitamin D in the diet or any dietary supplements. Also, the low serum magnesium levels, while not reported, might contribute to peripheral PTH resistance.

Another thing to note is that advances in this field should be anticipated. For example, the use of parathyroid hormone replacement therapy and the advent of calcilytics (which are not yet marketed), would interfere with the action of the parathyroid calcium sensing receptor preventing a decrease in the set point for circulating calcium suppression of parathyroid hormone production or release.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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