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Case Report:

Obstetric Anesthesia Management of Pregnant Patient with Gilbert Syndrome and Systemic Lupus Erythematosus with Hemolytic Anemia – A Rare Case Report

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ABSTRACT

Gilbert Syndrome (GS) is a rare benign condition due to mutation in glucoronyl transferase enzyme, characterized by recurrent mild unconjugated hyperbilirubinemia [4].Systemic lupus erythematosus (SLE) is autoimmune disease affecting multiple systems, with female preponderance, having onset during reproductive age group and hemolytic anemia is one of the diagnostic criteria and has bad prognosis (50% mortality in 10 years) [10]. GS and SLE in pregnancy are associated with higher maternal and fetal mortality and morbidity. The literature is scarce on anesthesia management during caesarean delivery of pregnancy with GS, SLE and hemolytic anemia. The case is reported due to its rarity.

We report anesthesia management of 22 years old female (G2P1D1 with 33 weeks of gestation) diagnosed case of GS and SLE with hemolytic anemia posted for elective caesarean section. This case report highlights that spinal anesthesia remains a better option over general anesthesia in management of such pregnancy with these comorbidities.

Key Words -Gilbert syndrome, Systemic lupus erythematosus, caesarean section, spinal anesthesia.

Introduction

Gilbert syndrome (GB) is characterized by recurrent mild unconjugated hyperbilirubinemia with serum bilirubin often <3mg/dl in 7% cases [4]. Mutation in glucoronyl transferase enzyme reduces one third of normal enzyme activity. It is diagnosed often at/after puberty with male predominance over female by 1.5:1 to >7:1[11]. The sex hormone induces glucoronyl transferase enzyme, thereby pregnancy seems to have protective effect in GS [11].

Systemic lupus erythematosus (SLE) is commonest autoimmune disorder that affects women during reproductive age group having incidence 1.4-24/100,000 worldwide, Female to male ratio is 9:1. During childbearing years ratio is 15:1 and 1:1000 women. Estrogen may play an important role in causing SLE [10].

GS and SLE in pregnancy are associated with higher maternal and fetal mortality and morbidity. In literature, there is no report about anesthesia management for cesarean delivery of pregnancy associated with both GS and SLE.

Case Details

A 22 year old female (G2P1D1, 33 weeks of gestation, weight 55kg) was planned for elective caesarean section. She was diagnosed having SLE along with autoimmune haemolytic anaemia and GS 2years back and was highly anxious about baby's wellbeing due to previous adverse foetal outcome. Clinical Examination was within normal limits.

Laboratory investigations- haemoglobin- 10.3gm/dl, total leukocyte count- 11.3, platelets 2.63 lakhs. Total bilirubin 4.9mg/dl, direct bilirubin 1.08 mg/dl, SGOT/SGPT: 38/42, Prothrombin Time-12.3 and INR 1.02, ECG/CXR normal. High risk informed consent ensured. Pre-medication tab. lorazepam 2mg was given on night before surgery and was scheduled first on the list at 7.30am. A 5% dextrose solution was started in the morning, changed to normal saline intraoperatively. Antiemetic IV ondansetron 4mg was given. Preparation for difficult intubation was kept ready.

Spinal anaesthesia was given at L3-L4, with 25guage Quincke's spinal needle, 2cc heavy bupivacaine (0.5%). Spinal action was set at T6 level. Healthy baby weighing 2800gm was delivered with APGAR score 9/10 at 1/5 minutes. Intra operatively mean arterial pressure (MAP) was maintained >70 mmHg. IV midazolam 0.5mg was given for sedation (to avoid anxiety and surgical stress after baby delivery [12] Oxytocin 20 unit infusion was given slowly. Intra operatively vitals were stable. Post operative management included tramadol 50mg IV for analgesia, adequate hydration and oxygen supplementation.

Discussion

GS described by Augestine Gilbert and Pierre Lerebullet in 1901 is also known as Zheel Bayrs syndrome, constitutional hepatic dysfunction and familial non-hemolytic jaundice [16]. Mutation in enzyme reduces activity to 10-30% of normal. Bile pigment exhibit a characteristic increase in bilirubin monoglucoronides [4]. About 30% are asymptomatic, other present with yellow color of sclera/skin, nausea, vomiting, diarrhea, fatigue, abdomen discomfort [11]. Factors precipitating rise in bilirubin are infection, dehydration, stress, lack of sleep, fasting, alcohol intake. Treatment includes choosing healthy lifestyle, exercise, adequate sleep, well hydration and balanced diet [11].

SLE is an autoimmune disease leading to cells and organs damage involving musculoskeletal cutaneous, nervous, renal, cardiac, gastrointestinal and reproductive systems [5]. Prevalence of SLE in United States is 20-150/100,000 women (90% women are of childbearing age) [10]. Clinical manifestations of SLE are malar rash, oral/nasal ulcer, synovitis, arthritis, seizure, loss of pregnancy, hemolytic anemia, joint pain etc. [8, 10]. Diagnosis is by antinuclear antibody, Anti ds DNA antibody, Anti sm antibody, Anti RNP antibody, Anti Ro antibody, Antiphospholipid antibody [10]. Prognosis is poor-50% mortality in 10years and is associated with high serum creatinine levels, hypertension, nephrotic syndrome, anemia (Hb<12.4gm/dl), hypoalbuminemia, antiphospholipid antibody, male sex, low socioeconomic status [10]. Rate of fetal loss increases 2-3 folds in women with SLE, correlates with high disease activity, antiphospholipid or active nephritis. Active SLE in pregnant women is controlled with hydroxychloroquine and azathioprine [10].

Obstetric risks includes coexisting pre-eclamsia(20-30%), gestational hypertension, pregnancy loss(20%), preterm birth due to pre-eclamsia/fetal distress/premature membrane rupture, severe IUGR or neonatal lupus. Also risk of

flaring of SLE, features of flares mimicking pre-eclamsia and possibility of lupus nephropathy should be vigilantly evaluated and managed.

Clinical features in our case- female patient, of reproductive age 22 years, G2P1D1 with 33 weeks of gestation. She was diagnosed with hemolytic anemia 4 years ago during antenatal checkup of previous pregnancy with multiple blood transfusions. She had first fetal loss at 7 months of gestation probably due to undiagnosed SLE. Two years post-delivery patient had 1 episode of mild jaundice and anemia followed by detailed work up, which lead to the diagnosis of SLE with autoimmune hemolytic anemia with GS. Then patient had recurrent episodes of jaundice, bilateral pedal edema and decreased appetite.

ANA antibody, dsDNA, antiSMA antibody were positive in our patient. Thereafter patient conceived spontaneously 1 year later. On rheumatologist and gastroenterologist's opinion she was advised, that she could continue the pregnancy if she had regular antenatal checkups for close fetal monitoring [8]. Blood investigations as reported above showed raised bilirubin. It was essential to ensure that anaemia is pre-operatively corrected to help cope with autoimmune anaemia superimposed on gestational dilutional anaemia keeping in mind to avoid exacerbation of GS [11] USG abdomen showed spleenomegaly of 13 cm and grade 1 fatty liver. Patient was on tablet prednisolone 10mg BD, tablet azathioprine 50mg BD, tablet hydroxychloroquine 200mg BD, tablet vitcofol since 5 months of amenorrhea.

Anesthetic management in patient with SLE should be based on the degree of involvement of various systems and severity of the disease [10]. Glucoronyl transferase is responsible for metabolism of many drugs, due to unavailability of this enzyme, drugs may get accumulated and leads to adverse outcome [2]. Preparation for anticipated difficult airway should be done in SLE due to laryngeal and subglottic involvement which may be aggravated in pregnancy [13]. Additionally nonerosive arthritis is common in SLE leading to increase risk of subluxation of antlanto-axial joint [7]. Pulmonary involvement should be assessed in SLE for pleural effusion, interstitial lung disease [9]. Difficult airway was to be anticipated, so endotracheal tubes with smaller diameters were kept ready [13. Vertebral involvement in SLE leads to difficult spinal anesthesia. SLE may leads to deranged coagulation profile [10]. Adequate blood and blood products were kept ready. ECG, blood pressure, pulseoximetry, urine output was monitored throughout the procedure.] We preferred regional anesthesia over general anesthesia in our case for elective cesarean section. As fasting and dehydration can aggravate GS, cesarean section was scheduled first on the list, early in the morning, to avoid hypoglycaemia and related stress [11] Intra operatively dextrose was changed to normal saline to avoid intraoperative hyperglycemia due to stress induced by surgery and anaesthesia [12].

During cesarean section performed under spinal anesthesia MAP was maintained >70 mmHg, this helps in maintaining adequate hepatic perfusion and prevents worsening of Gilbert's syndrome [15]. Oxytocin infusion @ 0.3 U/min started slowly after the delivery of the baby and anxiolysis by 0.5 mg midazolam to avoid surgery and anaesthesia induced stress [12]. Cesarean section lasted for 35 minutes with 300cc of blood loss.

Post operatively, dextrose normal solution was infused to avoid hypoglycaemia and related stress [12] Judicious blood transfusion was advised to avoid precipitation of Gilbert's syndrome and simultaneously preventing exacerbation of auto immune haemolytic anaemia.[15] Inj tramadol 50 mg IV was given for post-operative pain

and pain induced stress. Non steroidal anti inflammatory drugs should be avoided to prevent precipitation of dormant lupus nephritis. [14] Paracetamol (PCM) was avoided keeping in mind deficiency of glucoronyl transferase, as it is common that the enzyme metabolising PCM is hampered in GS [12]

Conclusion

GS and SLE both are diseases of young age, but if occur in pregnancy lead to raised feto-maternal morbidity and mortality. During anesthesia management of pregnant patient with GS and SLE, thorough physical assessment and laboratory evaluation, screening for multi-organ damage, and knowledgeable planning along with wise selection of anesthesia technique for conduct of anesthesia is necessary.

The cesarean section of full term pregnant patient with known diagnosis of GS and SLE with hemolytic anemia was managed successfully under spinal anesthesia with good maternal and fetal outcome.

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