Infantile Tremor Syndrome: A Case Report

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ABSTRACT

Infantile Tremor Syndrome is a clinical state, characterized by anemia, skin depigmentation, tremors and developmental delay in children between age 5 months to 3 years. Nutritional deficiency is one of the most accepted theories, usually seen among breastfeeding vegetarian mothers. The present case report describes demographic, clinical, laboratory profile and treatment outcome of infantile tremor syndrome diagnosed in a 5 month old female child admitted to the pediatric ward of tertiary care hospital.

Key words: Infantile tremor syndrome, Nutrition, Vegetarian, Tremors, VitaminB_{12} deficiency, Pediatric.

INTRODUCTION

Infantile tremor syndrome (ITS) is a self–limiting disease in infants and young children (5 months to 3 years), most commonly seen in developing countries with poor socio-economic conditions such as Southeast Asia, Indian subcontinent and African countries. ITS is an insidious in onset or an acute type of mental and psychological changes, with acute regression of mental and motor milestones, pallor with megaloblastic anemia and tremors. Symptoms include bleating goat like cry, brown scanty hair, lethargy and other body site hyperpigmentation usually due to Vitamin B_{12} deficiency, magnesium deficiency and infections. Nutritional deficiency is one of the most accepted theories, usually seen among breastfeeding vegetarian mothers.[1-3] High protein diet, multivitamins, folic acid, iron, calcium, zinc and magnesium has been the choice of treatment for nutritional deficient individuals.[4]

CASE REPORT

A 5 month female child visited outpatient department with complaints of fever, loose stools, and hypopigmented lesions over the trunk and lower limbs (Figures 1 and 2) and vomiting as soon as she was breast fed. On examination her pulse was 110/min, Respiratory rate-28/min, weight 4kgs, pallor was observed and she was admitted to pediatric ward. Developmental history (gross motor, fine motor, language, social) milestone were up to date at the time of admission. Dermatological evaluations establish scabies+atopic dermatitis.

Later, the developmental milestones, degraded during the course of treatment and tremors were also observed. Complete Blood Count (CBC) investigations at different stages during course of treatment showed low hemoglobin (Hb) (Table 1). Malignant cells were not identified in bone marrow aspiration and peripheral smear impression stated severe macrocytic anemia with relative lymphocytes and thrombocytopenia. 80 ml whole blood and 60 ml packed cell volume (PCV) blood transfusion was done over 4.5 hr. The next day, again 80 ml of blood was transfused and repeat CBC was performed which reveals Hb was increased from 5.0 to 18.0% but after few days it was dropped to 5% again. With the observed characteristic findings she was diagnosed

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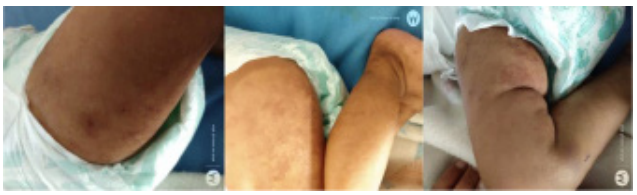

Figure 1: Hypopigmented lesions over lower limbs.

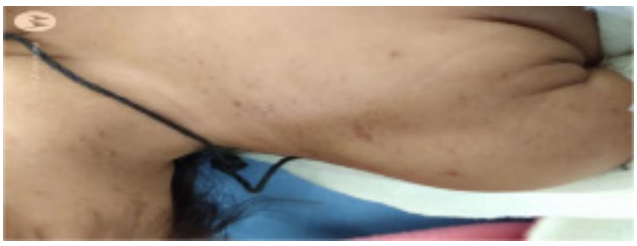

Figure 2: Hypopigmented lesions over the trunk.

Table 1: Hematological Investigations.

Test parameters	Pretreatment values	In-between treatment values	On discharge	Reference value
Neutrophils	21.6	50.4	32.4	40-75%
Lymphocytes	73.5	45.8	63.8	25-40%
Monocytes	2.7	1.2	2.6	2-8%
RBC	1.08	5.95	5.21	3.8-4.8million
Hb	5.0	18.0	5.0	11.6-14%
PCV	12.0	53.0	45.3	36-46%
MCV	111.1	89.1	86.9	80-100fl
MCH	46.3	30.3	28.8	27-32pg
MCHC	41.7	34.0	33.1	31.5-34.5%
Platelet count	1.08	0.35	0.14	1.5-4lakhs
ESR	140	-	-	5-20mm 1sthr
RDW	33.3	19.8	15.9	11.6-14%
Reticulocyte production index	0.282	-	-	0.5-2.5%

as an infantile tremor syndrome. The patient was then managed with *Permethrin* (5% w/w), *Hydroxyzine syrup* and *Physiogel lotion* for scabies and dermatitis. Subsequently child started receiving Vitamins (A, D, B complex and C), elemental iron, lysine, folic acid along with minerals (zinc, magnesium, calcium) and supportive treatment. Tremors were minimal and self-limiting so no drug was given. The standard therapy was followed and general condition of child improved and was discharged.

DISCUSSION

Exact incidence of ITS is not known but hospital statistics has revealed 0.77%–2.5% of the pediatric ward admissions to be due to ITS. The syndrome has been reported from many states of India including Karnataka. The literature reveals more incidence in during summer and winter/rainy seasons.[5] ITS has male preponderance in the majority of the studies reported and commonly affects infants between age range 40 days to 36 months with typical association of family with poor socio economic status where mother are often vegetarian and are often ignorant of animal foods in their diet. Thus, multiple nutritional deficiencies with underlying pernicious anemia are often associated with maternal health in ITS cases. The clinical presentation of ITS infants in a typical scenario often appears malnutrition characteristic (kwashiorkor and marasmus) with anemia, some reported with edema, multiple micronutrient and Vitamin A deficiencies.[5,6] Tremors, usually of coarse character (involving facial, laryngeal muscle) are one of the most significant characteristic features of ITS allowing immediate recognition of the syndrome. They are generally absent early in the course of illness, Tremors are intermittent initially, precipitate usually through emotional or physical stimuli, they are sometimes constant throughout the day but disappears or persist at reduce intensity in sleep. Laryngeal involvement renders a distinctive tremulous character to the vocalization/cry in these infants resembling to the bleating of a goat.[5,6] Chorea or myoclonus is often described coexisting with tremors.[5,7] Generally, there are no systemic symptoms and signs unless the course of illness has been complicated by inter current infections which are one of the reasons

for child's hospital visit. Mild hepatomegaly with or without splenomegaly is frequently reported sign in ITS. Congestive cardiac failure secondary to severe anemia has also been reported.[5] Though anemia is always present in ITS infants but is not a universal finding. Total leukocyte count is variable and may be affected by associated illness. Bone marrow findings have varied from predominantly normoblastic through dimorphic to predominantly megaloblastic.[5]

Kidney and liver function, calcium, blood glucose tests are often normal or do not point to specific etiology. Infants with ITS has been reported with low serum albumin, magnesium and zinc deficiency. Almost 50% of the infants with ITS has iron deficiency. Low serum Vitamin B_{12} is the laboratory diagnostic marker of Vitamin B_{12} deficiency. Also, low maternal serum Vitamin B_{12} is an indirect measure of Vitamin B_{12} deficiency in infants.[5]

Most often, ITS infants were treated symptomatically with multivitamins/ mineral supplements and a combined modified dietary approach, and reported gradual recovery over weeks to months irrespective of the treatments. Others have been treated successfully with dietary modification along with the treatment of anemia with folic acid, Vitamin B_{12} and iron, indicating that dietary deficiency of some kind was likely responsible for the manifestations of the syndrome.[5]

Successful treatment with Vitamin B_{12} alone has been observed with uniform pattern of response resulting in dramatic improvement in symptoms with rapid hematological and neurological recovery.[5] In some cases, the literature reveals tremors appeared first after initiation of treatment with Vitamin B_{12} and it was also observed that the tremors did not diminished early in those who received Vitamin B_{12} against those who did not, prompting some studies to negate Vitamin B_{12} deficiency as the cause of ITS. However, a comprehensive literature exist providing strong epidemiological, clinical, and laboratory evidence in favor of Vitamin B_{12} deficiency as the cause of ITS.[5]

Supportive care in the form of intravenous fluids to treat and prevent dehydration, antibiotics for associated infections, and other medications to treat associated complications are commonly used during acute phase. Tremors have been treated with propranolol, sedatives, carbamazepine, and emetine, but their role in treatment required evaluation through controlled studies.[5] Most of the ITS infants eventually improve, neurological deficits (cognitive and language skills) often persist, long-term mortality though rare but usually a result of inter-current illness.

CONCLUSION

Infantile tremor syndrome is a nutritional deficiency syndrome with a characteristic predominant neurological presentation along with consistent findings with megaloblastic anemia. ITS typically reported in families with poor socio economic status where mother are often vegetarian and are deprived of proper balanced nutritional diet. Multivitamin therapy especially Vit B_{12} and Treatment of other associated nutritional deficiencies and supportive therapy is essential for comprehensive management of ITS. Early diagnosis and management is warranted to avoid long term cognitive impairment.

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CONFLICT OF INTEREST

The authors declare that no conflict of interest exists.

ABBREVIATIONS

ITS: Infantile tremor syndrome; **RBC:** Red Blood Cell; **Hb:** Heamoglobin; **PCV:** Packed Cell Volume; **MCV:** *Mean Corpuscular Volume*; **MCH:** Mean Corpuscular Hemoglobin; **MCHC:** Mean Corpuscular Hemoglobin Concentration; **CBC:** Complete Blood Count.

SUMMARY

Infantile tremor syndrome is a rare clinical disorder characterized by coarse tremors, anemia and regression of motor and mental milestones in children of around one year of age. Exact cause is not known but poor hygiene environment and multiple nutritional deficiencies and underlying anemia are often reported in mothers with ITS affected children. Supportive therapy and management of nutritional deficiencies in affected children are essential to avoid long term cognitive impairment.

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