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Case Report

Nephrogenic Diabetes Insipidus with Intracranial Calcifications in a Child with Thalassemia Minor

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Abstract

Introduction: There are numerous causes for intracranial calcification in children. We describe an unusual cause of intracranial calcifications in a child, namely, nephrogenic diabetes insipidus (NDI).

Case Report: A 12-year-old boy presented with seizures and developmental delay. MRI of the brain revealed intracranial calcifications. Evaluation showed findings suggestive of NDI.

The lack of evidence of any other metabolic defect suggests that these calcifications were secondary to NDI. He also had anemia for which he was investigated and diagnosed as thalassemia minor.

Detailed literature review failed to reveal any reported association between NDI and thalassemia minor.

Conclusion: We report this case to emphasize the importance of early diagnosis and treatment of NDI to prevent organic brain damage.

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Introduction

Nephrogenic diabetes insipidus (NDI) is a condition in which the kidneys are unable to concentrate urine, despite normal or elevated plasma concentrations of antidiuretic hormone [1]. It can be congenital or acquired. In the congenital type, 90% of cases are inherited as X-linked recessive whereas 10% are inherited as autosomal recessive [2]. Causes of acquired NDI include lithium therapy, protein energy malnutrition, hypercalcemia, hypokalemia, the release of urinary tract obstruction [3], dysplastic kidneys, renal tubular acidosis and sickle cell disease. Early manifestations of the disease include polyuria, excessive thirst, irritability, poor feeding and poor weight gain. Children may present with repeated episodes of fever due to dehydration [4]. Intracranial calcification is an unusual complication of NDI.

We report a 12-year-old male with thalassemia minor who presented to us with seizures and developmental delay. Further work-up revealed intracranial calcifications. Other laboratory results as well as therapeutic interventions indicated that the child was suffering from NDI.

Case Report

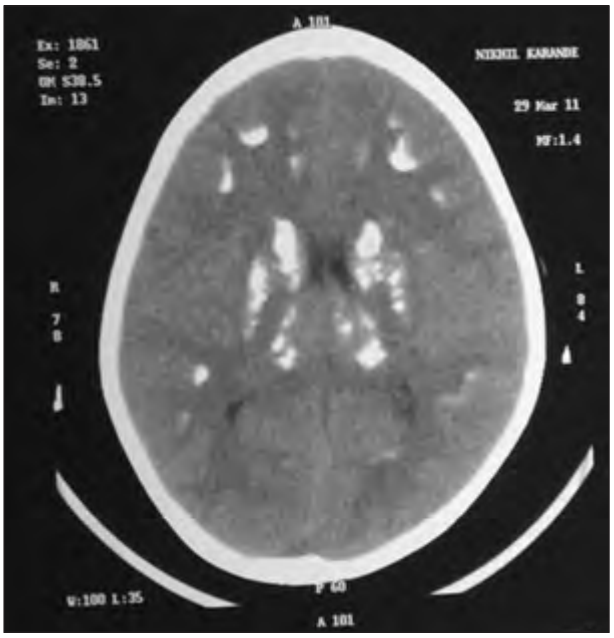
A 12-year-old boy presented with history of developmental delay and seizures. He was the only child of non-consanguineous parents. His gestational history and delivery were normal. He had repeated episodes of febrile illnesses during infancy for which he was admitted to hospital on three to four occasions. His parents had noticed polyuria and polydipsia during early childhood but he was not investigated for that. He also had nocturnal enuresis, his milestones were delayed, and he had repeated attacks of generalized tonic clonic convulsions during the previous two years. His seizures were persistent despite being maintained on anticonvulsants; accordingly he was referred for further management.

On examination he was conscious, markedly stunted with a height of 117 cm, head circumference of 48 cm and a body weight of 20 kg. His optic fundi were normal. Muscle tone was increased in all four limbs and tendon reflexes were exaggerated with bilateral extensor plantar response. He had discrete motor coordination defects and a broad based gait. On the Vineland Social Maturity Scale, the child attained an IQ of 75, suggestive of borderline mental sub-normality. The rest of his clinical examination was normal.

His MRI brain showed extensive bilateral subcortical calcifications involving the fronto-parietal regions, basal ganglia, thalamus and cerebellar white matter (Figure-1). His blood investigations showed serum sodium of 170 mmol/L, potassium of 3.2 mmol/L, calcium of 7.9 mg/dL and phosphorus of 2.4 mg/dL. His blood urea nitrogen (BUN) was 31.6 mg/dL, serum creatinine 1.8 mg/dL and blood sugar 106 mg/dL. His urine volume was 12 mL/kg/hr, with an osmolality of 169 mosmol/kg and a corresponding serum osmolality of 361 mosmol/kg. Vasopressin response test, one hour after intramuscular injection of 5 units of vasopressin did not show any significant increase in urine osmolality, from 197 mosmol/l to 228 mosmol/l, confirming the diagnosis of NDI. Electroencephalogram was abnormal with generalized slow waves and polyspikes. Serum PTH level was normal and ADH level was 18 pg/ml (normal range 1-5 pg/ml). He was also found to have thalassemia minor with hemoglobin-F (3.4%) and hemoglobin-A2 (5.4%).

Evaluation for secondary causes of NDI in the form of serum calcium, parathyroid hormone, serum potassium, urinary calcium/creatinine ratio, and ultrasound scanning of the kidneys, ureter and bladder for nephrocalcinosis

Figure-1: MRI Brain showing intracerebral calcifications involving bilateral frontoparietal, basal ganglia and thalamus region



and dysplastic kidneys were non-contributory. Sickling test and serological screening for TORCH group of infections were negative. There was no history of a similar illness in the family.

He was started on hydrochlorthiazide (3 mg/kg/day) and amiloride (0.3 mg/kg/day), and advised to drink plenty of oral fluids in order to avoid further episodes of dehydration. Two weeks after initiation of therapy his serum sodium was normalized to 144 mmol/L, calcium to 9.6 mg/dL, BUN to 12 mg/dL and serum creatinine to 0.8 mg/dL. Six months after initiation of therapy his frequency of nocturnal enuresis had decreased and he had no more convulsions.

Discussion

Intracranial calcification is an uncommon manifestation of NDI. Episodes of recurrent hypernatremic dehydration can cause necrosis of endothelial cells and dystrophic calcification in the affected areas. Occurrence of calcification in and around the blood vessels in NDI supports this hypothesis [5, 6].

The developmental delay described in this patient might be due to repeated hyperosmolar insults to the developing brain. In a brief description by Tomio Nozue *et al* of seven patients with intracranial calcifications and DI,

all patients had delayed psychomotor development and five of them had seizures despite normal serum calcium levels [7]. Hypernatremia has been found to be associated with mild hypocalcemia, the mechanism for which is unknown [8, 9]. Some studies suggest that it may be due to an alteration of extracellular and skeletal calcium, and is typically seen when hypernatremia is associated with mild hypokalemia [9]. So far, no prior association was reported in the literature regarding the co-existence of NDI and thalassemia, as seen in our patient.

General management of NDI requires family education, liberal fluid intake and avoidance of dehydration [2, 10]. Further treatment includes a combination of oral hydrochlorthiazide and amiloride; though indomethacin is also known to have a role [2, 10].

We hereby emphasize on the importance of timely diagnosis and early intervention in patients with NDI to prevent psychomotor delay, growth failure and seizures [11].

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