Indian Journal of Pediatrics (February 2024) 91(2):206
https://doi.org/10.1007/s12098-023-04870-9

SCIENTIFIC LETTER

Severe Hemolytic Anemia due to Erythrocyte Adenylate Kinase Deficiency due to a Novel Missense Mutation (c.518T>G)

Kalpana Panda[1] · Ipsita Sahoo[1] · Swarup Kumar Bisoi[1] · Mrutunjay Dash[1]

Received: 8 June 2023 / Accepted: 11 September 2023 / Published online: 2 October 2023

To the Editor: An 8-y-old girl from Odisha, product of non-consanguineous marriage with uneventful antenatal and postnatal history was referred to us for workup of severe anemia. She became symptomatic from 6 mo of age, receiving regular blood transfusions at 1–2 mo intervals. On examination, she had severe pallor and icterus with splenohepatomegaly. Lab investigations were suggestive of hemolytic picture {Hb: 3.0 g/dl, LDH: 1775, Reticulocyte count: 13.5%, peripheral smear: normocytic normochromic, unconjugated hyperbilirubinemia [Bilirubin (Total/Direct): 6.9/0.7]}. HPLC of the child and both parents were normal. Direct Coombs test and osmotic fragility test were also non-contributory. Hence, a strong probability of erythrocyte enzymopathies was kept, however, G6PD and pyruvate kinase were in normal range. So, possibility of other rare enzymopathies was considered, but as their estimation is not commercially available, Next-generation sequencing (NGS) was conducted which revealed a novel homozygous missense mutation in exon 7 of Adenylate kinase (*AK1)* gene (c.518T>G) causing amino acid substitution of Glycine for Valine at codon 173 (p. Val173Gly).

Erythrocyte adenylate kinase (AK) deficiency is an extremely rare cause of congenital hemolytic anemia [1], to date described only in 14 unrelated families worldwide. It is inherited in autosomal recessive manner and 11 specific mutations in *AK1* gene have been described in literature so far [2]. Our patient had a novel homozygous missense mutation of *AK1* gene that has not yet been reported in literature. Moreover, this is the fourth case of AK deficiency to be reported from India and first such case from eastern part of country [3, 4].

In conclusion, AK deficiency should be kept in differential diagnosis of hereditary anemias unexplainable by hemoglobinopathies, RBC membrane defects or common enzymopathies like G6PD deficiency. However, enzyme assay for such rare enzymopathies is not readily available commercially, posing a diagnostic challenge to clinicians. Such cases mandate NGS for confirmation of diagnosis.

Declarations

Conflict of Interest None.

References

1. Abrusci P, Chiarelli LR, Galizzi A, et al. Erythrocyte adenylate kinase deficiency: characterization of recombinant mutant forms and relationship with nonspherocytic hemolytic anemia. Exp Hematol. 2007;35:1182–9.
2. He S, Chen H, Guo X, Gao J. Red cell adenylate kinase deficiency in China: molecular study of 2 new mutations (413G > A, 223dupA). BMC Med Genomics. 2022;15:102.
3. Dongerdiye R, Sampagar A, Devendra R, Warang P, Kedar P. Rare hereditary nonspherocytic hemolytic anemia caused by a novel homozygous mutation, c.301C > A, (Q101K), in the AK1 gene in an Indian family. BMC Med Genomics. 2021;14:191.
4. Sivasankaran M, Reddy VK, Kumar V, Munirathnam D. Hereditary non-spherocytic hemolytic anemia (HNSHA): four children with rare hereditary red cell enzymopathies. Indian Pediatr. 2021;58:993–4.

✉ Mrutunjay Dash
m.dash74@gmail.com

[1] Department of Pediatrics, Institute of Medical Sciences & SUM Hospital, Bhubaneswar, Odisha, India