Infantile Tremor Syndrome

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Introduction

Infantile tremor syndrome (ITS) is a rare clinical disorder characterized by coarse tremors, anaemia and regression of motor and mental milestones in children of around one year of age. Exact incidence is not known. In India, it accounts for 0.2 to 2 % of paediatric hospital admissions (1-2% in 1960s, 1.1 % in 1975-77 and 0.2% in mid-1990s) [1]. Improvement in nutritional status, living conditions and better weaning practices could explain the reducing incidence rates over the 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 [2]. Various nutrient deficiencies (e.g. Vit B₁₂, Magnesium, Zinc, Vit C etc.) have been found to be associated with ITS. Other causative theories include viral encephalitis and degenerative processes.

Case Report

Three children presented with tremors within a span of six months. Mean age of the patients was 14 months (Table 1). There were two boys and one girl. Two children had protein energy malnutrition (PEM) grade II and the third one had grade III PEM. All of them had plump appearance with dull, expressionless face and sparse, hypopigmented hairs (Fig. 1). All children were exclusively breast-fed. All three had anaemia, cutaneous hyperpigmentation and regression/delayed developmental milestones. Two children had severe coarse tremors involving limbs, head and tongue, while in the third child the tremors were more marked in distal parts of the limbs. Tremors were initially intermittent and disappeared during sleep. Bleating cry was present in all three children, at the peak of tremors. All children had some infection at the time of presentation : 2 had respiratory tract infection and 1 had gastroenteritis. Peripheral smears were suggestive of varied pictures (hypo-micro-macro-polychromasia). Electroencephalogram (EEG) showed high voltage sharp waves and spikes in 2 cases. Computed tomography (CT) scan and magnetic resonance imaging (MRI) of brain showed cerebral cortical atrophy in all cases. Based on clinical and radiological

evidence, they were diagnosed to have 'Infantile tremor syndrome' and were started on vitamin B₁₂ and folic acid (which was continued for six weeks), thiamine, pyridoxine, iron and proteins. Tremors decreased within 10-20 days of therapy and previously lost milestones were regained within six weeks to six months.

Discussion

A classical picture of ITS is a plump looking infant between 6 to 18 months with presence of malnutrition (as was seen in all three cases). Usually, these children are listless, apathetic and disinterested in surroundings. Scalp hair is sparse and light coloured. 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

Fig. 1 : Dull expressionless face, with hypopigmented hairs in a child of ITS (Case 2).

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Table 1**Comparison of the three cases of ITS**

Case	Age (months) & Sex	Breast feeding history	Grade of PEM	Co-morbidity	Hb level (gm%) & PBS	EEG findings	CT/MRI brain
1	11 M	Exclusive breast feed	II	Gastroenteritis	9 Macrocytic	Abnormal	Cerebral atrophy
2	15 M	Exclusive breast feed	III	Bronchopneumonia	7.6 Microcytic	Normal	Cerebral atrophy
3	16 F	Exclusive breast feed	II	Bronchitis	5.8 Macrocytic	Abnormal	Cerebral atrophy

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 cases. Tremors have been attributed to structural and functional alterations of extrapyramidal system [3]. There is presence of anaemia, which may be macrocytic, microcytic or normocytic.

The etiology of ITS is still elusive. Among various theories, 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 cerebrospinal fluid (CSF) may be responsible for the neurological features of this syndrome [4]. Iron, magnesium and zinc deficiency have also been postulated to cause ITS. It is usual to find direct or indirect evidence of associated other nutritional deficiencies like protein, vitamin A, D, C and B-complex and other micronutrients [1,5,6]. Other speculations for its etiology include viral encephalitis and degenerative processes.

ITS is essentially a clinical diagnosis with peripheral smear suggestive of anaemia (mostly megaloblastic anaemia, macrocytosis (MCV>95), hypersegmented polymorphs, and megaloblastic bone marrow). Vitamin B₁₂ levels may be low (Serum levels of homocystiene are increased in deficiency of folate and B₁₂ but levels of methylmalonic acid (MMA) are increased in B₁₂ deficiency only. Even increased urinary levels of MMA are considered diagnostic of B₁₂ deficiency). CSF levels of Vit B₁₂ and TC II may be reduced [6]. Vitamin B₁₂ levels in the mother may also be low suggesting low levels in the breast milk. Serum levels of zinc, ascorbic acid and magnesium may be low. Cortical atrophy and prominence of subarachnoid space and ventricular system are the commonest findings in CT/ MRI of brain, and were seen in our cases [7].

Treatment consists of therapy for anaemia and nutritional deficiency. Vitamin B₁₂ in high doses may be required if B₁₂ levels are low. Multivitamins, vitamin C,

iron, protein, zinc and magnesium supplements may also be necessary [8]. If the tremors are severe, phenobarbitone (3-5 mg/kg/day) may be required to decrease the intensity [9]. The tremors subside slowly. Initially there is gradual reduction in the amplitude and severity, then the tremors become intermittent and finally stop. Propranolol and chlorpromazine are other drugs, which can be used to control tremors. Pigmentary changes in skin and hair take months to clear. Mental dullness and sluggishness takes years to come back to normal (six months in our case).

To summarise, infantile tremor syndrome needs to be considered in a young child presenting with malnutrition, developmental delay, tremors and typical cry.

Conflicts of Interest

None identified

References

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