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Case Report

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Is there a role of erythropoetin in congenital hemolytic anemia?

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Introduction

The role of erythropoietin in renal insufficiency and in patient on dialysis is already established. In newborn infants the erythropoietin is produced by the liver and at the end of the year the renal tissue picks up the production.[1] However in patients with congenital hemolytic anemia such as red cell enzyme deficiencies the new born infants have invariably hepatic dysfunction as the excessive bilirubin generated from the hemolysis is difficult to handle for the liver. In these patients the erythropoietin level is low. These groups of patients who are born with jaundice and with the anemia due to hemolysis invariably are treated with the transfusion. These patients can avoid the transfusions and the risks associated with it both immediate and long term if EPO is used as a treatment to tide over the crisis until at least the infant is one year old when renal tissue will start making EPO. Here is a case report of the patient with PK deficiency born with jaundice and anemia responded well to EPO avoiding transfusion.

Case History

The patient was born to the parents of different ethnic origins. The father was American white and the mother was of East Indian ethnic origin. This was their first child and mother was gravida I para 0. The pregnancy was uneventful and the delivery was also uneventful. The new born was female sex and born with the hemoglobin of 5.4 gm and the white cell count was around 14000 with normal differential with the plate count of 368000/cmm. The infant was jaundice and weighed 6 pounds. The clinical examination was normal with no evidence of hepato- splenomegaly. The cardio vascular examination was normal. The infant was lethargic and slightly irritable.

Laboratory

The review of the peripheral blood smear revealed no evidence of the schistocytes or fragmented red cells. There was polychromasia with occasional nucleated red cell. The white blood cells were normal morphologically with the normal distribution other than slight neutrophilia.[2] The reticulocyte count was high indicating hemolysis. There was no red blood cell antigenic incompatibility between mother and the infant and the husband and the wife. The red cell enzyme a study was under taken confirming the PK deficiency the G6PD was normal. The renal functions were normal and liver functions showed indirect bilirubin of 16 and normal hepatic enzymes. The erythropoietin level was less than 20.

Discussion

The clinical picture of PK deficiency is variable, from hydrops fetalis to neonatal jaundice and anemia.[3] In our patient jaundice and anemia was present. In patients with kernicterus sometimes exchange transfusion is advised. In some patients with anemia and jaundice splenomegaly is noted. In contrast in adults this could be diagnosed as incidental mild hemolysis with mild anemia. There are no specific clinical findings as no other tissue other than red cells is affected in PK deficiency.[4] Besides accumulation of 2-3DPG makes the oxygen dissociation curve shift the right resulting better tolerance of anemia. The PK deficiency is the most common enzymopathy of the glycolytic pathway inherited as autosomal recessive form. The PK catalyzes the conversion of phosphor-enol pyruvate (PEP) to pyruvate. This is one of the two glycolytic reaction resulting ATP production. The incidence of this in general white population is 1in 20,00 births as assessed by the gene frequency studies.[5] More than 220 different gene mutations have been identified on PKLR gene on chromosome 1. At one time PK deficiency was noted to be consequence of decrease production of structurally normal enzyme. But now it is known that most of the PK variants are abnormal proteins which differ in their biochemical kinetics and physical properties.

The PK deficiency leads to impaired glucose utilization and there by decreased pyruvate and lactate production. In addition to glycolytic intermediates proximal to block accumulate in the red cells. The deficiency of the PK leads to accumulation of the substances like 2-3 DPG three times that of normal The increase concentration of the 2-3DPG leads to the shift in the oxygen dissociation curve to the right in PK deficient cells resulting low oxygen affinity and the delivery of the oxygen to the tissues with the low hemoglobin concentration. These patients thus tolerate anemia better as low hemoglobin content will deliver same amount oxygen to the tissues as that of the normal hemoglobin. Though the oxygen will reserves limited.

Normally these infants are treated with transfusion to keep hemoglobin above 8 gm% to permit normal fetal growth and development. This can result in frequent transfusions and associated short and long term complications. In addition to increasing the iron storage, as the iron load increases due to hemolysis as well as transfusion. Thus knowing the importance of accumulation of 2-3 DPG and its effect on the oxygen dissociation curve I was reluctant to transfuse the patient. There is a single case of successful bone marrow transplantation in a 5year old boy.[6] Hence taking into consideration the physiology of erythropoietin production in infants and excess accumulation of 2-3 DPG I knew to increase oxygen reserve one needs to improve hemoglobin production. The transfuse blood does not last long hence my intentions were to find how to improve hemoglobin concentration that will last longer. The principle

hormone regulating the erythropoiesis is Erythropoetin (EPO) which is principally produced in the kidney except in fetal and neonatal life.[7] The hepatocytes are the major source for the erythropoietin production in fetal and neonatal life. Besides hypoxia is the major stimulus for the production of EPO and as hypoxia is not the feature of PK deficiency due to accumulation of 2-3 DPG. As the EPO came back to low after obtaining the consent from the parents proceeded with the replacement of EPO. The 100 units three times a week subcutaneously were started. The hemoglobin rose very promptly as the hemoglobin became 12gm in 2weeks. The EPO was maintained once week subsequently till the first year was completed. The case illustrates that judicious use of EPO resulted in avoiding transfusions and raising the hemoglobin level to the optimum level. Thus the judicious use of EPO in the neonatal period is appropriate to avoid transfusions and its complications as well as avoiding bone marrow transplantation.

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Conflict of interest

The author declares no conflict of interest.

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