

# Salvage Intrapartum Splenectomy for the Treatment of Transfusion-refractory Anaemia in a $\beta$ -thalassemia Intermedia Patient

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## ABSTRACT

Thalassemia intermedia (TI) patients may need a transfusion during physiological stress conditions, such as pregnancy. We present a case of a female TI patient with emerging transfusion-refractory anaemia during pregnancy, which resolved after splenectomy performed simultaneously with cesarean delivery. A 26-year pregnant woman at 29<sup>th</sup> gestational weeks was referred with a diagnosis of TI due to emerging anaemia which was refractory to transfusion. Splenectomy at term was decided to improve anaemia, and transfusion response. A preterm infant was delivered by cesarean section due to threatened preterm labour. Once the uterine incision was closed, an open splenectomy was performed. Postoperative follow-up was uneventful. To the best of our knowledge, the present case is the first open splenectomy performed during cesarean delivery as a salvage option for the management of transfusion-refractory anaemia.

**Key Words:** *Thalassemia intermedia, Splenectomy, Pregnancy, Hemolytic anaemia.*

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## INTRODUCTION

$\beta$ -Thalassemia results from >300 different mutations of the  $\beta$ -globin gene, causing reduced production of  $\beta$ -globin chains.<sup>1</sup>  $\beta$ -Thalassemia is classified as transfusion-dependent thalassemia (TDT) and non-transfusion-dependent thalassemia (NTDT) according to the severity of phenotype.<sup>2</sup> Thalassemia intermedia (TI) is a clinical entity where anaemia is mild or moderate, requiring no or occasional transfusion. TI patients may need a transfusion during physiological stress conditions, such as infections and pregnancy, which cause erythroid stress and subsequent hemolysis. Later in life, they may develop transfusion dependence.

We present a case of a female TI patient with transfusion-refractory anaemia during pregnancy, which resolved after splenectomy performed concurrently with cesarean delivery.

## CASE REPORT

A 26-year pregnant woman with a diagnosis of TI was referred due to emerging anaemia which was refractory to transfusion.

She was at 29<sup>th</sup> gestational week, gravida 1 para 0. She was pale, anxious, and had massive hepatosplenomegaly. The transfusion history included 14 units packed with red blood cells (RBCs). The laboratory evaluation revealed haemoglobin (Hb) level of 5.2 g/dl, and platelets of  $69.9 \times 10^9 / \mu\text{L}$ . The leukocyte count was  $8.6 \times 10^9 / \mu\text{L}$ , whereas, serum vitamin B12 and folic acid levels were within normal limits. Peripheral blood smear showed nucleated RBCs, anisocytosis, severe microcytosis, and hypochromia with target cells and spherocytosis. The direct and indirect antiglobulin tests were positive.

Capillary electrophoresis (CE) revealed a normal level of HbA2 (3.1%); HbA and HbF levels were 61.3% and 35.6%, respectively. TI diagnosis was confirmed by molecular analysis of the  $\beta$ -globin gene, which was harboring a homozygous  $\beta$  point mutation Hemoglobin  $\beta$  (HBB): c.315+1G>A. Until the last year, she has not been transfused. The clinical picture was consistent with hemolytic anaemia with decreased haptoglobin of 3 mg/dl (Normal: 30-200 mg/dl), and elevated serum lactate dehydrogenase (LDH) level of 969 U/L (Normal: 135-200 U/L). Serum ferritin was 233 ng/dL (Normal: 4.63-204 ng/mL). The spleen size seemed to be unexpectedly large for TI disease. The osmotic fragility test was negative. The patient was also evaluated for portal hypertension (PH) and Gaucher's disease. No clinically significant PH and esophageal varices were detected. No glucosylceramidase deficiency was documented. No compatible cross-matched RBCs were available for transfusion. Alloantibodies with probable autoantibodies were considered. To disso-

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ciate the alloantibodies, an elution test could not be performed due to insufficient technical equipment and autoimmune hemolysis association could not be excluded. Low-dose methylprednisolone was started as 1 mg/kg/day with a minimum transfusion plan. Splenectomy at term was planned to improve anaemia and transfusion response. She was vaccinated against *S. pneumoniae*, *N. meningitidis*, and *H. influenzae* type b and anticoagulant prophylaxis with low molecular weight heparin was started.

Antenatal betamethasone course was completed due to uterine contractions at 32 gestational weeks. Tocolytics did not suppress the labour. Due to cephalopelvic disproportion, cesarean delivery was planned. The preoperative Hb level was 4.6 g/dl. Under general anaesthesia, cesarean delivery was performed with a median skin incision. A preterm female infant weighing 1520 g (Apgar score of 7 at 1 minute, and 9 at 5 minutes, respectively) was delivered. Following uterine closure, splenic vein was ligated and three units of packed RBCs were transfused by the surgery team. The duration of the operation was 45 minutes and the estimated blood loss was 750 ml. Postoperative follow-up was uneventful. On 2<sup>nd</sup> postoperative day, Hb level increased to 8 g/dl, and platelets to  $375 \times 10^9 /\mu\text{L}$ . The patient was discharged on heparin prophylaxis to prevent thromboembolic complications. The newborn was followed up in the neonatal intensive care unit due to respiratory distress for 5 weeks after birth and was discharged without any sequelae.

## DISCUSSION

The TIs are genotypically and clinically a heterogeneous group of blood disorders. The disease severity ranges from asymptomatic carrier state to the severe symptomatic state dependent on blood transfusion. Anaemia deteriorates in pregnancy in combination with gestational anaemia with a possible contribution of fetal  $\text{O}_2$  consumption and leads to different obstetric complications such as spontaneous abortion, intrauterine growth restriction (IUGR), and preterm delivery.<sup>3</sup> Most centres transfuse pregnant women aiming to maintain Hb of  $>10 \text{ g/dL}$  to ensure appropriate fetal growth.<sup>4</sup> Approximately 30% of these patients have no previous history of transfusion.<sup>5,6</sup> Despite following this approach, IUGR may be present, suggesting the role of other fetoplacental and maternal factors. On the other hand, pregnancy and transfusion may contribute to acquired red-cell antibodies which result in difficulties to find out matched RBC units.<sup>4</sup>

Each TI patient planning pregnancy should have a detailed blood group analysis, screened for acquired red-cell alloantibodies and transfused accordingly. Unfortunately, this patient's detailed blood group analysis and determination of alloantibody specificities could not be performed due to previous transfusions. If a woman diagnosed with TI has massive splenomegaly and transfusion-refractory severe anaemia develops, splenectomy should be recommended in preconceptional period.<sup>7</sup> In the current case, our concern was focused on the risk of maternal-fetal hypoxia that may develop due to transfusion-resistant severe anaemia. Cesarean

delivery was preferred because of the borderline findings in pelvic examination and the possible risk of fetal hypoxia during labour. After discussing all opportunities with the patient and receiving the informed consent, it was decided to perform the splenectomy simultaneously during cesarean delivery. It is known that thromboembolic complications occur more frequently in TI patients compared to thalassemia major patients with a higher risk in splenectomised patients. This is related to the fact that damaged RBCs, which are normally removed by the spleen, persist in the systemic circulation and trigger thrombin generation. Therefore, anticoagulation was started.<sup>8</sup> Splenectomy during pregnancy is a rarely used treatment modality and requires surgical experience. Open surgery is recommended to be performed during the second trimester.<sup>9,10</sup> In the current case, which was refractory to transfusion, completing two major surgeries in the same session was the preferred option for eliminating the splenic sequestration and increasing the Hb level. To the best of our knowledge, this is the first case, where a splenectomy was performed during cesarean section as a salvage option.

In conclusion, with the increasing number of immigrants, physicians should be prepared to face severe hemoglobinopathies related to ethnic background and unplanned pregnancies. Transfusion policies and thromboembolism prophylaxis are the main steps. Planned splenectomy may definitively reduce blood requirements with improved Hb levels and could be performed under secure conditions.

## PATIENT'S CONSENT:

Informed consent was obtained from the patient.

## COMPETING INTEREST:

All authors declared no competing interests.

## AUTHORS' CONTRIBUTION:

TSS, AO and MO: Searched the literature.

TSS, MO: Wrote the manuscript with support from SKB.

SKB, MT: Supervised the manuscript.

All the authors have approved the final version of the manuscript to be published.

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