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Sideroblastic Anaemia - Anaesthetic Considerations during Emergency Ophthalmic Surgeries

Dr. Shobha Ravishankar

Senior Consultant, Medical Research Foundation

Abstract: ***The sideroblastic anemias comprise a heterogeneous group of acquired and congenital disorders which that have in common: (1) anemia; (2) the presence of ring sideroblasts in the bone marrow; and (3) impaired heme biosynthesis. Elevation in iron levels is secondary to a deficiency in mitochondrial physiology. Patients exhibit mild to moderate hemolysis due to peripheral red blood cell destruction, and often require regular blood transfusions. The purpose of this case report was to describe the anaesthetic management of a child with congenital sideroblastic anemia—a rare hematologic disorder for an emergency ophthalmic surgery and to emphasize how important it is for anaesthetists and ophthalmologists to be cognizant of a patient's hematologic profile before attempting to perform procedure. The timing of the patient's transfusions regarding the scheduling of surgery is crucial for successful management and anticipation of possible complications.***

Keywords: Sideroblastic anaemia, Congenital disease, Anaesthetic management, Haemolysis

1. Introduction

Sideroblastic anemias are a unique group of disorders that can rise from primary or secondary defects of mitochondrial metabolism and are characterized by ring sideroblasts in the bone marrow and impaired heme biosynthesis (Fig.1). These ring sideroblasts consist of erythroblasts containing excessive iron levels in the mitochondria[1]. This characteristic feature appears as Prussian blue-positive iron granules[2] (Fig.2) .The high iron levels are the result of the mitochondria's inability to utilize it in hemoglobin synthesis, producing hypochromic microcytic erythrocytes[3] .

Clinical manifestations of sideroblastic anemias present in a myriad of forms. The patient commonly suffers from: fatigue, dizziness and decreased tolerance to activity. Hemoglobin levels range from 4 g/dl to 10 g/dl[1]. Patients exhibit mild to moderate hepatosplenomegaly[4] and hemolysis due to peripheral erythrocyte destruction. This disease's morbidity and mortality is due in large part to iron overload rather than deficiency[5] . High iron levels may interfere with growth and development. In addition, iron overload leads to cardiac arrhythmias and congestive heart failure[4] .Thus, serum ferritin levels and transfer in saturation should be routinely monitored to detect iron overload[1].

2. Course in the hospital

A 4 year old male child weighing 16.6 kgs came to our institute following trauma to the right eye as an emergency. The patient was scheduled for lid exploration and repair under general anaesthesia.

The patient was born full term with normal developmental mile stones. At the age of 2 years , baby was investigated for repeated episodes of fever and was diagnosed to have Sideroblastic Anaemia. The haemoglobin levels were 4gms/dl. Subsequently the patient was receiving blood transfusion once in 20 days.

After 6months of diagnosis a bone marrow transplant was attempted, the donor being the child's father. Unfortunately this failed and baby was again on periodical blood transfusions.

On the day of surgery, the haemogram was as follows:
Hb : 11 gms/dl (Patient has had transfusion 4 days ago)
Blood Sugar (R) : 118 mgs/dl
Coagulation profile : Normal

S. Ferritin : 1968 ng/ml
Peripheral smear : mild hypochromic microcytic RBC with occasional burr cells, schistocytes and pencil cells.

Current drug regimen:
T. Asunra (Desferrioxamine) 600mgs OD
T. Pyridoxine 40 mgs at night
T. Thiamine 50 mgs at night
T. Folic acid 5 mgs at night

After obtaining the haematologists clearence and an informed consent the
child was taken up for emergengy surgery.

Universal fasting guidelines were followed and the patient was premedicated with Inj. Glycopyrolate 0.004 mgs/kg I.M. After inhalational induction, an IV access was obtained and 0.45% DNS was started. I.V. Fentanyl 1.5mcg/kg was given for analgesia. Trachea was intubated with an appropriate sized tube after paralysis with Atracurium 0.5mg/kg. Vitals remained stable throughout the procedure which lasted for two hours. The patient was extubated awake at the end of the surgery after reversal.

3. Discussion

Sideroblastic anemia is classified based on its mechanism of transmission[1]. The acquired form is the most common, and it occurs as the result of medications and toxins. The hereditary form follows primarily by way of X-linked mutations and generally occurs in males. Sideroblastic anemia can also be of an idiopathic origin or associated with myelodysplastic syndromes, malignancy, or other systemic

disorders[6] .

Advances in molecular medicine have proven useful in the search for the etiology of sideroblastic anemia. Investigation into hereditary or X-linked sideroblastic anemia has concluded that the disease's etiology may be a mutation in the gene found on the X chromosome encoding for erythroid specific 5-aminolevulinic acid synthase (ALAS-2)[4,7] . ALAS-2 is the first and rate controlling enzyme of heme synthesis in erythroid cells. This defect results in the excessive iron levels that typify sideroblastic anemias. The mutation commonly follows an X-linked pattern of transmission, but has also been found in other forms[8].

A second group of hereditary X linked sideroblastic anemia results from defects in another gene that encodes an ATP-binding cassette protein[9]. Other types of sideroblastic anemia involve primary mitochondrial defects, including 2.7 kb to 7.767 kb deletion lesions of mitochondrial DNA[6] .

Nuclear DNA mutations have been found in both autosomal dominant and recessive forms.

Sideroblastic anemia can present as a component of several syndromes characterized by partial deletion of mitochondrial DNA[10,11] (Table 1). Pearson's syndrome has been identified as a 4977 bp deletion in mitochondrial DNA, responsible for oxidative phosphorylation. Clinical presentation is similar to the clinical expression of sideroblastic anemia, though there is a less marked genetic transmission; the anemia is diagnosed as macrocytic and hyperchromic[12] . Diagnosis is also made earlier in life, and up to a quarter of affected infants are diagnosed prior to their first month of life.

The mitochondrial myopathy and sideroblastic anemia (MSA) syndrome was initially described by Rawles and Weller in 1974. MSA is a rare autosomal recessive disorder of oxidative phosphorylation and iron metabolism[13] . Although no specific gene has been identified as being responsible for the disease, an area of chromosome 12q24.33, and the PUS1 gene have been identified as candidate loci[14,15].

Case reports have linked the Kearns Sayre syndrome to diabetes and Addison's disease[16-18] .The onset of symptoms is prior to age 20, and it has been proposed that this condition is the late stage representation of Pearson's syndrome

Treatment of severely anemic individuals suffering from sideroblastic anemias generally involves routine blood transfusions to: (1) maintain hemoglobin levels; (2) manage symptoms; and (3) allow normal growth and development[1,4]. A potential risk of these interventions is the development of autoimmunity to recurring transfusions, particularly if initiated at a young age. These patients are often on deferroxamine which is the current standard therapy for elimination of excess iron. Pursuit of a curative treatment for sideroblastic anemia has led to investigation of hematopoietic stem cell transplantation (HSCT) and nonmyeloablative allogenic hematopoietic stem cell transplantation (NST).

4. Conclusion:

The management of children with blood dyscrasias from an anaesthetists perspective can present a significant challenge for an emergency surgery under general anaesthesia and it is likely to be further complicated if these cases are associated with mitochondrial myopathies. Thus an indepth knowledge of the underlying pathology is very useful for a successful anaesthetic outcome.

5. Conflict of Interest

Nil

6. Financial interest

Nil

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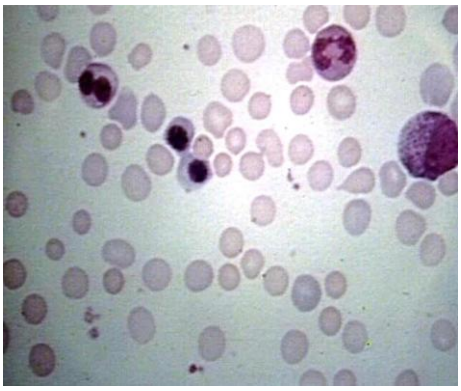

Figure 2: Prussian blue stain

Figures

Figure 1

Table 1: Syndromes of Mitochondrial Metabolism Linked to Sideroblastic Anemia

Pearson's syndrome (Pearson's marrow pancreas syndrome)	Mitochondrial myopathy and sideroblastic anemia (MSA) syndrome	Kearns-Sayre syndrome
Refractory sideroblastic anemia	Severe muscle weakness	External ophthalmoplegia
Pancreatic dysfunction	Anemia in middle to late childhood	Pigmentary retinopathy
Vacuolization of marrow cells		Cardiac conduction abnormalities
Hyperparathyroidism		Endocrine dysfunction
Metabolic acidosis		Muscular abnormalitiesr
Pancytopenia		
Failure to thrive		