CORRESPONDENCE

Anemia in a Child with Deafness: Be Vigilant for a Rare Cause!

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To the editor,

A toddler was advised cochlear implant for sensori-neural deafness. During pre-anesthetic checkup, she was noted to have diabetes mellitus, anemia and deafness which lead to diagnosis of thiamine responsive megaloblastic anemia (TRMA). TRMA is an autosomal recessive disorder caused by the deficiency of thiamine transporter protein characterized by triad of diabetes mellitus, anemia and deafness [1]. The only gene known to be associated with TRMA is SLC19A2, which encodes the high-affinity thiamine transporter [2]. Here we describe the above case.

A 2-year-old Muslim girl from eastern Uttar Pradesh, product of a consanguineous marriage, presented with history of pallor since the age of one year. Her first complete blood count at 1-year of age showed hemoglobin (Hb)-5.4 g/dl, mean corpuscular volume-93femtolitres, total leucocyte count (TLC)- $13.3 \times 10^9/L$ with 29 % neutrophils and platelet- $40 \times 10^9/L$. Her Hb improved to 6.3 g/dl after therapy with oral iron, and multi-vitamin including vitamin-B12 and folic acid. Almost a year later, the Hb again dropped to 5.7 g/dl after discontinuation of iron and vitamin-B12. At 21-months of age she was diagnosed with deafness and cochlear implantation was planned. She was detected with diabetes mellitus and decreased visual acuity at the same time. There was no family history of similar illness. On examination, she had pallor, sensori-

neural deafness and an ejection systolic murmur. Bone marrow aspiration smears were aperticulate and hemodilute. Imprint smears showed poor cellularity with partial degeneration of cells. The erythroid cells were megaloblastic with ringed sideroblasts. Only an occasional megakaryocyte was seen. Echocardiography showed small patent ductus arteriosus. Audiometry confirmed bilateral profound hearing loss for that cochlear implantation was done. Fundus showed pale disc with macular degeneration. With the above findings, a diagnosis of TRMA was made. Sequence analysis of coding and flanking intronic region of the SLC19A2 gene revealed a homozygous mutation of SLC19A2 gene, showing a nonsense mutation of protein p.Glu66X (p.E66X) at exon 1 (c.196G > T) which results in an in-frame single amino acid deletion (p.Gly335del). She was started on thiamine 50 mg orally daily and her insulin therapy was continued. A month later, her reports showed Hb-9.1 g/dl, TLC- $12.7 \times 10^9/L$ and platelet- $4.01 \times 10^9/L$. She has been on thiamine for the last 12-months and maintains a mean Hb of 10.1 g/dl (9.1–12.1 g/dl).

A homozygous c.196G > T mutation in SLC19A2 gene confirmed the diagnosis of TRMA in our case. Both parents were heterozygous carriers for the same mutation. This mutation has previously been described in three children from two consanguineous families from Pakistan [3]. Diabetes mellitus is non-type 1 in nature with onset from infancy to adolescence. Decrease in insulin requirement with institution of high-dose of thiamine has been reported [4]. This was observed in our case also. She is off insulin now and maintaining sugars on oral hypoglycemic agent, glimepiride 0.5 mg orally daily. Progressive sensori-neural deafness, which is irreversible is due to selective inner hair cell loss, occurs in early life [5]. Role of high-dose thiamine in improving hearing loss is not clear; however

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animal studies have shown reversibility of hearing loss with thiamine supplementation [6]. Her vocabulary has improved markedly after cochlear implant. As in our case, combination of megaloblasts and ringed sideroblasts characterizes TRMA. Treatment of TRMA involves life-long use of thiamine at a dose of 25–75 mg/day compared to recommended daily allowance of 1.5 mg/day. Anemia can recur when thiamine is withdrawn as seen in our case.

Be vigilant for TRMA as a cause while dealing with a child with anemia and deafness. Early interventions are critical for prevention of visuo-linguistic problems in a growing child. Molecular diagnosis is definitive and thiamine is the cornerstone of therapy.

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