CASE REPORT

RARE CASE WITH MEGALOBLASTIC ANAEMIA

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A nine years old boy presented with history of pallor and anaemia since early infancy along with neural hearing loss responding to empirical multivitamin and folic acid therapy started on basis of blood complete picture showing anaemia and megaloblastic anaemia. On investigation he was diagnosed with Thiamine Responsive Megaloblastic Anaemia, a very rare condition in our settings.

Keywords: Megaloblastic Anaemia, Thiamine Responsive Megaloblastic Anaemia, Thiamine, Sensorineural Hearing Loss

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INTRODUCTION

Thiamine-responsive megaloblastic anaemia (TRMA) syndrome usually associated with diabetes mellitus, anaemia and deafness, due to mutations in SLC19A2, encoding a thiamine transporter protein which leads to deficient absorption and the body is unable to effectively utilize thiamine from the diet.[1] To date, 33 families with 28 distinct mutations have been identified.[2]

The diagnosis of TRMA should be suspected in patients with syndrome of hearing loss, megaloblatic anaemia, and history of diabetes mellitus. Consanguinity and family history is also very important. The bone marrow aspirate shows Megaloblastic anaemia picture.[3]

The syndrome occurs because of mutation in the SLC19A2 gene encoding a thiamine transporter protein leading to abnormal thiamine transportation and vitamin deficiency in the cells.[4]

CASE

A 9 years old boy was admitted from emergency department to child health department with history of progressive pallor. On taking comprehensive history from mother, the boy was second among four siblings. He was delivered normal in social security hospital and pregnancy was uneventful. He was noticed to have pallor for first time at the age of 4 months and he was taken to hospital where red cell concentrate was transfused without doing any workup. Again at the age of one year parents noticed that child was not responding to sound and his pallor started to manifest. He was taken to ENT department and after initial screening brain stem evoked response audiometry (BERA) was advised and it showed severe sensory neural hearing loss and child was advised hearing aid. Initially parents applied hearing aid but it did not give much difference so parents abandoned it on their own. For pallor, work up was done and it showed Megaloblastic anaemia. Vitamin B-12 and folic level were sent and child was stared on multivitamin syrup along with folic acid. Though vitamin B-12 and folic acid level turned to be normal yet he responded to both of drugs and his pallor improved. As soon as parents stopped the drugs pallor again manifested, so parents continued the drugs on and off.

This time the child presented to hospital after lapse of about 3 years with history of progressive pallor as he was not taking multivitamin and folic acid. Physical and systemic examination showed an anaemic child with sensory neural deafness. Initial laboratory investigations showed anaemia with Haemoglobin (Hb) of 4.7 gm/dl, and MCV of 114.2 fl/l. Peripheral blood smear showed macrocytosis. Blood sugar (fasting) was 89 mg/dl to rule out diabetes mellitus. Vitamin B-12 level were 219 (176–686 mmol/L), and Folate levels were 13.0 (6.25–45.3 pmol/L). Bone marrow examination was performed to determine the cause of macrocytosis. Megaloblastosis with hyper-cellular marrow was seen.

Genetic studies were being planned but could not be performed due to non-availability of such facilities. Child was started on thiamine (Vitamin B-1) with dose of 25 mg tds as no other treatment was initiated apart from thiamine except dietary advice. Hb after 4 weeks of follow up increased to 9.1 gm/dl. Hb after 6 weeks of follow up increased to 11.7 gm/dl and MCV was 93.9 fl.

DISCUSSION

Thiamine responsive megaloblastic anaemia is the association of thiamine responsive megaloblastic anaemia with insulin deficient diabetes and sensorineural deafness. Diabetes may respond to thiamine, but all patients develop an insulin requirement in the long term.[5]

In the UK not all diabetics presenting in childhood is autoimmune type 1. Apart from increasing type 2 diabetes, maturity onset diabetes of the young, iatrogenic diabetes, rare syndromic forms of diabetes including Roger syndrome have

been identified in children.[6] It is an autosomal recessive disorder caused by the deficiency of thiamine transporter protein.[7] Mutations in SLC19A2 (a membrane bound thiamine transporter) cause this recessive disorder.[4]

The water-soluble micronutrient thiamine is required for normal tissue growth and development in humans. Progressive hearing loss is one of the cardinal findings and is known to be irreversible as early diagnosis and treatment with oral thiamine could not prevent deafness[8] but it may be effective in preventing deafness if started before two months.[2] Heart rhythm abnormalities and structural cardiac anomalies have been detected in TRMA patients.[9] Bone marrow examination reveals megaloblastic anaemia with erythroblasts often containing iron-filled mitochondria (ringed sideroblasts). All individuals with the diagnostic phenotypic triad evaluated by sequence analysis showed identifiable mutations in the SLC19A2 gene, which encodes the high-affinity thiamine transporter, only gene known to be associated with TRMA.[10]

In affected individuals treatment of TRMA focuses on lifelong use of pharmacologic doses (25–75 mg per day) of thiamine (Vitamin B1).[11] This normalizes haematological abnormalities along with improvement in the diabetic control but has no effect on deafness.[12]

Follow up of patients with TRMA should be done at least yearly to monitor the efficacy of the oral thiamine therapy as well as disease progression which includes hematologic tests CBC, reticulocyte count, assessment for glucose intolerance (fasting serum glucose concentration, OGTT, urine analysis), hearing, ophthalmologic, and cardiac evaluations.[13]

TRMA is inherited in an autosomal recessive manner. Prenatal testing is available for families in which the disease-causing mutations have been identified.[14]

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