

Case Report:**Primary hypoparathyroidism presenting as refractory status epilepticus**Mukut Roy¹, Nilanjan Sengupta², Pranab Kumar Sahana³, Chanchal Das⁴, Ranen Dasgupta⁵**Abstract:**

A case of adult onset primary hypoparathyroidism is reported highlighting the effect of phenytoin therapy on calcium metabolism. This patient of brain calcinosis syndrome (BCS) presented with refractory status epilepticus despite on full dose phenytoin. Seizures were controlled with correction of hypocalcemia. A change of anti-epileptic therapy to lamotrigine and supplementation with calcium and calcitriol kept the patient seizure free for last 10 months till last follow up.

Key Words: Idiopathic primary hypoparathyroidism, phenytoin, refractory status epilepticus.

Introduction:

Idiopathic hypoparathyroidism presenting in adulthood as refractory status epilepticus is quite rare.¹ We report an underdiagnosed metabolic effect of anti-epileptic therapy leading to the refractory nature of status epilepticus in this case of adult onset idiopathic hypoparathyroidism (IHP) with brain calcinosis syndrome (BCS).

Case report:

A 50 year old post-menopausal female presented to the emergency room with status epilepticus. Intravenous lorazepam was given with no improvement, phenytoin infusion was initiated and she was admitted to the medicine ward. Initial electrolytes reports revealed: normal sodium (140meq/l) (ref range: 136-146meq/l), potassium (3.6meq/l)

(ref range: 3.5-5.0mmol/l), magnesium (2.1mg/dl) (ref range: 1.5-2.3 mg/dl) levels with hypocalcemia (4.3mg/dl) (ref range: 8.5-10.5mg/dl). Subsequently, parenteral calcium infusion was given with continuous cardiac monitoring. Phenytoin was stopped and sodium valproate infusion also was initiated. With this, seizures controlled but she remained in a confusional state. Endocrinology consultation was sought for evaluation of hypocalcemia.

Enquiry revealed that she had similar attack about a month back & was treated in another hospital. Previous discharge summary mentioned that seizures responded with parenteral diazepam and subsequently a CT scan brain showed multiple hyperdense lesions. On refusal for further stay to that hospital, she was discharged next day with an advice to continue oral phenytoin (300mg/day) therapy.

Despite being on phenytoin, she presented to our hospital with recurrent status epilepticus. Her past, personal and family histories were non-contributory.

After recovery from the status, on clinical examination, she had positive Chvostek and Trousseau sign. Resting tremor and rigidity were present. However, other systemic and fundus examinations did not reveal any abnormality. Routine blood, urine examination and chest x-ray were normal. Blood urea was 28 mg/dl (ref. 15-45 mg/dL) and creatinine 1.2mg/dl (ref. <1.5 mg/dL). CT brain was showing evidence of calcifications involving bilateral basal ganglia and periventricular region (figure 1).

1. Mukut Roy, M.B.B.S, MD (Medicine), Post Doctoral Trainee (Endocrinology)
2. Nilanjan Sengupta, MD(Medicine), DM (Endocrinology), Associate Professor
3. Pranab Kumar Sahana, MD(Medicine), DM(Endocrinology), Associate Professor
4. Chanchal, Das, M.B.B.S(Cal), DCH(Cal), MD(Medicine), Post Doctoral Trainee (Endocrinology)
5. Ranen Dasgupta, MD(Medicine), DM (Endocrinology), Professor & Head

All the authors work in Department of Endocrinology, N.R.S. Medical College & Hospital, Kolkata-700014, West Bengal, India

Corresponding Author:

Dr. Mukut Roy, M.B.B.S, MD (Medicine), Post Doctoral Trainee (Endocrinology), Department of Endocrinology, N.R.S. Medical College & Hospital, Kolkata-700014, West Bengal, India, Email: mukutdoc@gmail.com

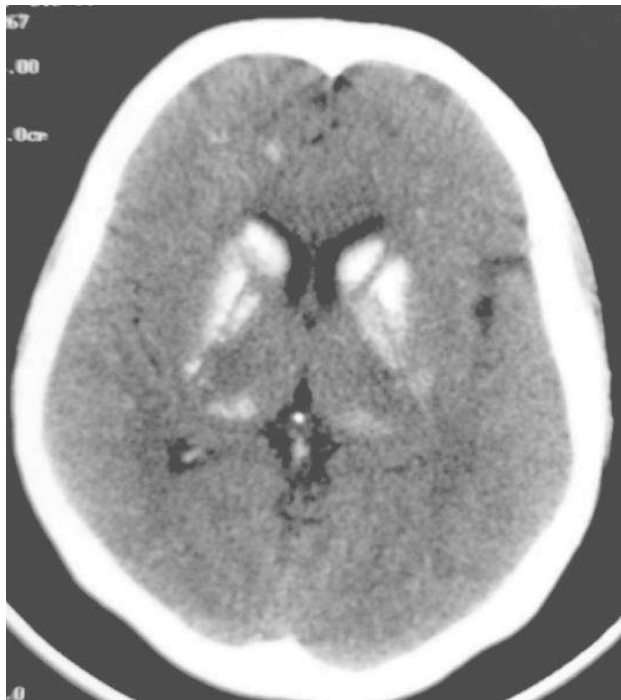


Figure 1: CT scan brain showing multifocal calcifications

A provisional diagnosis of brain calcinosis syndrome was made. Then resting EEG revealed background 8-10 Hz, 30-40 microvolt alpha activity and paroxysmal slow waves in right temporal region with secondary generalization (figure 2).

On endocrine evaluation, related salient biochemical parameters were elucidated (table 1) with biochemical profile of hypocalcemia, hyperphosphatemia and inappropriately low PTH. A final diagnosis of primary hypoparathyroidism was made. Her related family members had normal calcium levels. She had normal free T4 and TSH levels. She also had no evidence of any autoimmune diseases and normal levels of anti TPO antibodies. Subsequently, she was classified as having idiopathic primary hypoparathyroidism.

Parameters	Value
Calcium (mg/dl) (8.5-10.5)	4.3
Phosphorus (mg/dl) (3-5)	8.7
25-OH vitamin D (ng/dl) (11.1- 42.9)	20
Albumin (g/dl) (2.8- 4.9)	4.1
iPTH (pg/ml) (15- 65)	8.06
Magnesium (mg/dl) (1.8- 2.6)	2.3
24 hour urine calcium(mg) (<300)	380
TSH (micro IU/ml) (0.43- 4.8)	1.39

Table 1: Important biochemical parameters on endocrine evaluation.

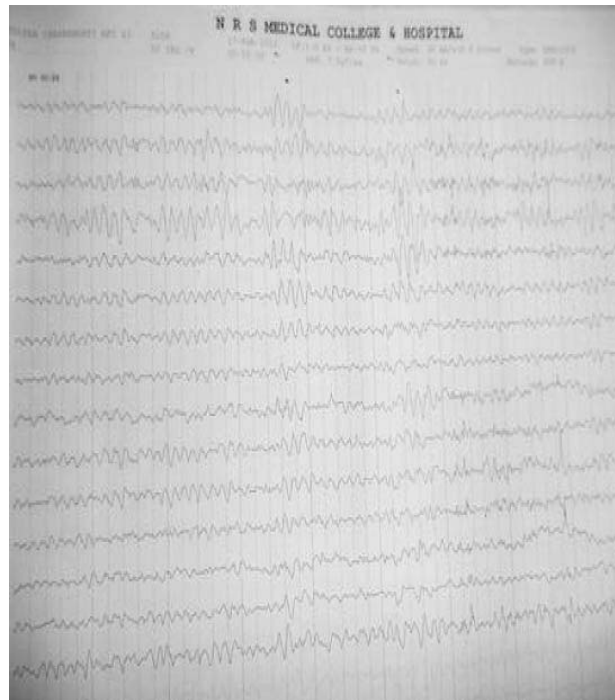


Figure 2: Resting E.E.G showing background alpha activity and paroxysmal slow waves

Oral calcium was initiated with a dose of 2g/day in divided doses and calcitriol of 0.5 µg/day. Phenytoin was stopped and lamotrigine was chosen as oral antiepileptic after a discussion with neurologist. With this approach, even after 10 months, she remains seizure free till last follow up. Serum calcium is being maintained at low-normal levels and serum phosphorus had normalized with a normal 24 hour urinary calcium excretion.

Discussion:

Hypoparathyroidism (HP) can be of varied etiology.¹ Hypoparathyroidism for long-standing duration can lead to brain calcinosis syndrome (BCS) which is defined as bilateral calcium accumulation in the brain parenchyma, most often within the basal ganglia.² Clinically, basal ganglia calcification may have diverse presentations including mental deterioration, disorders of cerebellar or extra-pyramidal function, movement disorders, chorea and parkinsonian features.²

Primary hypoparathyroidism presenting as refractory status epilepticus in adulthood is rare.¹ This case of primary hypoparathyroidism, at 50 years of age, presented for the first time without any history of hypocalcemic symptoms earlier. Subsequently, she was diagnosed as isolated idiopathic hypoparathyroidism (IHP) and brain calcinosis syndrome. The patient also developed refractory status epilepticus despite on anti-epileptic therapy (phenytoin).

When status epilepticus (SE) is refractory to first and second line anticonvulsants, the condition becomes critical

and requires ICU management. Earlier, a metabolic cause for SE was reported by Murthy et al. (11%).³ Metabolic factors like acute or severe symptomatic hypocalcemia in hypoparathyroid patients should be managed aggressively with intravenous calcium.¹ Long-term treatment is done with oral calcium and calcitriol supplementation.¹ Our patient also improved after initiating calcium and calcitriol supplementation and changing phenytoin to lamotrigine. In this case, phenytoin can be presumed as the aggravating if not the precipitating factor ultimately leading to refractory status epilepticus.

Hypocalcemic seizures are underdiagnosed complications of long-term therapy with anti-epileptics. Anticonvulsants should be used cautiously because most of the anticonvulsants may aggravate hypocalcemia, which further exacerbates the seizures. The inducers of the cytochrome P450 enzymes like phenytoin and carbamazepine are known to enhance vitamin D catabolism.^{4,5} Valproic acid is not an enzyme inducer but its metabolites act as anions and thus, binding plasma calcium ions and for this reason may cause hypocalcemia.⁵ For treatment of these patients, non-enzyme-inducing anticonvulsants are preferred. So far the knowledge goes; lamotrigine does not have any effect on calcium and bone dynamics.⁶

Despite the evidence suggesting adverse effects of different anti-epileptics including valproic acid on bone & calcium metabolism, there appears to be a lack of awareness among medical fraternity about these possible metabolic effects.

Also, in presence of hypoparathyroidism, phenytoin therapy could be potentially epileptogenic, by aggravating hypocalcemia, as in our case. So for the prevention of these potentially preventable effects, choosing the right anti-epileptic would be crucial in patients with seizure disorders secondary to abnormalities in calcium metabolism.

References:

1. Shoback D. Clinical practice. Hypoparathyroidism. *N Engl J Med* 2008; 359:391-403.
2. Manyam BV, Walters AS, Narla KR. Bilateral striopallidodentate calcinosis: clinical characteristics of patients seen in a registry. *Mov Disord* 2001; 16: 258-64.
3. Murthy JM, Jayalaxmi SS, Kannikannan MA. Convulsive status epilepticus: the clinical profile in a developing country. *Epilepsia* 2007; 48: 2217-23.
4. Gough H, Goggin T, Bissessar A, Baker M, Crowley M, Callaghan N: A comparative study of the relative influence of different anticonvulsant drugs, UV exposure and diet on vitamin D and calcium metabolism in out-patients with epilepsy. *Q J Med* 1986; 59:569-577.
5. Kulak CA, Borba VZ, Bilezikian JP, Silvado CE, Paola L, Boguszewski CL: Bone mineral density and serum levels of 25 OH vitamin D in chronic users of antiepileptic drugs. *Arq Neuropsiquiatr* 2004; 62:940-948.
6. Sheth RD, Hermann BP: Bone mineral density with lamotrigine monotherapy for epilepsy. *Pediatr Neurol* 2007; 37:250-254.