

## A mentally challenged adult with tonic convulsions, dysmorphic face and sebopsoriasis

John M, Sudeep K, Thomas N, Thomas M\*

Department of  
Endocrinology and  
\*Neurological Sciences,  
Christian Medical  
College, Ida Scudder  
Road, Vellore – 632 004,  
Tamil Nadu, India

**Correspondence:**

Mathew John,  
E-mail:  
drmathewjohn@yahoo.com

Received : 14-11-05

Review completed : 30-01-06

Accepted : 28-02-06

PubMed ID :

J Postgrad Med 2006;52:145-7

A 21-year-old man presented with increased frequency of intermittent tonic spasms of 3 weeks' duration. There was also history of fever and extensive cutaneous lesions involving the body, scalp and nails of 6 weeks' duration. From the age of 17 years, he experienced spontaneous paroxysmal tonic spasms involving extremities and trunk with retained consciousness and was on treatment with Carbamazepine and Sodium valproate. Behavioral problems were treated with Chlorpromazine, Nitrazepam and Trihexyphenidyl. For a week prior to admission, he was on treatment with Cefotaxime and Gentamicin for the febrile episode. He was born of a non-consanguineous union. Birth history and family history were non-contributory. Motor and mental milestones were delayed and he attended a school for the mentally challenged.

On examination, he was of normal stature (25<sup>th</sup> percentile), febrile and delirious. He had myoclonic movements of both upper limbs with tonic posturing of fingers. He had a dysmorphic face with low set ears, hypertelorism, narrow palpebral fissures and a broad forehead. The uvula was normal. There was no limb weakness. Ocular examination showed early posterior subcapsular cataract and papilledema. Well-defined scaly plaques with peripheral erythema with fissuring over the forearm, neck, face, scalp, groin and legs with palm and sole involvement, suggestive of sebopsoriasis were present. He also had sub-ungual hyperkeratosis with distal discoloration of the nails. Pubertal status was appropriate for age. On clinical assessment, he was judged to have moderate mental retardation.

On formal IQ testing, his intelligence quotient (IQ) was 60 (Binet Kamat scale for intelligence)

Biochemical investigations and blood cultures were ordered and an urgent CT scan of the brain [Figure 1] was performed, which was followed by a lumbar puncture.

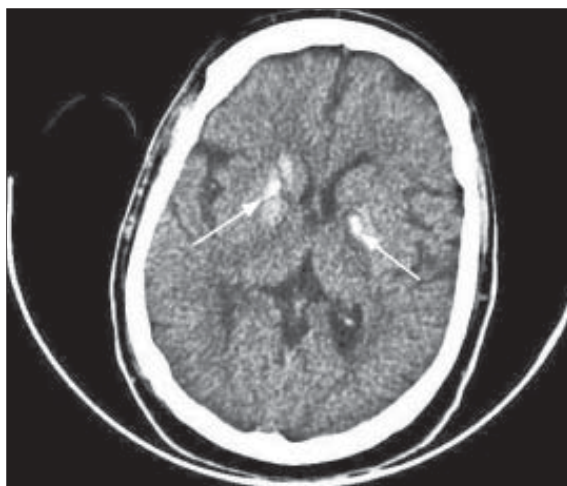


Figure 1: Non-enhanced CT scan of brain showing bilateral basal ganglia calcifications (Arrows)

### *What is the differential diagnosis for this presentation?*

This patient had paroxysmal episodes of spontaneous tonic spasms involving the limbs and extremities without loss of consciousness: paroxysmal non-kinesigenic dyskinesia (PNKD). PNKD can be familial (with an autosomal dominant inheritance) in nature. The secondary causes of PNKD include multiple sclerosis, perinatal hypoxia encephalitis, cystinuria, hypoparathyroidism, pseudohypoparathyroidism, Wilson's disease, thyrotoxicosis, head injury, hypoglycaemia, basal ganglia calcification, acquired immune deficiency syndrome (AIDS), diabetes mellitus, meningioma, cerebro-vascular accidents and Leigh syndrome. In view of fever with associated central nervous system symptoms, a lumbar puncture was also undertaken.

The non-enhanced CT scan showed bilateral basal ganglia calcifications. The ventricular systems and basal cisterns were prominent and reflected the degree of cerebral atrophy.

Name the conditions that would be included in the differential diagnosis in the light of CT scan findings.

The various causes for bilateral basal ganglia calcification are given in [Table 1].<sup>[1]</sup>

**Table 1: Differential diagnosis of basal ganglia calcification\***

- Idiopathic: with aging
- Endocrine: hypoparathyroidism, pseudohypoparathyroidism, hyperparathyroidism
- Metabolic diseases: Fahr's disease, mitochondrial cytopathies, Leigh's disease
- Post-infective: congenital TORCH infections, congenital HIV, neurocystercosis
- Congenital: Tuberous sclerosis, Down's syndrome, Neurofibromatosis
- Miscellaneous: Post-anoxia, cranial radiation, carbon monoxide poisoning, lead poisoning

\*Modified from reference 1

The results of biochemical investigations were as follows: venous plasma glucose: 106 mg/dl (80-120), Serum calcium: 3.3 mg/dl (8.5-10.5), Serum Phosphorus: 8.8 mg/dl (2.5-4.5), Serum albumin: 3.4 mg/dl (3.5-5), Serum magnesium: 1.32 mg/dl (1.8-3.0), serum creatinine: 0.9 mg/dl (0.8-1.2 mg/dl), Testosterone: 3.92 ng/ml (3-10), FSH: 3.12 IU/L (1.4-9.6), Cortisol: 18.8 mcg/dl (>18), PTH: 8 pg/ml (10-65), TSH: 1.14 mIU/ml (0.5-4.5), FT4: 1.88 ng/dl (0.8-2.0), Sodium: 143 meq/l (135-145), Potassium: 4.3 meq/l (3.5-5), Bicarbonate: 23 meq/l (22-29), Chloride: 94 meq/L (98-106), 25-OH Vitamin D: 7.9 ng/ml (10-40) Cerebrospinal fluid: Cells: 2 lymphocytes/mm<sup>3</sup> (0-5 cells/mm<sup>3</sup>), Glucose: 93 mg/dl, Protein: 17 g/dl, Measles IgG Antibody: negative. Brainstem Auditory Evoked Response: normal. 2D Echocardiogram: normal. Karyotype: XY. Blood cultures showed significant growth of Enterococci. Ultrasound study of the abdomen including the kidneys was normal.

#### *What do these biochemical investigations indicate?*

The investigations demonstrate the presence of hypocalcaemia, hyperphosphatemia and low PTH levels. This is suggestive of hypoparathyroidism. The other abnormal investigations in this group are hypomagnesaemia and low 25 hydroxy-vitamin D levels. The low vitamin D levels are likely to be due to the homebound state of the patient and chronic use of anticonvulsants. Low 25- hydroxy Vitamin D levels can sometimes cause a syndrome resembling pseudohypoparathyroidism.<sup>[2]</sup>

The possible causes of hypomagnesaemia in this patient are aminoglycoside usage, magnesium loss through the weeping skin lesions, reduced dietary intake and use of magnesium free intravenous fluids. Since, 25-30% of magnesium is bound to albumin, hypo-albuminemic states may lead to spuriously low magnesium values.<sup>[3]</sup> The presence of intra-cerebral calcifications establishes the fact that hypocalcemia is long-standing. The low chloride levels are likely to be related to increased cutaneous loss of chloride.

The presence of dysmorphic facies and mental retardation is in favour of a congenital onset of diseases. The various aetiologies of congenital hypoparathyroidism in this setting are summarized in [Table 2].<sup>[4]</sup>

**Table 2: Congenital hypoparathyroidism (modified from ref 4)**

- Idiopathic: with aging
- 22q11 deletions: DiGeorge syndrome, Velocardiofacial syndrome
- 10p13 deletion
- CHARGE syndrome
- Congenital hypoparathyroidism (X linked, Autosomal dominant, Autosomal recessive)
- Syndrome of hypoparathyroidism, deafness, renal dysplasia (HDR)
- Hypoparathyroidism-Retardation-Dysmorphism (HRD) syndrome: Kenny-Caffey syndrome, Sanjad-Sakati syndrome
- Type 1 autoimmune polyendocrinopathy
- Mitochondrial DNA mutations e.g. Kearns Sayre syndrome and MELAS

#### *How do you treat hypocalcaemia in this patient?*

In the acute phase, calcium gluconate may be given intravenously. This should be followed by an intravenous infusion of calcium at 0.5-2 mg/kg/hour. Simultaneously, oral replacement of calcium and vitamin D should be started: 2-4 g of calcium carbonate and 0.25 to 0.5 mg of Calcitriol. Alphacalcidol can also be used instead of Calcitriol. Hypomagnesaemia should be considered in situations predisposing to the same. A low serum magnesium level (<1 mg/dl) indicates magnesium deficiency, but magnesium deficiency can exist even with normal serum magnesium levels.<sup>[3]</sup> As the serum calcium level has normalized, elevated serum phosphate concentrations generally decline.<sup>[5]</sup>

The patient was treated with 10 ml of 10% calcium gluconate diluted in 10% dextrose given over 10 minutes, following which he was started on a calcium gluconate infusion. Two gram of 50% magnesium sulfate (16.6 mEq) diluted in saline was given intravenously over 60 minutes. This was gradually replaced with Calcitriol (0.5 µg/day) and Calcium carbonate (2 g/day). Magnesium replacement as an oxide salt was continued for two weeks. The enterococcal septicaemia was treated with Ampicillin and Amikacin for 10 days.

#### *What are the neuropsychiatric manifestations of hypoparathyroidism?*

Patients with hypoparathyroidism can present with parasthesias, tetany, choreoathetosis, mutism, locked jaw, papilledema and generalized tonic clonic epilepsy.<sup>[6]</sup> They can have gait disturbances, cognitive dysfunction, extrapyramidal signs, muscle spasms, seizures and psychosis.<sup>[7]</sup> Myopathy, sensorineural deafness and idiopathic intracranial hypertension have been described in hypoparathyroidism. Cerebellar signs and myelopathy due to vertebral lamina overgrowth can be present in long standing disease.<sup>[8]</sup> A reversible form of peripheral neuropathy that recovered following correction of hypocalcemia has also been described in hypoparathyroidism.<sup>[9]</sup>

#### *What are the skin manifestations of hypocalcaemia?*

Psoriasis vulgaris, pustular psoriasis and impetigo herpetiformis have been reported in hypoparathyroidism. Vitamin D and its analogues appear to affect cell differentiation and cell proliferation and hypocalcaemia may damage cell adhesion

molecules such as cadherins, which depend on calcium.<sup>[10]</sup> A patient with generalized psoriasis associated with hypoparathyroidism and HDR syndrome, cured by normalization of calcium has also been reported.<sup>[11]</sup> Patients with autoimmune polyendocrinopathy syndromes can have associated mucocutaneous candidiasis, alopecia and vitiligo as manifestations.

In patients with idiopathic hypoparathyroidism without other endocrine autoimmunity, antibodies to calcium sensing receptor have been demonstrated and a T cell mediated autoimmune destruction of the parathyroid glands has been postulated. The study also showed an increased occurrence of the HLADRB1\* 01 or DRB1\*09 alleles among the hypoparathyroid patients.<sup>[12]</sup> The fact that HLD –DR associations and T cell activation are major factors that underlie the pathogenesis of psoriasis may be another reason for the association between psoriasis and hypoparathyroidism.<sup>[13]</sup> Our patient was treated with topical steroids with significant clearing of the skin lesions within 2 weeks of therapy.

#### *How will you monitor treatment in hypoparathyroidism?*

The target of treating hypocalcaemia is to maintain calcium in the low normal range (corrected calcium 8.0-8.5 mg/dl) and preventing hypercalciuria simultaneously at the same time. This is done by monitoring serum calcium and urinary calcium (by either using a 24 hour urinary calcium estimation or calcium/creatinine ratio). Since there is an absence of the PTH effect on conservation of renal calcium, there can be hypercalciuria despite having low normal serum calcium values.<sup>[5,14]</sup> In the event that a complication of hypercalciuria or hypercalcemia develops, a reduction in the dose of calcium supplements and/or calcitriol is necessary. Annual ultrasound to screen for nephrocalcinosis should be undertaken. Ocular assessments should be undertaken yearly to assess the progress of posterior subcapsular cataract.<sup>[14]</sup>

Our patient has chronic hypoparathyroidism of congenital origin with dysmorphic features. This case highlights various issues in the management of hypocalcaemia and an interesting association with sebopsoriasis. The patient is currently on follow up maintaining normal biochemical parameters and free of involuntary movements. There is no recurrence of sebopsoriasis after correction of hypocalcemia.

## References

1. Deepak S, Jayakumar B, Shanavas. Extensive Intracranial Calcification. J Assoc Physics India 2005;53:948.
2. Shriram M, Bhansali A, Velayutham P. Vitamin D deficiency masquerading as pseudohypoparathyroidism type 2. J Assoc Physics India 2003;51:619-20.
3. Tong GM, Rude RK. Magnesium deficiency in critical illness. J Intensive Care Med 2005;20:3-17.
4. Singh J, Moghal N, Pearce SH, Cheetham T. The investigation of hypocalcaemia and rickets. Arch Dis Child 2003;88:403-7.
5. Levine AM. Hypoparathyroidism and Pseudohypoparathyroidism. In: Avioli LV, Krane SM (Editors) Metabolic Bone Disease and Clinically Related Diseases. 3<sup>rd</sup> ed. Academic Press: San Diego; 1998. p. 501-29.
6. Idris MN, Sokrab TE. Unusual neuropsychiatric manifestations of hypoparathyroidism: report of two cases. East Afr Med J 1998;75:127-8.
7. Chiu JS, Wang YF, Chen CA, Lin SH, Lin YF, Chu P. Rocks in the head: extensive intracranial calcification. Intern Med J 2005;35:362-3.
8. Jay CA, Abrams GM. Other endocrinopathies and the nervous system. In: Aminoff MJ (editor) Neurology and General Medicine. 3<sup>rd</sup> ed. Churchill Livingstone: Philadelphia; 2001. p. 383-96.
9. Goswami R, Bhatia M, Goyal R, Kochupillai N. Reversible peripheral neuropathy in idiopathic hypoparathyroidism. Acta Neurol Scand 2002;105:128-31.
10. Lee Y, Nam YH, Lee JH, Park JK, Seo YJ. Hypocalcaemia-induced pustular psoriasis-like skin eruption. Br J Dermatol 2005;152:591-3.
11. Aksoylar S, Aydinok Y, Serdaroglu E, Coker M, Ozdemir F, Ozkinay F. HDR (hypoparathyroidism, sensorineural deafness, renal dysplasia) syndrome presenting with hypocalcemia-induced generalized psoriasis. J Pediatr Endocrinol Metab 2004;17:1031-4.
12. Goswami R, Brown EM, Kochupillai N, Gupta N, Rani R, Kifor O, *et al.* Prevalence of calcium sensing receptor autoantibodies in patients with sporadic idiopathic hypoparathyroidism. Eur J Endocrinol 2004;150:9-18.
13. Nickoloff BJ, Nestle FO. Recent insights into the immunopathogenesis of psoriasis provide new therapeutic opportunities. J Clin Invest 2004;113:1664-75.
14. Goltzman D, Cole DE. Hypoparathyroidism. In: Favus MJ (Editor) Primer on Metabolic Bone Disease and Disorders of Mineral Metabolism. 4<sup>th</sup> ed. Lippincott Williams & Wilkins: Philadelphia; 1999. p. 226-9.