World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

Case report: Pyruvate kinase deficiency in an infant

Ishwarya B * and N K Kalappanavar

Department of pediatrics, SSIMS and RC Davangere, India.

World Journal of Advanced Research and Reviews, 2023, 18(03), 1060–1062

Publication history: Received on 15 February 2023, revised on 16 June 2023, accepted on 18 June 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.18.3.0439

Abstract

Pyruvate kinase deficiency is a rare cause of hemolytic anaemia. We report a case of Non-spherocytic hemolytic anaemia due to a deficiency of the red cell Pyruvate kinase enzyme due to a homozygous type of autosomal recessive inheritance. The child underwent a double volume Exchange Transfusion and received blood transfusions for Rapid Hemolysis on the first day of life. In this report, we stress the need for consideration of Red cell Pyruvate kinase enzyme deficiency as one of the differentials of Non-immune hemolytic anaemia. The study will help human geneticists and paediatricians with early identification or screening.

Keywords: Non-spherocytic Hemolytic anemia; Red cell Pyruvate Kinase; Deficiency; Human geneticists

1. Introduction

Pyruvate kinase deficiency is a Congenital hemolytic anaemia occurs in people homozygous or compound heterozygous for autosomal recessive genes that cause either a marked reduction in red blood cell (RBC) pyruvatekinase (PK) or the production of an abnormal enzyme with decreased activity resulting in impaired conversion of phosphoenol pyruvate to pyruvate 1, 2, 3. The generation of adenosine triphosphate (ATP) in RBCs at this step is impaired, and low levels of ATP, pyruvate, and the oxidized form of nicotin amide dinucleotide (NAD+) are found. As a consequence of decreased ATP,RBCs cannot maintain their potassium and water content, the cells become rigid, and their lifespan is considerably reduced [4,5].

2. Case report

A girl child born to a third-degree consanguineously married couple, third in order delivered by caesarean section in view of fetal distress, her prenatal history was uneventful. Family history of previous two sibling deaths at 3 months of age for haematological disease requiring blood transfusions in early infancy. She was found to be pale and have yellow discoloration of skin and sclera 6 hours after birth, which was highly suggestive of hemolytic anaemia, which progressed to palms and soles by 24 hours of life, with normal colour of urine and stools. Her pulse rate was 150 beats per minute, and she was well hydrated. She had no fever or hypothermia. She did not have any dysmorphic features, Lymphadenopathy, or splenomegaly. A non tender hepatomegaly was just palpable. Examination of other systems was normal. Evaluated for hemolytic anaemia like a complete hemogram (haemoglobin 12.5 g/dl), total count of 20,958 cells/mm3, platelets 2.71 lakh/mm3, a peripheral smear (macrocytic blood picture), a reticulocyte count of -27%, The direct Coombs test was negative, Serum Bilirubin levels were 13.6 mg/dl by 24 hours of life, Liver Function was normal, Septic screen was negative .S he was screened for G6PD deficiency and was found to have a normal G6PD enzyme level. The baby was given a double volume exchange transfusion and phototherapy on suspicion of a possible rare blood group incompatibility, although direct Coombs was negative. The baby was discharged on day 10 in stable condition. A month later, she presented with symptoms of anaemia requiring blood transfusion and was transfused with Packed Red cells.

*Corresponding author: DrIshwaryaB

A clinical exome sequence was sent, which revealed a homozygous mutation in Intron 5, c. 694+2T>C (5' splice site), and red cell pyruvate kinase, and she was advised to follow up on a regular basis.

3. Discussion

Pyruvate kinase deficiency leads to anaemia with various patterns in the first month of life. It should be investigated in newborn with unexplained anaemia and jaundice even in absence of Reticulocytosis and strongly suspected with positive family history. Early and timely treatment of Anemia reduces mortality and morbidity among neonates and infants. This patient highlights a novel pathogenic variant Intron 5, c.694+2T>C (5' splice site) in the PKLR gene, which is consistent with non-spherocytic hemolytic anemia, most likely PKD. Interestingly, she was homozygous for the mutation which is extremely rare. There are several reported cases of PKD with different pathogenic genetic variants in different populations. The first report was in 1961 in three patients with congenital non- spherocytic anemia [3]. This individual was homozygous for a novel pathogenic variant Intron 5, c.694+2T>C (5' splice site) in the PKLR gene, consistent with PKD. PK enzyme assay was not performed. However, her clinical presentation was consistent with PKD. The exclusion of other etiologies for her clinical presentation further strengthens the diagnosis of PKD. Moreover, the genetic variant found in her PKLR gene is predicted to affect splicing of the mRNA transcript, and a pathogenic base substitution at the Intron 5, c.694+2T>C ,5' splice site been reported and abolishes the 5' donor splice site indicating that this locus is critical to normal PKLR gene expression. Genetic testing is essential for definitive diagnosis and diagnostic in cases where enzyme assay results are equivocal.

Figure 1 Schematic view of Pyruvate kinase deficiency in an infant

4. Conclusion

In conclusion, this is a novel genetic variant in the PKLR gene, which is consistent with PKD, detected in an early infancy, and has not been described previously. It could be one of there are causes of Non Spherocytic hemolytic anemia requiring blood transfusion.

Compliance with ethical standards

Acknowledgments

We would like to acknowledge to the all key officers of our Institution for their moral supports.

Disclosure of conflict of interest

There is no conflict of Interest between Institution and any other funding agency.

Statement of informed consent

Consent obtained from the patient care takers .

References

[1] Grace RF, Zanella A, Neufeld EJ, et al. Erythrocyte pyruvate kinase deficiency: 2015 statusreport.AmJHematol.2015, 90:825–30.

[2] Zanella A, Fermo E, Bianchi P, et al. Red cell pyruvate kinase deficiency: molecular and clinical aspects. *Br J Haematol*.2005, 130:11–25.

[3] Valentine WN,Tanaka KR, Miwa SA. Specificery throcyteglycolytic enzyme defect(pyruvate kinase) in three subjects with congenital non spherocytic haemolytic anaemia. *Trans Asssoc Am Physicians*. 1961, 74:100–10.

[4] Min-OoG, FortinA, Tam MF et al. Phenotypic expression of pyruvate kinase deficiency and protection against malaria in a mouse model. Genes Immun. 2004, 5:168–75. https:// doi. org/10.1038/sj. gene. 6364069.

[5] WijkRI, Van Wesel AC, Thomas AA et al. Exvivo analysis of aberrant plicing induced by two donor site mutations in PKLR of a patient with severe pyruvate kinase deficiency. *Br JHaematol*.2004, 125:253–63. https://doi.org/10. 1111/j.1365- 2141.2004. 04895.x.

[6] Viprakasit V, Ekwattanakit S, Riolueang S et al. Mutations in Krüppel-likefactor 1 cause transfusion-dependent hemolytic anemia and persistence of embryonic globin gene expression. Blood. 2014, 123:1586–95. https://doi. org/ 10. 1182/blood-2013- 09- 526087.