INTRACTABLE SEIZURES CAUSED BY A RARE TREATABLE CONDITION

Hussein A. Algahtani, MD, FRCPC.
College of Medicine, King Saud Bin Abdulaziz University
Jeddah, Saudi Arabia

ABSTRACT
A case of a young man who presented with generalized tonic clonic seizures and intracranial calcification due to primary hypoparathyroidism was reported. He was diagnosed with primary generalized epilepsy for many years in a periphery hospital. His seizures were intractable despite treatment with three antiepileptic drugs. Further evaluation in our center revealed low calcium level, high phosphate, low parathyroid hormone and cerebral calcification on computed tomography imaging. Diagnosis of primary hypoparathyroidism was established and treatment started. He responded well to treatment and currently he has been seizure-free for eight years.

Keywords: Hypoparathyroidism, Seizures, Hypocalcemia, Intracranial calcification.

Address for Correspondence
DR. HUSSEIN A. ALGAHTANI
King Abdulaziz Medical City
P.O. Box 12723
Jeddah 21483
Saudi Arabia
e-M: halgahtani@hotmail.com

Submitted Date: 2/7/2012
MS Approved Date: 30/11/2012
INTRODUCTION
Hypoparathyroidism is a clinical disorder that results from insufficient secretion or weak action of the parathyroid hormone (PTH). It has a wide spectrum of clinical manifestations, ranging from being asymptomatic to intermittent tetany and intractable seizures. The objective of this report is to increase awareness of physicians to such a rare reversible cause of seizures and to consider hypoparathyroidism in the work up of these patients.

CASE REPORT
A 24-years-old right-handed Saudi gentleman presented with generalized tonic clonic seizures that started at the age of 12 years. His seizures were not preceded by aura and each attack lasts for one minute with postictal confusion and sleepiness for one hour. For years, he was labeled as a case of primary generalized epilepsy. He had cataract extraction surgery on the right eye. Family and social history were unremarkable.

His medications included valproic acid 1000 mg twice daily, carbamazepine 400 mg twice daily, and phenytoin 100 mg twice daily.

His vital signs, weight and height were normal with no dysmorphic features. General and systemic examinations were unremarkable. Neurological examination, including higher mental functions, cranial nerves, motor, sensory, reflexes and coordination examination, were normal.

His laboratory investigations showed hypocalcemia of 1.46 mmol/L (2.15-2.5 mmol/L) with a high phosphate of 2.4 mmol/L (0.87-1.45 mmol/L) and low PTH at < 1 pg/ml (10-69 pg/ml). Thyroid function test, liver function test, glucose and renal profile were all normal. Work-up for mitochondrial disease including ophthalmologic assessment, lactate and pyruvate were normal as well (the patient refused to go for a muscle biopsy). Work up for mitochondrial disorders is part of the investigations done for patients presenting with seizures and basal ganglia calcification on neuroimaging.

Computed tomography (CT) scan of the brain (Figure 1a and 1b) showed symmetrical distribution of calcification in the basal ganglia (lentiform nuclei, caudate nuclei and both thalami), dentate nuclei and corticomedullary junction in both cerebral (frontal) and cerebellar hemispheres with no evidence of focal lesion or mass effect. Magnetic resonance imaging (MRI) (Figure. 2a and 2b) confirmed the CT scan findings with symmetrical increase signal intensity in T1 and low signal intensity in gradient Echo with no evidence of mesial temporal sclerosis (MTS). Electroencephalography (EEG) obtained twice were reported as normal.

The patient was diagnosed to suffer from primary hypoparathyroidism and was started on oral calcium Caltrate 600 mg twice daily and Vitamin D 800 IU twice daily. His biochemical profile normalized, his seizures frequency improved dramatically, and eventually his antiepileptic drugs were stopped. First, carbamazepine was discontinued slowly over two months followed by phenytoin and finally valproic acid.
Intractable Seizures Caused by a Rare Treatable Condition

Hussein A Algahtani

DISCUSSION

Hypoparathyroidism is a clinical disorder that results from insufficient secretion or weak action of the PTH\(^1\). Figure 3 is demonstrating the control of mineral metabolism by PTH. The most common cause of hypoparathyroidism is inadvertent surgical damage to the parathyroid glands during thyroidectomy, radical neck dissection, or surgical management of primary hyperparathyroidism. It may also develop as a feature of autoimmune endocrinopathies, inherited disorders such as Kearns-Sayre syndrome and DiGeorge syndrome, and due to destruction from infiltrative process or radiation\(^2\).

Hypoparathyroidism has a wide spectrum of clinical manifestations, ranging from being asymptomatic, detected only by biochemical screening, to intermittent tetany and intractable seizures\(^3\). The duration, severity, and rate of development of hypocalemia determine the clinical presentation. Symptoms of hypocalemia include paraesthesia with tingling around the mouth and in the distal extremities, facial twitching, carpopedal spasm, laryngeal stridor, apathy, lethargy, and depression. Latent tetany can be demonstrated by contracture of the facial muscles on tapping the facial nerve in front of the ear (Chvostek sign) or by evoking carpal spasm by inducing ischemia in the arm with an inflated blood pressure cuff (Trousseau sign)\(^4\). Patients may also present with symptoms of congestive heart failure resistant to standard therapy but responsive to normalization of serum level of calcium. Dementia and psychosis have been described, with varying degrees of improvement, after correction of serum calcium concentration. Although seizures, usually generalized, are a well-recognized feature of hypoparathyroidism, they are often overlooked\(^5\). In addition, focal motor, atypical absence or akinetic seizures may occur. Hypoparathyroid-induced seizures are frequently misdiagnosed as idiopathic epilepsy, especially in children\(^6\). They tend to be frequent and respond poorly to antiepileptic drugs. Seizures are thought to occur due to hypocalemia.
and generalized bursts of spikes have been frequently reported. EEG may demonstrate slowing but may also be interpreted as normal. Attention should be directed toward correcting serum calcium concentration. Seizures diminish in frequency initially and finally stop when the level of serum calcium is raised to normal levels.

Reversible impairment of PTH secretion or PTH action with intact underlying secretory function

- Severe magnesium depletion
- Hypermagnesemia
- Constitutively active Calcium sensing receptors (CaSRs)

Genetic disorders of PTH biosynthesis and parathyroid gland development

- PTH gene mutations (familial hypoparathyroidism)
- Mutations or deletions in transcription factors and other regulators of the development of the parathyroid glands; DiGeorge syndrome and the closely related velocardiofacial syndrome
- Mutations in mitochondrial DNA (Kearns-Sayre syndrome, Pearson marrow pancreas syndrome, mutation of long-chain 3-hydroxyacylcoenzyme A dehydrogenase)

Resistance to PTH action

- Pseudohypoparathyroidism types 1a, 1b, and 2

and intracranial calcification that occurs in vascular and perivascular locations. Sometimes, seizure may be the sole presenting symptom of hypocalcemia. Nonconvulsive status epilepticus has also been reported. Attention should be directed toward correcting serum calcium concentration. Seizures diminish in frequency initially and finally stop when the level of serum calcium is raised to normal levels.

Although non-specific, electroencephalographic changes have been frequently reported. EEG may demonstrate slowing and generalized bursts of spikes. No correlation was found between calcium levels and EEG changes; thus changes typically revert to normal with correction of the serum calcium levels. The diagnosis of hypoparathyroidism is made based on clinical symptoms, hypocalcemia, hyperphosphatemia, and low or undetectable plasma PTH levels.

Intracranial calcifications are common in hypoparathyroidism and are best seen using CT scan. It most commonly affects the basal ganglia, however, the thalami, dentate nuclei, cerebral cortex, centrum semiovale, and mesencephalic gray matter may also might be involved. In 1855, Virchow and Bamberger independently described the histology of bilateral basal ganglia calcifications. In 1939, the association of basal ganglia calcification with chronic hypoparathyroidism was recognized by Eaton et al. Calcification of the basal ganglia really refers to calcareous deposits in the floor of the cortical convolution, the artery of centrum semiovale, the striatum, and the pallidum. Occasionally, the thalamus, red nucleus, subthalamic nucleus of Luys, dentate nucleus and white matter.

The calcifications are usually asymptomatic, but a variety of hypokinetic and hyperkinetic movement disorders have been seen in hypoparathyroidism. These include parkinsonism, choreoathetosis, dystonia, torticollis and hemiballismus. Symptoms may be reversible with appropriate treatment. Increased intracranial pressure with papilledema has been reported with hypoparathyroidism. The mechanism is unexplained and the cerebrospinal fluid (CSF) pressure returns to normal with correction of serum calcium levels. Hypoparathyroid myopathy with raised serum creatine kinase (CK) levels is another less common neurological syndrome.

Other rare systemic features include sensorineural hearing loss, premature cataracts, dry rough skin, coarse brittle hair, alopecia, and mucocutaneous candidiasis. Children may have enamel hypoplasia, dental caries and failure of secondary dentition.

Vitamin D and calcium supplements are the primary therapy for most forms of hypoparathyroidism. They are effective in relieving tetany and in restoring the serum calcium and phosphate levels to normal. Oral calcium is given with a dose of two to three grams of elemental calcium per day. Alternatively, dihydrotachysterol, 0.125 mg/day, can be prescribed. It is critical to monitor therapy closely since overtreatment may result in hypercalcemia, hypercalciuria, renal stones, and nephrocalcinosis.

CONCLUSION

Hypoparathyroidism is a rare but treatable cause of seizures. For any patient presenting with new onset seizures, simple laboratory investigations, including calcium profile, might reveal the underlying etiology. This patient’s diagnosis was missed by the peripheral hospital for a long period of time. Treatment should be targeted toward correcting the metabolic abnormality with calcium and vitamin D supplements. Our patient responded well to treatment with complete resolution.
of his seizures and dramatic changes in the quality of his life. To the best of our knowledge, this is the first case of hypocalcemic seizures due to hypoparathyroidism coming from Saudi Arabia.

REFERENCES


