ANAESTHETIC MANAGEMENT OF A PATIENT WITH SICKLE β+
THALASSEMA WITH CHOLELITHIASIS
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ABSTRACT: The clinical picture of Sickle cell disease (SCD) is remarkable for striking heterogeneity in presentation, progression and severity. The intermittent vaso-occlusive crisis and anemia due to chronic hemolysis often leads to acute to chronic pain and organ damage. Enhanced bile secretion in SCD with chronic hemolysis requiring multiple transfusions predisposes to the development of cholelithiasis. Sickle cell disease is quite common in the state of Chhattisgarh affecting mainly 10% of the population. We report the successful management of a 16 year old tribal girl diagnosed with sickle cell disease with β+ thalassemia with cholelithiasis, who underwent cholecystectomy under general anesthesia. Anesthetists have to be extremely vigilant about the increased perioperative complications and device a careful strategy to prevent them, and in a worst scenario, manage them.

KEYWORDS: Sickle cell disease, sickle β+ thalassemia, cholecystectomy, anesthesia.

INTRODUCTION: Sickle cell disease is a common hereditary hemoglobinopathy resulting from a mutant version of the β-globin gene and defined by the presence of hemoglobin S (HbS). While, sickle cell anemia (homozygous HbSS) is the commonest form, other forms of SCD result from co-inheritance of HbS, with other abnormal β globin chain variants viz, sickle hemoglobin C (Hb– SC) and 2 types of sickle β thalassemia, sickle Beta positive thalassemia (HbS β+ Thal.) and sickle Beta Zero thalassemia (HbSβ0 Thal.), inherited as autosomal recessive.¹ Persistent hemolysis with increased bilirubin turnover is a recognized attributable risk factor for the development of Cholelethiasis.² The case of a 16 old tribal girl diagnosed with sickle cell anemia and B+ Thalassemia is reported here. She was investigated and posted for cholecystectomy. With the increase in knowledge of pathophysiology of SCD and clinical spectrum, newer therapeutic protocols and anesthetic procedures, the management of these patients has vastly improved resulting in successful outcome.

CASE REPORT: A 16 year old female patient, belonging to tribal community was referred to medical college hospital, presented with frequent pain in the right hypochondrium & recurrent episodes of jaundice. She gave history of episodes of pain, vomiting, fever and steatorrhea. She required hospitalization in remote community health centre twice for enteric fever. Careful history revealed that she had received blood transfusions twice previously, but none in the last one year.

She was thin-built and on examination she was found to have pallor, moderate icterus and characteristic facies of SCD, which included frontal bossing, depressed nose bridge, prominence of cheek and muddy brown sclera. The right hypochondrium was tender, without any obvious lump. There was no organomegaly. Systemic examination did not reveal any other abnormality. USG showed contracted GB with diffuse thickening and multiple echogenic calculi within the lumen of gall bladder. Hemogram showed total Hb to be 8.6 g/dL.
Her liver function test results were abnormal. (Table 1). Keeping in view a very high prevalence of hemoglobinopathies in this tribal dominated region, Hb variant analysis was performed. (Table 2) She was diagnosed as a case of sickle beta positive thalassemia with cholelithiasis. She was transfused with one unit of packed RBC, and Hb variant analysis was repeated. The patient and attendants were explained the nature of operation and anesthesia; informed consent was taken. She was given alprazolam 0.25 mg the night before surgery; Adequate hydration was maintained with IV ringer lactate solution.

Her urine output was maintained over 1ml/kg/hr. She was given inj. ranitidine 50mg, ondansetron 4mg and inj. glycopyrrolate 0.2mg as preoperative medication. A nasopharyngeal probe was inserted for monitoring and maintain temperature between 36-37°C. She was preoxygenated with 8 l/min 100% oxygen. Induction was done with inj. Propofol 2mg/kg and inj. Atracurium 0.5mg/kg. Patient was mechanically ventilated and maintained on oxygen and isoflurane. Nitrous oxide and Sevoflurane were purposely avoided. Standard intraoperative monitoring was accomplished with pulse-oximetry, NIBP, ECG, Temperature and EtCO2 measurements. Patient was shifted to ICU for continued postoperative monitoring.

**DISCUSSION:** Sickle cell disease is a congenital hemoglobinopathy, characterized by chronic hemolytic anemia, recurrent episodes of intermittent vaso-occlusion and severe pain and progressive organ damage.¹ Vaso-occlusion is triggered by delayed passage of RBC through microcirculation, mechanical obstruction to flow, vaso-occlusion & infarction in a vicious cycle. Sickling is caused by extensive polymerization and gelation of hemoglobin-S after deoxygenation.³ Factors like infection, acidosis, hypothermia predispose RBCs for sickling. While the instable HbS exposes erythrocyte cell membrane to the destructive oxidant potential of intra-cellular iron, an impaired nitric oxide (NO) signaling pathway disrupts the vascular endothelial function.⁴,⁵

Resultant pain crisis or vaso-occlusive crisis (VOC) is an intricate patho-physiological process, involving vaso-constriction, leucocyte adhesion & migration, platelet activation & adhesion, and coagulation. The lumber spine, abdomen, femoral shaft and knee are the recognized common sites of acute pain.⁶ The Bone pain arises either from cortical infarction or from marrow infarction.⁷ Abdominal pain may arise from bowel dysfunction, organ infarction or be referred from the ribs.

The acute chest syndrome (ACS), an acute pneumonia like serious complication of SCD is characterized by alveolar consolidation excluding atelectasis, chest pain, pyrexia, tachypnea, precipitated by infections, fat embolism and surgical procedures.⁸,⁹ Therefore; it is almost customary to start broad–spectrum antibiotics in the peri-operative period. Streptococcal infections are common in these patients, owing to functional hypo-splenism. Pulmonary complication can be effectively prevented by prophylactic continuous positive air way pressure and incentive spirometry.¹⁰

Stroke is a devastating complication of SCD, may be infarction or hemorrhagic in origin. Nephropathies attributable to SCD include glomerular disease and papillary necrosis, presenting with varying degrees of hematuria and proteinuria.¹¹

In contrast to sickle cell trait, SCD patients have marked perioperative complications. Therefore, assessment must include type of operative procedure, disease activity, patient details, and organ dysfunction consequent on disease progression. Surgical trauma, anesthetic agents used along with additive factors like vascular stasis, compromised ventilation, alterations in fluid volume,
oxygen tension, pH contribute and enhance the risk of end organ ischemic infarcts.\textsuperscript{1} The morbidity of SCD patients undergoing major surgeries has been reported to be 40%.\textsuperscript{12}

Chronic hemolysis with accelerated bilirubin turnover, increased bile secretion from liver, than the gallbladder can hold and thick bile sludge leads to a higher incidence of cholelithiasis. Gall stones could be cholesterol laden or pigmented, black or brown.\textsuperscript{13,14} The overall occurrence of cholelithiasis increases considerably with age, while, gall stones occur in approximately 30 to 50 % of children with SCD, it rises to about 50-70% in adults.\textsuperscript{15,16}

For medical management various agents including hydroxyurea to enhance the production of HbF, inhibiting HbS polymerization, oral magnesium supplement to reduce RBC dehydration and induced hyponatremia to decrease HbS concentration have been used with varying degree of success.\textsuperscript{17,18,19} Prophylactic continuous positive airway pressure and incentive spirometry effectively prevents pulmonary complication.\textsuperscript{10}

Cholecystectomy is the preferred surgery in cases of SCD when high degree of adhesions is anticipated. The choice of anesthesia is of great relevance owing to various complications which follow silent infarctions of end organs. Adequate hydration to minimize viscosity of blood and increase dilution of sickle cells, enhance Hb levels and PCV between 30 and 50% is of utmost importance. Perioperative exchange transfusion depends on general condition of patient and type of surgical procedure, it does wonders to reduce the circulating HbS concentration, minimize sickling and prevent SCD-specific complications.\textsuperscript{20} Another important recognizable complication of hemolytic anemia is pulmonary artery hypertension (PAH) resulting from deranged NO pathway and impaired vascular endothelial function. Therefore, nitrous oxide should preferably be avoided.\textsuperscript{21-22}

SCD is a common clinical entity in this tribal dominated region in the districts of Bastar, Narayanpur & Surguja of Chhattisgarh State. There are large variations in prevalence of sickle hemoglobin in various tribal population of the state. Among Gond group of tribals the prevalence rate of sickle hemoglobin generally varies from 10 to 25 percent whereas in the Bhil group of tribals the prevalence rate varies from 15 to 33 percent.\textsuperscript{23}

Therefore, it is pertinent that, as a policy the clinically suspected of SCD requiring major surgical interventions are investigated thoroughly including Hb variant analysis. Anesthetists have to demonstrate a judicious planning of anesthesia and analgesia and meticulous execution of the strategies devised in all cases of Hemoglobinopathies.\textsuperscript{24-25}

In conclusion, maintenance of adequate hydration preoperatively, avoidance of acidosis, hypoxia, hypovolemia, hypothermia reduced the perioperative sickle- induced complications. Good intraoperative and postoperative pain relief, oxygen therapy, incentive spirometry sand regular ABG monitoring played an important role in successful management of the case.

| Investigation       | Observed value |
|---------------------|----------------|
| Total bilirubin     | 5.2 mg/dL      |
| Unconjugated bilirubin | 3.3 mg/dL    |
| SGPT                | 85 U/L         |
| SGOT                | 68 U/L         |
| Total protein       | 7.3 g/dL       |
| Albumin             | 3.2 g/dL       |

Table 1: Liver function test
Investigation | Observed value (%) | Pre transfusion | Post transfusion |
|---------------|--------------------|----------------|-----------------|
| Hb A          | 3.1                | 19.6           |
| Hb A2         | 2.5                | 3.2            |
| Hb F          | 19.8               | 16.5           |
| Hb S          | 74.6               | 60.7           |
| Hb D          | Absent             | Absent         |
| Hb C          | Absent             | Absent         |

Table 2: Hemoglobin variant analysis of blood (HPLC technique)

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