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Case Report

Thiamine-responsive megaloblastic anaemia syndrome – A case report

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ABSTRACT

Thiamine is a water-soluble vitamin which is helpful for tissue growth and development. Thiamine-responsive megaloblastic anaemia (TRMA), also known as Rogers syndrome, is caused by the mutation of a gene SLC19A2 which encodes for a thiamine transporter protein. TRMA is characterised by the triad of megaloblastic anaemia, progressive sensorineural hearing loss and diabetes mellitus. The onset of megaloblastic anaemia is between the extremes of infancy and adolescence, which can be corrected with pharmacological doses of thiamine. Progressive sensorineural hearing loss is generally early in onset, irreversible and may not be prevented by thiamine treatment.

Keywords: Thiamine-responsive megaloblastic anaemia, SLC19A2, Diabetes mellitus, Sensorineural hearing loss

INTRODUCTION

Thiamine-responsive megaloblastic anaemia syndrome (TRMA) is a rare autosomal recessive disorder.[1] It is characterised by megaloblastic anaemia, diabetes mellitus and sensorineural hearing loss. Mutation in the gene SLC19A2 which encodes for a high-affinity thiamine transporter disturbs the active process of thiamine uptake into the cells.[2]

Here, we report a 14-year-old male child with megaloblastic anaemia and diabetes mellitus. Sensorineural hearing loss was eventually recognised in the course of the hospital stay. Pharmacological treatment with thiamine resulted in dramatic normalisation of haemoglobin levels along with improvement of glycaemic control. This case report sensitises that early diagnosis and intervention with thiamine is required for patients presenting with anaemia, diabetes and deafness.

CASE REPORT

We hereby report a case of a 14-year-old male child, born out of non-consanguineous marriage, who is a known case of diabetes mellitus, presenting to the Paediatric Department at Cheluvamba Hospital, MMCRI, with the chief complaints of – progressive pallor, lethargy, tingling and numbness of limbs over the past 4 months.

He was on a basal-bolus regimen of injection actrapid and glargine with the insulin requirement being 2.1 IU/kg/day.

At presentation – vitals were stable. Head to toe examination was significant for severe pallor. Systemic examination was within normal limits.

Laboratory investigations revealed severe anaemia (Hb – 5.9 g%); peripheral smear showed features suggestive of megaloblastic anaemia. Corrected retic count was 3%. Periphersl smear for malarial parasite was negative. GRBS and HbA1c were 318mg/dl and 9.4% respectively. Cold agglutinin test was positive. Direct coombs test, ANA and anti TPO antibody tests were negative.

The liver function test and thyroid function test are within normal limits.

Serum Vitamin B12 was 129 pg/dl (Normal 160-950 pg/ml). Serum folic acid was 16.9 ng/ml (Normal 2.7-17 ng/ml)

Suspicion of TRMA syndrome prompted us to do a hearing evaluation of this patient. Audiometry test revealed mild sensorineural hearing loss, thereby completing the triad of TRMA syndrome.

The patient was initially managed with a blood transfusion to correct severe anaemia. Haemoglobin levels increased soon after transfusion, only to drop again after 7 days. By then, Rogers syndrome was suspected clinically. Pharmacological treatment with thiamine supplementation (100 mg per day) was initiated. Remission of anaemia along with further decreased insulin requirement was found in the subsequent follow-up visits of the patient. No improvement in the hearing loss was documented.

DISCUSSION

TRMA – it is responsive, rare, recessive, it is Rogers!

Thiamine is a water-soluble vitamin which is used for tissue growth and development. TRMA is caused by the mutation of a gene SLC19A2 which encodes for a thiamine transporter protein. Thiamine-responsive megaloblastic anaemia syndrome (TRMA) should be suspected in individuals who present with the following clinical features, which make up the triad as mentioned below:[3]

1. Megaloblastic anaemia
    a. Bone marrow examination reveals megaloblastic changes with ringed sideroblast seen often
    b. Vitamin B_{12}/folic acid levels are normal
    c. The anaemia is corrected with pharmacologic doses of thiamine (50–100 mg/day). However, it is found that anaemia can recur when thiamine is withdrawn.
2. Progressive sensorineural deafness: It is generally irreversible. Pharmacological correction with thiamine may not prevent the progression of hearing loss.
3. Diabetes mellitus: Thiamine replacement has been occasionally found to cause its remission.

The diagnosis of TRMA is made in a proband with megaloblastic anaemia with normal Vitamin B_{12}/folic acid levels, with or without diabetes mellitus or hearing loss in whom there is a response to pharmacological therapy to oral thiamine and/or identification of biallelic pathogenic variants in *SLC19A2* by molecular genetic testing.[4] Molecular genetic testing methods can include either single-gene testing or the use of a multigene panel.

In a child who presents with diabetes, refractory anaemia and hearing loss, TRMA should be considered as a possibility. Response to thiamine distinguishes TRMA from other syndromes such as Wolfram syndrome and Pearson syndrome. Although rare, prompt recognition of this syndrome at the earliest can induce remission or delay the development of diabetes and improve the quality of life in the patient.

CONCLUSION

Suspicion of TRMA must be made in a child completing the triad of the disease as mentioned earlier. Prompt recognition of the disease helps in early intervention and thus improves the quality of the patient.

Declaration of patient consent

Permission was obtained from the patient and the parents to publish the case report. Every attempt is made to ensure the anonymity of the patient.

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Conflicts of interest

There are no conflicts of interest.

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