

Case Report

Pearson syndrome masquerading diamond blackfan anemia: a case report

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ABSTRACT

Pearson syndrome (PS) is rare and often fatal multisystemic mitochondrial disorder. Many of those who survive develop signs and symptoms later in life of a related disorder called Kearns-Sayre syndrome (KSS). 13-month-old male child presented with transfusion dependent anemia since the age of 3 months and was initially labeled as a case of Diamond Black fan Anemia. Mitochondrial and pancreatic enzyme replacement therapy. Through this case report, we attempt to address the fact that possibility of PS, which is often labeled as DBA in initial stages, should be considered in cases of congenital anemia of uncertain etiology. Early diagnosis of PS and interventional therapy in the form of mitochondrial and pancreatic replacement can significantly prolong survival and improve quality of life.

Keywords: Mitochondrial disorder, Refractory anemia

INTRODUCTION

Pearson Marrow Pancreas Syndrome (PS) is an extremely rare multisystem mitochondrial disorder characterized by sideroblastic anemia, pancreatic insufficiency, metabolic acidosis, and other defects with less than 100 cases described in the literature so far.¹ A recent study from Italy estimates incidence of PS as 1 in million births.² Patients present in infancy with transfusion dependent severe macrocytic anemia often associated with variable degrees of neutropenia, thrombocytopenia, metabolic acidosis and tissue dysfunction.^{1,3}

The early onset of severe anemia, variable penetrance and sporadic genetic inheritance make it difficult to differentiate PS from Diamond BLACKFAN Anemia (DBA).⁴ About half of children with this severe disorder die in infancy or early childhood due to complications of

anemia or pancreatic insufficiency or liver failure.^{5,6} Many of those who survive develop signs and symptoms later in life of a related disorder called Kearns-Sayre syndrome (KSS).^{5,6} Here we report a 13-month-old male child with PS who was initially labeled as a case of DBA.

CASE REPORT

A 13-month old child born out of 2nd degree consanguineous marriage was referred to the pediatric hematology OPD with complaints of repeated episodes of blood transfusion since the age of 3 months and recurrent bleeding manifestations in the form of ecchymotic patches and epistaxis. The child presented first at the age of 3 months to the local pediatrician with complaints of progressive pallor. His first CBC revealed macrocytic anemia (Hb 3.6gm%, WBC 5600 /mm³, DLC N60%L46%, plt count 160000, MCV 104fl, corrected

retic 0.4%). Bone marrow examination performed at other center revealed erythroid hypoplasia and hence a provisional diagnosis of Diamond-Blackfan Anemia (DBA) was made. The child was put on oral steroid therapy. However, he continued to require blood transfusions at monthly interval. Subsequently, from the age of 8 months, the child also developed bleeding manifestations in the form of ecchymotic patches following trivial trauma. The child had failure to thrive and delayed motor development. He developed chronic diarrhea from the age of 9 months. At the age of 13 months, the bleeding episodes became more pronounced in the form of epistaxis for which the child was referred to our center.

On examination, he was grossly malnourished. His anthropometric parameters were weight 6.3kgs, height 88cms, HC 44cms. All were <3SD, as per WHO growth chart. He had features of florid rickets and other fat-soluble vitamin deficiencies in the form of dry coarse skin and bleeding manifestations. Investigative work up revealed Hb 3.8gm%, MCV 112fL, TLC 6300, Neutrophils 57%, Lymphocytes 33%, Platelets 142000. His coagulation profile was deranged (PT-INR 1.72, a PTT, control). A proximal renal tubulopathy was present as urine evaluation showed proteinuria and blood gas analysis revealed metabolic acidosis. His cardiac evaluation was normal.

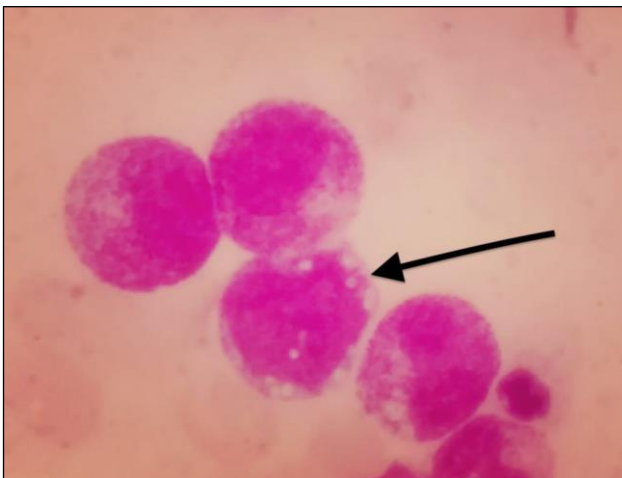


Figure 1: Image showing characteristic vacuolated myeloid precursors in Pearson syndrome.

Bone marrow examination revealed 'vacuolated myeloid and erythroid precursors' (Figure 1). Clinical picture of exocrine pancreatic insufficiency and acidosis associated with classic marrow findings was consistent with diagnosis of PS. Genetic testing confirmed 4977 bp mitochondrial DNA deletion.

The child was put on pancreatic and mitochondrial enzyme replacement which included Coenzyme Q at 15mg/kg/day, carnitine 100mg/kg/day, biotin 10mg/day, high dose thiamine and riboflavin. Supportive care in the

form of pRBC, FFP transfusion, oral sodium bicarbonate and Vitamin A, D, E, K supplementation was also given.

On follow-up after one month, there was significant improvement in general condition and appetite. There was improvement in motor milestones and the child was now able to stand with support. His CBC revealed Hb of 10gm%. At the latest follow-up at the age of 2 years, the child has become transfusion-free and continues to gain weight and milestones.

DISCUSSION

PS results from large deletions in mitochondrial DNA (mtDNA), which leads to metabolic acidosis and variable tissue dysfunction. Usually, the deleted mtDNA exists in varying proportions relative to normal mtDNA called heteroplasmy and changes in heteroplasmy is responsible for varied disease manifestations and evolution of the disease including spontaneous hematological remission and evolution to KSS or Leigh's disease.^{7,8}

PS and DBA have common clinical features like early onset of transfusion dependent anemia, sporadic genetic inheritance, and occasionally spontaneous hematologic remission.⁴ Because of these common features and lack of familiarity amongst clinicians about PS, it is often labeled as DBA in early stages and treated with steroids, which is not efficacious and can lead to clinical worsening in PS due to metabolic and infections complications.^{9,10}

Hence the early diagnosis of PS is imperative for better clinical outcome. Elevated serum lactate level and vacuolation in erythroid and myeloid precursors can help in early diagnosis of PS. Usually PS is diagnosed when exocrine pancreatic insufficiency becomes apparent. This underlines the importance of regular close follow up in patients with transfusion dependent anemia of unclear etiology.

To our knowledge this is first case report of PS from Indian subcontinent. In our case, although the child was initially labeled as DBA at the age of 3 months, when he presented to us at the age of 13 months, the disease was in evolving phase. He had additional findings of pancreatic insufficiency, failure to thrive, fat soluble vitamin deficiency, metabolic acidosis and characteristic bone marrow picture of vacuolated myeloid and erythroid precursors and erythroid hypoplasia, which prompted us to go for genetic evaluation.

However, there were no ringed sideroblasts, as has been reported in several studies.¹ Various studies have described concurrent neutropenia and thrombocytopenia, but these were not noted in our case 1 and the bleeding manifestations were attributed to Vitamin K deficiency secondary to pancreatic insufficiency. This case report addresses several important implications for the management of children with PS.

Early diagnosis of PS and interventional therapy in the form of mitochondrial and pancreatic replacement can prolong survival and significantly improve the quality of life.

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