Case Report

Congenital hypoparathyroidism presenting as recurrent seizures in an adult

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Abstract

Hypocalcemia due to hypoparathyroidism may manifest as serious neurologic symptoms such as seizures, movement disorders, or raised intracranial pressure. Several patients were observed to have these dangerous neurologic complications even without subtle signs of hypocalcemia like tetany, chvostek's sign or carpopedal spasms. We present a case of recurrent hypocalcemic seizures due to congenital hypoparathyroidism.

Key words: Hypoparathyroidism, seizures, hypocalcemia

INTRODUCTION

Neurologic manifestation of hypoparathyroidism can range from signs of latent tetany to frank seizures. Seizures in hypoparathyroidism can be due to hypocalcemia or rarely because of intracranial calcifications. This interesting case highlights the importance of hypoparathyroidism as an etiology of recurrent seizures.

CASE REPORT

A 17-year old female presented to us with a history of generalized tonic clonic seizures of 20 min duration. Leading questions revealed that the patient had similar episodes of seizures with a frequency of four to five times a month since she was 8 years of age. There was no history of head trauma in childhood. Detailed treatment history was not available. After seizures were controlled with anticonvulsants, the general physical examination revealed normal vitals, mild pallor, peculiar facies in the form of long face, prominent forehead, broad and depressed bridge of nose, small philtrum, hypertelorism, and bilateral lenticular cataracts [Figure 1]. Carpopedal spasm was present and other signs of latent tetany such as Chovstek's sign and Trousseau's sign were present. CVS and RS examinations were normal. CNS examination revealed moderate mental retardation in higher function testing.

Investigations revealed a normal hemogram. RBS was normal. TLC and DLC were within the normal range. Serum Na^+, K^+ were normal; serum calcium—total 5.2 mg% (normal 9–11 mg%), serum ionic calcium—1 mg/dl (normal 4.5–5.5 mg/dl). KFT and LFT were normal; serum parathyroid hormone level—2.76 pg/ml (normal

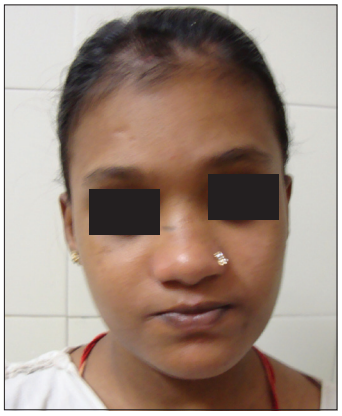

Figure 1: The typical facies of DiGeorge's syndrome

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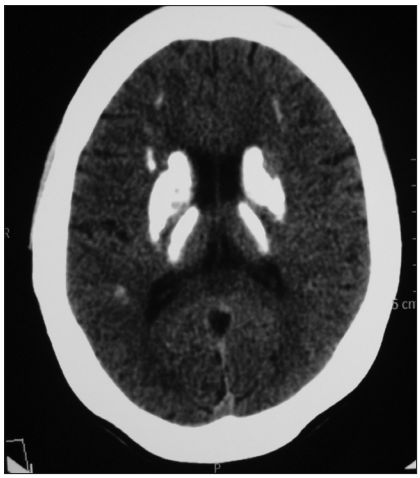

Figure 2: CT scan of brain showing symmetric calcification in bilateral caudate nucleus, lentiform nucleus, and gangliocapsular region.

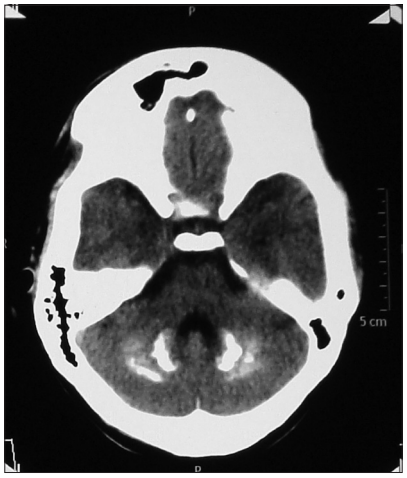

Figure 3: CT scan of brain showing symmetric calcification in the dentate nuclei of posterior fossa

8–51 pg/ml), ECG–QTc—0.48 s. A 2 D ECHO study was normal. CT brain revealed extensive intraparenchymal calcifications [Figures 2 and 3].

A diagnosis of congenital/hereditary hypoparathyroidism was made. The patient was treated with anticonvulsants, oral calcium 1 g/day and vitamin D 1 mg/day. During the hospital stay of 10 days, she had two attacks of seizures with documented hypocalcemia. After 2 months of follow-up, frequency of seizures were slightly decreased (three attacks) and evidence of latent tetany were absent.

DISCUSSION

Intracranial calcification is rarely physiological.[1] Physiological intracranial calcification occurs in about 0.3–1.5% of cases. It is asymptomatic and detected incidentally by neuroimaging. Among the pathological causes [Table 1], one of the important endocrine causes is hypoparathyroidism.

Table 1: Causes of intracranial calcification on neuroimaging

Classification	Causes
Physiological	Aging
Familial idiopathic cerebral calcification	Fahr's syndrome
Infections	CMV Toxoplasmosis Measles Mumps Rubella Acquired immunodeficiency syndrome (especially in children) Coxakie B Varicella
Endocrine disorders	Hypoparathyroidism Pseudohypoparathyroidism Pseudopseudohypoparathyroidism Hyperparathyroidism
Toxins and drugs	Carbon monoxide intoxication Lead poisoning Radiation therapy Methotrexate therapy
Mitochondrial disorders	Leigh's disease Kearns–Sayre syndrome Melas Merrf
Congenital	Down's syndrome Neurofibromatosis Tuberous sclerosis Lipoid proteinosis
Others	Cockayne's syndrome

Hypoparathyroidism can be congenital/ hereditary, iatrogenic (e.g., drugs, removal of the parathyroid glands during thyroid or parathyroid surgery, radiation), infiltrative (e.g., metastatic carcinoma, Wilson's disease, sarcoidosis), suppression of parathyroid function such as in hypomagnesemia, infective (HIV/AIDS), or idiopathic which is a diagnosis of exclusion.[2] Prevalence of hypoparathyroidism is equal in men and women and occurs in all age groups. Basal ganglia calcification is a known association of hypoparathyroidism, the most common site being globus pallidus.[3] Extensive intracranial calcification as in this case is a rare phenomenon.

Basal ganglia calcification can manifest as seizures, mental deterioration, cerebellar ataxia, Parkinsonism, chorea, and rarely it can be asymptomatic.[4] The emergence of CT has led to the finding that sporadic calcification is the most common form, present in up to 1.5% of all brain scans.[5]

Decreased PTH levels, hypocalcemia, and hyperphosphatemia in our case suggest primary hypoparathyroidism. As

Table 2: Description of congenital/inherited causes of hypoparathyroidism

Disorder	Genetic abnormality	Clinical features
Familial hypoparathyroidism	Mutation of a transcription factor, glial cell missing (GCMB) (6p23)[6]	Same as hypoparathyroidism
X-linked recessive hypoparathyroidism	Deletion/insertion of DNA near the *SOX3* gene at Xq26-Xq27.[7] Interstitial deletion–insertion involving chromosomes 2p25.3 and Xq27.1, near SOX3.	Same as hypoparathyroidism
Kenny–Caffey syndrome	Mutations in the chaperone protein, TBCE 1q43-44.[8]	Deep-set eyes Beaked nose Long philtrum, thin upper lip Micrognathia Large floppy earlobes Macrocephaly Dwarfism Hypoparathyroidism
Hypoparathyroidism, deafness, renal dysplasia (HDR)	1q43-44.[9] Mutation of the transcription factor GATA3	Hypoparathyroidism Renal dysgenesis Deafness
Sanjad-Sakati Syndrome	(OMIM 241410) locus to chromosome 1q42-43[10]	Long narrow face Deep set small eyes, beaked nose Large floppy ears Micrognathia Mild to moderate mental retardation
(1) Kearns–Sayre syndrome. (2) Mitochondrial trifunctional protein	Mitochondrial myopathies[11]	Complete heart block Hypoparathyroidism Progressive external opthalmoplegia
DiGeorge's syndrome	Microdeletion of 22q11.21-q11.23[12] t(2;22)(q14;q11) balanced translocation Chromosome 22q11 deletion Deletion of the *TBX1* Gene Terminal 10p deletions or interstitial 10p13/10p14 deletions	Typical facies Hypoparathyroidism MR Cardiac defects (may not be present in incomplete forms) Immunodeficiencies (T cell) Cataracts
Recessive autoimmune polyglandular syndrome, Type 1	Mutations in the autoimmune regulatory gene (AIRE).[13]	Hypoparathyroidism Vitiligo Addison's disease Chronic mucocutaneous candidiasis Pernicious anemia
Other inherited forms of hypoparathyroidism	—	Lymphedema dysmorphism, renal cardiac abnormalities,[14] Or isolated abnormalities

discussed, abnormal facies, mental retardation, bilateral lenticular cataracts, extensive intracranial calcifications, and most importantly manifestation of the disease from early childhood suggests congenital/hereditary etiology. Long-standing hypocalcemia associated with hyperphosphatemia (observed with PTH deficiency or resistance) leads to calcification of the basal ganglia and mineral ion deposits in the lens leads to cataract formation.

The differential possibilities of congenital/hereditary hypoparathyroidism with their predominant features are described [Table 2].

The typical facies in our case was of DiGeorge's syndrome. DiGeorge's syndrome occurs sporadically and is associated with an embryologic defect in the formation of the third, fourth, and fifth branchial pouches, resulting in the absence of parathyroid glands. DiGeorge's syndrome may, in fact, be a neurocrestopathy, because ablation of the premigratory cephalic neural crest in chick embryos produces the same phenotype.[15] The contribution of homeobox genes to parathyroid development and their potential relationship to DiGeorge's syndrome also has been demonstrated by the absence of thymic and parathyroid tissue, accompanied by cardiac and craniofacial abnormalities, in mice lacking the homeobox gene *hoxa3*.[16]

Absence of cardiac defects and T-cell dysfunction can occur in incomplete penetrance of DiGeorge's syndrome. Florescent *in situ* hybridization (FISH) to detect the abnormal chromosome could not be done in our case because of financial constraints.

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