Hypoparathyroidism: A rare treatable cause of epilepsy – report of two cases

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Hypoparathyroidism occurs due to insufficient production of parathyroid hormone to maintain extracellular calcium levels within the normal range. The acute clinical symptoms and signs of hypoparathyroidism are those of hypocalcaemia, ranging from tingling and numbness of limb extremities to intractable seizures. Often seizures are mistaken for epilepsy. Though hypoparathyroidism is not uncommon, the diagnosis is often missed due to its unusual clinical manifestation. This is the first documented report with vitamin D, Parathormone levels and urinary biochemical parameters from India. We present two cases of hypoparathyroidism who presented with seizures along with a short review of literature.

Introduction

Parathyroid hormone (PTH) works in conjunction with vitamin D to regulate the total body calcium. Hypoparathyroidism is a syndrome caused by insufficient secretion or weak action of parathormone leading to hypocalcemia and intermittent tetany. Hypoparathyroidism is commonly diagnosed during the workup for hypocalcemia. Symptoms caused by hypocalcemia are dominant and they are signs of disturbed neuromuscular balance. Seizures occur in 70% of patients with symptomatic hypoparathyroidism. Biochemical hallmarks of PTH insufficiency are hypocalcemia and hyperphosphatemia. Hypocalcemia resulting from hypoparathyroidism can be treated with good outcome. Overall, mortality rate depends on the cause of the hypoparathyroidism. Hypoparathyroidism presenting as seizures are reported in western literature [1]. There are case reports from India [2] of clinical, biochemical and radiological features of hypoparathyroidism. To the best of our knowledge, this is the first report of hypoparathyroidism presenting as seizures in India documented with parathormone and vitamin D levels.

Case reports

Case 1

A 16-year-old female presented with a first episode of generalized tonic–clonic seizure, recent onset cramps and chronic headache. There was no past or family history of epilepsy. General examination revealed grade 4 Trouseau’s sign and grade 1 Chvostek sign. There was no focal neurological deficit. A clinical diagnosis of hypocalcaemia was made. Biochemical and hormone investigations revealed hypocalcemia with low intact parathormone (Table 1). Electroencephalography (EEG) showed generalized burst of spike and slow wave discharges during hyperventilation and photic stimulation (Fig. 1). Computerized tomographic scan (CT scan) of the head showed bilateral basal ganglia and cerebellar calcification (Fig. 2).

Case 2

A 23-year-old male presented with a single episode of generalized tonic–clonic seizure. He had a past history of focal seizure at the age of 6 years after which he was not on medication. There is no family history of epilepsy. EEG showed background slowing to delta activity. There was bilateral basal ganglia and cerebellar calcification in the CT scan of the head. The patient did not have any symptoms of hypocalcemia. As there was bilateral basal ganglia calcification on the CT scan, he was investigated for hypocalcemia. Biochemical and hormone reports of the patient revealed hypocalcemia with low PTH levels (Table 1).

No history of drug intake, neck irradiation or chronic disease was identified in any of the patients. Both the patients did not have any history of any drug intake, neck irradiation or any chronic illness in the past.

Both patients had hypocalcemia, hyperphosphatemia with low serum PTH levels. The biochemical profile favored the diagnosis of idiopathic hypoparathyroidism. Both patients were started on daily supplementation of 0.5 µg of calcitriol and 1000 mg of elemental calcium (calcium carbonate).
Deficient PTH secretion can be due to post-surgical or idiopathic causes. Idiopathic cause is further categorized into congenital or acquired. Congenital hypoparathyroidism is a condition in which the person is born without parathyroid tissue. They usually have no family history of the disease. The inherited form tends to arise from abnormal genes. The acquired form of the disease typically arises because the immune system has developed antibodies against the parathyroid tissues in an attempt to reject it as a foreign body. In response to this, the parathyroid stops synthesizing and secreting PTH [3]. Idiopathic hypoparathyroidism presents mostly in the age group of 5–10 years [4].

Primary hypoparathyroidism is a state of inadequate PTH activity. In the absence of adequate PTH activity, the ionized calcium concentration in the extracellular fluid falls below the normal reference range. Hypoparathyroidism results in hypocalcemia, which has a spectrum of clinical manifestation. The history should focus on eliciting signs and symptoms of neuromuscular irritability, paraesthesias involving fingertips, toes, circumoral area, hyperirritability, fatigue, anxiety, mood swings and/or personality disturbances, seizures, hoarseness, wheezing and dyspnea (due to bronchospasm), muscle cramps, diaphoresis, biliary colic, hypomagnesemia, hypokalemia and alkalosis. Physical symptoms include muscle cramps and increased neuromuscular irritability demonstrable at the bedside by eliciting Chvostek sign and Trousseau sign. Other rare presentations include extrapyramidal choreoathetoid syndromes, Parkinsonism, dystonia, hemiballismus, oculargic crises and psychosis. Idiopathic hypoparathyroidism may also exhibit various neurological manifestations and/or psychiatric abnormalities.

Hypoparathyroidism usually starts insidiously, with slowly increasing episodic symptoms dominated by increased neuromuscular irritability. Clinically, hypoparathyroidism as part of the polyglandular autoimmune syndrome (type 1) does not differ from idiopathic hypoparathyroidism [4]. Intracranial calcifications have been attributed to hypocalcemia and may be a

### Table 1 Biochemical and hormonal investigations

<table>
<thead>
<tr>
<th>S.Ca (mg/dl)</th>
<th>S.P (mg/dl)</th>
<th>SAP (IU/l)</th>
<th>S.Cr (mg/dl)</th>
<th>Ur.Cr (mg/day)</th>
<th>Ur.Ca (mg/day)</th>
<th>Ur.P (mg/day)</th>
<th>Total volume (ml/day)</th>
<th>25(OH)D (ng/ml)</th>
<th>ntactPTH (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.5</td>
<td>9.5</td>
<td>14</td>
<td>0.9</td>
<td>456</td>
<td>60</td>
<td>408</td>
<td>2400</td>
<td>42</td>
<td>&lt;6.4</td>
</tr>
<tr>
<td>6.1</td>
<td>6.9</td>
<td>63</td>
<td>0.9</td>
<td>1480</td>
<td>72</td>
<td>340</td>
<td>4000</td>
<td>36</td>
<td>&lt;6.4</td>
</tr>
</tbody>
</table>

Normal values. S.Ca, serum calcium (8–10.5 mg/dl); S.P, serum phosphorus (2.5–4.8 mg/dl); SAP, serum alkaline phosphatase (<90 IU/L); S.Cr, serum creatinine (<1.5 mg/dl); Ur.Cr, urine creatinine/day (800–2000 mg); Ur.Ca, urine calcium/day (<250 mg); Ur.P, urine phosphorus/day (300–1300 mg); 25(OH) D, 25 hydroxy Vitamin D (>20 ng/ml); ntact-PTH, parathyroid hormone (intact) (>13–54 pg/ml).
function of its duration, seen commonly in idiopathic hypoparathyroidism and pseudohypoparathyroidism, and less commonly in surgically induced hypoparathyroidism [5]. Basal ganglia calcifications are most common but may rarely affect the symmetrical cortex, predominantly in the frontal lobe, subcortical white matter, thalamus, and cerebellum [6]. The mechanism of calcium deposition remains unclear but may be caused by a chronic abnormality of intra- and extracellular calcium and phosphate concentrations [7]. EEG changes have been frequently reported [8]. EEG may demonstrate slowing and generalized bursts of spikes. Nagashima and Kubota [9] reported bilaterally synchronous sharp and slow wave discharges of unusually long duration in idiopathic hypoparathyroidism and called it parathyroid epilepsy. Serum calcium and the extend of intracranial calcification might influence the EEG changes in idiopathic hypoparathyroidism. EEG changes may be seen with clinical type of seizures or who have no seizures at all. There is irregularity and fragmentation of postcentral background activity, a shift in frequency from $\delta$ (< 4 Hz) to $\theta$ (4–8 Hz), and increased low voltage fast activity. Lower calcium levels cause paroxysmal bursts of high voltage slow waves at 2–5 Hz. Irregular sharp spike and slow pattern appear at calcium levels lower than 6.5 mg/dl, resembling the pattern seen in hyperventilation. These irregularities may persist with the normalization of the calcium levels, but the abnormal background and photic response may persist for weeks to months [10]. The pathophysiology of most neurological syndromes accompanying hypoparathyroidism is accounted for by hypocalcemia. Hypocalcemia in the background of acidosis does not produce seizures. Tetany, muscle cramps and seizures respond quickly following calcium replacement.

Isolated hypoparathyroidism, in which PTH deficiency is not associated with other endocrine disorders or developmental defects, is usually sporadic, but it may occur on a familial basis. The age of onset is generally within the first decade, although hypocalcemia may be undetected until adult life. The diagnosis of hypoparathyroidism should be considered in any patient who has hypocalcemia and low parathormone levels. Sometimes hypocalcemia may be undetected. Investigation of new onset epilepsy is often a dilemma. There are no practice parameters which guide the physician to a unanimous investigation for a patient who presents to the clinic with a single episode of seizure. Most often biochemical investigation and neuroimaging are carried out without knowing what to expect out of the results. In fact, because of the yield of the routine investigations are low, they are usually not ordered. Yet there may be cases that might have been missed in initial evaluation of seizures and later investigations are ordered to detect metabolic abnormalities because of the worsening of seizures or development of other neurological or non-neurological symptoms. Hypocalcemia may present in 30 etiopathogenic variants and, consequently, being a problem for many clinical disciplines [11]. Case 1 had symptoms and signs of hypocalcemia, which encouraged us to investigate. Case 2 presented with a single episode of seizure with no symptoms or signs of hypocalcemia. Because of the presence of bilateral basal ganglia and cerebellar calcification on CT, the patient was investigated for hypoparathyroidism. The biochemical and hormonal investigation shown in Table 1 are diagnostic of the hypoparathyroidism. Patients were asymptomatic 1 year on follow-up.

Both cases of hypoparathyroidism presented as seizures. Secondary causes of epilepsy might occasionally be missed in the first seizure clinic. In the work up in a patient with new onset seizures, electrolytic disturbances such as hypocalcemia, hypercalcemia, hypoglycemia as well as endocrine disorders should be excluded.

References