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Case Report

Pyruvate kinase deficiency: A rare cause of hemolytic anemia: A case report from North-Eastern India

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ABSTRACT

Pyruvate kinase, liver and RBC (PKLR) gene located on chromosome 1q21 encodes erythrocyte pyruvate kinase enzyme. Pyruvate kinase conveys the concluding tread of the glycolytic pathway, along with production of the 50% red cell total adenosine triphosphate. Pyruvate kinase deficiency (PKD) is a rare autosomal recessive disorder causing congenital non-spherocytic hemolytic anemia (CNSH). Biallelic pathogenic variation in the PKLR gene is responsible for PKD. It is the most common glycolytic defect resulting in CNSH. This case report highlights different pathogenic variants in PKLR gene detected in a patient having severe PKD.

Keywords: Pyruvate kinase, liver and RBC gene, Pyruvate kinase deficiency, Congenital non-spherocytic hemolytic anemia

INTRODUCTION

Mature erythrocytes are deficient in mitochondria and are hence reliant on glycolysis intended for adenosine triphosphate (ATP) production. Pyruvate kinase (PK) a central enzyme in glycolysis, generating 50% ATP, is encoded by the PKLR gene (PK, liver, and red cell isoform) which is sited on chromosome 1q21. CNSHA an inherited autosomal recessive trait is primarily caused due to PK deficiency.[1] The disease-anticipated predominance is 51 per one million people of Western ancestry. Approximately 200 alterations have been recognized in pyruvate kinase deficiency (PKD). Most prevalent are missense mutations, encompassing c.1529G>A, (p.Arg510Gln) within the USA and Northern and Central Europe; c.1456C>T, (p.Arg486Trp) in Southern Europe; and c.1468C>T, (p.Arg490Trp) in Asia.[1,2] This report highlights PKD to be an atypical reason for hemolytic anemia in a patient born out of non-consanguineous marriage from North-Eastern India.

CASE REPORT

A 6-year-old Indian Bengali girl, the first child of non-consanguineous parents, presented with anemia and unconjugated hyperbilirubinemia in the Hematology OPD of Nil Ratan Sircar Hospital and Medical College, Kolkata. Features of hemolytic facies and lymphadenopathy were absent and splenomegaly of 4 cm below the left costal margin was present. The age at first blood transfusion was 5 months, subsequently requiring blood transfusion once a month. Bone marrow aspirate was hypercellular for age, with erythroid hyperplasia with normal maturation. However, myeloid maturation was normal and the numerals of megakaryocytes were also within the normal span, thus ruling out red cell aplasia, myelodysplastic syndrome, and congenital dyserythropoietic anemia. The corrected reticulocyte count was 10%. The diseases excluded in the study were iron and B12/

folate deficiencies as well as hemoglobinopathies such as sickle cell anemia, thalassemia syndromes, hereditary spherocytosis, G6PD deficiency, and autoimmune hemolytic anemia. Due to repeated blood transfusion, PK enzyme activity and 2,3-bisphosphoglycerate level were not assessed. Subsequently, next-generation sequencing was undertaken for the PKLR gene, to confirm multifaceted heterozygosity of the PKLR variants. Two heterozygous alternatives were found in exon 8 – NM_000298.6 (PKLR): c. 1174G>A (p.Ala392Thr) and exon 10 – NM_000298.6 (PKLR):c.1456C>T, (p.Arg486Trp) of the gene, confirming diagnosis of PKD. Further, the Sanger sequencing technique validated the presence of compound heterozygous variants.

DISCUSSION AND CONCLUSION

The missense variant c.1174G>A (p.Ala392Thr) is highlighted by Lenzner *et al*. (1994) and Kager *et al*. (2016) amid patients with PKD, leading to CNSHA.[3,4] The missense variant c.1456C>T, (p.Arg486Trp) is the chief most prevalent pathogenic variant reported in the literature causing PKD.[5,6] PKD may be missed by conventional techniques including biochemical enzyme activity assays due to numerous aspects including recent blood transfusions and leukocyte contamination of tested red cells. Treatment options for PKD include Packed Red blood cell transfusions, mitapivat, an oral drug enhancing PK activity, and splenectomy for refractory cases. Our patient is on PRBC transfusion and tablet folic acid and is planned for splenectomy. Thus, the patient makes obvious an atypical finding of PKD causing hemolytic anemia and, therefore, necessitates boosting of a higher threshold for diagnosing PKD.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Grace RF, Zanella A, Neufeld EJ, Morton DH, Eber S, Yaish H, *et al*. Erythrocyte pyruvate kinase deficiency. Am J Hematol 2015;90:825-30.
2. Zanella A, Fermo E, Bianchi P, Valentini G. Red cell pyruvate kinase deficiency: Molecular and clinical aspects. Br J Haematol 2005;130:11-25.
3. Lenzner C, Nürnberg P, Thiele BJ, Reis A, Brabec V, Sakalova A, *et al*. Mutations in the pyruvate kinase L gene in patients with hereditary hemolytic anemia. Blood 1994;83:2817-22.
4. Kager L, Minkov M, Zeitlhofer P, Fahrner B, Ratzinger F, Boztug K, *et al*. Two novel missense mutations and a 5bp deletion in the erythroid-specific promoter of the PKLR gene in two unrelated patients with pyruvate kinase deficient transfusion-dependent chronic nonspherocytic hemolytic anemia. Pediatr Blood Cancer 2016;63:914-6.
5. Montllor L, Mañú-Pereira MD, Llaudet-Planas E, Ramírez PG, Navarro JS, Vives-Corrons JL. Red cell pyruvate kinase deficiency in Spain: A study of 15 cases. Med Clin (Barc) 2017;148:23-7.
6. Jamwal M, Aggarwal A, Palodhi A, Sharma P, Bansal D, Trehan A, *et al*. Next-generation sequencing-based diagnosis of unexplained inherited hemolytic anemias reveals wide genetic and phenotypic heterogeneity. J Mol Diagn 2020;22:579-90.

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