Case Report

Rare association of thin corpus callosum with infantile tremor syndrome in a 5.5-month-old infant

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ABSTRACT

Infantile tremor syndrome (ITS) is a clinical disorder characterized by coarse tremors, anemia and regression of motor and mental milestones, presenting in malnourished children aged between 5 months and 3 years. Few reports of neuroimaging abnormalities in children with ITS are present. The most common finding of neuroimaging in ITS is cerebral atrophy with ex-vacuo enlargement of ventricles and subarachnoid space, some recent reports also showed pontine myelinolysis and cerebral hyperintensities. We did not find any report of thin corpus callosum associated with ITS in the literature.

Key words: Infantile tremor syndrome, thin corpus callosum, Vitamin B12

Introduction

Infantile tremor syndrome (ITS) is a clinical syndrome of acute or gradual onset of mental and psychomotor changes, pigmentary disturbances of hair and skin, pallor, and coarse tremors in malnourished children aged between 5 months and 3 years. It has been primarily reported from India and South East Asia and has also been reported from other developing countries in Asia and Africa. Various nutrient deficiencies (e.g. Vitamin B12, magnesium [Mg], zinc [Zn], Vitamin C, etc.,) have been found to be associated with ITS. Other causative theories include viral encephalitis and degenerative processes. Clinically the presence of tremor has been attributed to structural and functional alterations of extrapyramidal system, but routine neuroimaging studies with computed tomography (CT) scan and magnetic resonance imaging in past revealed non-specific structural changes in ITS.

Here, we report a classical case of ITS with a rare association of thin corpus callosum. To the best of our knowledge, this is the first reported case of such an association in the literature.

Case Report

A 5.5-month-old female infant presented with pallor for 1-month, tremors of hands and feet for 2 days and delayed development. There was no history suggestive of fever, bleeding, rash, lymphadenopathy, hepatosplenomegaly,
jaundice, or seizures. The child was born at term gestation with no antenatal, natal, or postnatal complications. The child was exclusively breastfed. The child weighed 5.5 kg, had a length of 66 cm and head circumference of 41.5 cm. On physical examination, the child had sparse hair, pallor, and hyperpigmented knuckles [Figure 1]. There were coarse tremors in all four limbs, the perioral and periorbital region in awake as well as sleep state [Video 1]. Tremors were less in sleep stage. There was increased tone in all 4 limbs, but no paresis of limbs or cranial nerve palsies. There was no fracture or bruise. Investigations revealed anemia (hemoglobin = 6.6 g%), mean corpuscular volume (MCV) (103.7 fl), mean corpuscular hemoglobin (MCH) (38 pg), MCH concentration (37.4%), with normal leucocyte count (11,400/mm$^3$), and platelets (4 lakh/mm$^3$). Peripheral smear suggested dimorphic anemia. Serum B12 level was 202 pg/ml (200–900 pg/ml) and serum folic acid was 6.3 ng/ml (5–21 ng/ml). Cerebrospinal fluid (CSF) examination revealed no red blood cells or neutrophils, normal protein, sugar, and sterile cultures. CT scan of the brain revealed cerebral atrophy with thin corpus callosum [Figures 2 and 3].

Based on the clinical features, child was diagnosed as ITS. Initially, we have given her propranolol, B12, Mg, and multivitamins, but there was no improvement in her condition. Then, we started carbamazepine after 4 days and a dramatic response was observed after 7 days, as appetite improved, tremors disappeared during sleep and decreased in amplitude in the awake state. After 1-month of follow-up, the child is active, gaining weight (6 kg), hemoglobin has improved (9.4 g%), and tremors stopped. After 2 months of follow-up, propanol and carbamazepine have been tapered and stopped.

**Discussion**

A classical picture of ITS is a plump looking infant between 6 and 18 months with the presence of malnutrition. Usually, these children are listless, apathetic, and disinterested in surroundings. Scalp hair is sparse and light colored. Dark pigmentation is present over dorsal aspects of hands, nail folds, feet, knees, ankles, buttocks, and axillae. There is regression of milestones in the recent past. Tremors have an acute onset following an acute infection or stress. Initially, they are intermittent but become continuous in a few days. They are more prominent in distal parts of limbs, head, face, and tongue. These tremors disappear during sleep. Most of the classical findings were present in our case. Tremors have been attributed to structural and functional alterations of extrapyramidal system.[3] There is presence of anemia, which may be macrocytic, microcytic, or normocytic.

The etiology of ITS is still elusive. Malnutrition, vitamin and mineral deficiency (e.g., Mg and Zn), infections, toxins, degenerative brain disease, enzyme defects (e.g., tyrosine) all have been postulated as the causation of ITS.[1] Among various theories, the nutritional theory is the most accepted. Vitamin B12 deficiency has been found to be associated with ITS in many studies.[1] It is usually seen in children who are exclusively breast-fed for prolonged periods by vegetarian mothers. The low levels of Vitamin B12 and its
transport protein transcobalamin II (TC II) in the CSF may be responsible for the neurological features of this syndrome. Iron, Mg, and Zn deficiency have also been postulated to cause ITS. It is usual to find direct or indirect evidence of associated other nutritional deficiencies such as protein, Vitamins A, D, C, and B-complex and other micronutrients. Other speculations for its etiology include viral encephalitis and degenerative processes.

ITS is essentially a clinical diagnosis with peripheral smear suggestive of anemia (mostly megaloblastic anemia, macrocytosis (MCV >95), hypersegmented polymorphs, and megaloblastic bone marrow). Vitamin B12 levels may be low. CSF levels of Vitamin B12 and TC II may be reduced. Vitamin B12 levels in the mother may also be low suggesting low levels in the breast milk. Serum levels of Zn, ascorbic acid, and Mg may be low.

Only a few reports of neuroimaging in ITS are available. Most reports have shown normal neuroimaging findings or cerebral atrophy, ventricular prominence and/or prominence of the subarachnoid space, pontine myelinolysis, and cerebral hyperintensities. In our case, CT scan showed cerebral atrophy along with thin corpus callosum.

Thin corpus callosum is usually present in premature babies and is associated with poor neurological outcome and neuropsychological performance, but our case was delivered at term gestation and her antenatal, natal, and postnatal course was uneventful. To the best of our knowledge, thin corpus callosum has never been reported in ITS in the past.

Treatment consists of therapy for anemia and nutritional deficiency. Vitamin B12 in high doses may be required if B12 levels are low. Multivitamins, Vitamin C, iron, protein, Zn, and Mg supplements may also be necessary. If the tremors are severe, phenobarbitone or carbamazepine may be required to decrease the intensity. The tremors subside slowly. Initially, there is a gradual reduction in the amplitude and severity, and then the tremors become intermittent and finally stop. Propranolol and chlorpromazine are other drugs, which can be used to control tremors.

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Conflicts of interest
There are no conflicts of interest.

References