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Thalassemia Major: A Catastrophe in the Pregravid Patient: Case Report

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Introduction

The red blood cell contains approximately 500 to 600 million hemoglobin molecules, the predominant one in the adult is hemoglobin A (HbA) formed by four polypeptide chains, two alpha chains and two beta chain, in addition to the HEM group formed by iron and protoporphyrin. In any normal adult, three types of hemoglobin are found: HbA ((α2 β2) in more than 90%, hemoglobin A2 (HbA2) formed by 2 alpha polypeptide chains and two delta (α2 δ2) and fetal hemoglobin (HbF) which contains two alpha chains and two gamma chains (α2 γ2) [1,2]. Thalassemia is an inherited blood disorder, which are produced by alterations in the hemoglobin molecule, which may be due to defects, in the complete or partial synthesis of hemoglobin chains. This pathology is named according to the chain in which the deficiency is found [3].

Severity and type of anemia in beta thalassemia, are determined by the affected genes on chromosome 11, resulting in a lack of synthesis of beta globin chains. This determines the type of presentation or complications [3]. Iron deposition is the most important complication of Thalassemia and the biggest obstacle in management. In patients who do not receive transfusions, abnormal iron absorption results in an increase in iron stores of 2 to 5 g per year. If iron deposition progresses, the capacity of serum transferrin, the main iron transport protein, that binds and detoxifies iron may be exceeded and an unbound fraction may promote the generation of hydroxyl free radicals, which causes damage and in the absence of chelation therapy iron accumulation results in progressive heart dysfunction liver and endocrine glands [4].

The survival of patients with beta thalassemia is determined by the amount of iron deposited within the heart [4]. Because pregnancy is a hypercoagulability state, the thrombotic tendency with thalassemia will triple, and will increase the risk of bleeding if there is a deficiency of coagulation factors, potentially increased catastrophic complications. In women with thalassemia major, chronic hypertransfusion leads to iron overload, risk of alloimmunization and transmission of infections, which increases the risk of pregnancy complications [3].

The course of action to follow is to prescribe supplements with folic acid and iron. Depending on the severity of the syndrome, regular blood transfusions are used to maintain a hemoglobin level within an optimal range. Alloimmunization against erythrocyte antigen. as a result of genetic differences between the donor and the recipient, it is a risk that must be considered. This phenomenon brings with it the production of alloantibodies against one or more of these antigens that will complicate the subsequent administration of heme components [5].

Betathalassemia is an obstetric risk factor for oligohydramnios, preterm birth, preeclampsia, premature rupture of membranes and gestational diabetes. For this reason, timely diagnosis is of utmost importance to anticipate possible adversities [5]. Based on the above, the objective was to determine the implications of thalassemia anemia on mortality in pregnant patients and the fetus, as well as describing the pathophysiology of the disease and their behavior during pregnancy, in addition, to specify the complications that occur in this type of patients through a case report.

Case Presentation

Female patient, 21 years old, from Los puertos de altagrasia, Zulia, Venezuela. With LMP 17/02/2022 (34.5 weeks), who comes to the emergency department because of a acute-onset frontal headache of strong intensity, oppressive character, without irradiation, which does not yield to the administration of analgesics Dizziness and generalized weakness were also added to the clinical picture, and for this reason, after medical evaluation, her admission was decided.

She was diagnosed with thalassemia major at 4 years of age, treated with folic acid 10mg daily, oral order, and hypertension

diagnosed 2 years ago and treated with losartan. Primigestation patient, who during pregnancy refers lower urinary tract infection: acute cystitis in the 2nd trimestre, treated with ceftriaxone 1 g every 12 hours for 7 days. She denies other important antecedents.

On physical examination; vital signs blood pressure (BP): 130/83mmhg, mean arterial pressure (MAP): 93mmHG, heart rate (HR): 80 beats per minute, respiratory rate (RR): 19 breaths per minute. Patient in bad clinical conditions, afebrile, hydrated, eupneic, with accentuated icteric tinge in skin and mucous membranes, capillary filling <2 seconds.

She has normoexpandable symmetrical thorax, audible vesicular murmur in both lung fields without aggregates, rhythmic heart sounds without murmurs, turgid breasts with colostral secretion. Abdomen with hydro-aerial sounds present and normal in all quadrants, globular at the expense of the pregnant uterus, hepatomegaly 4cm below the costal rim, splenomegaly 2cm exceeding the costal rim, pregnant uterus, single fetus longitudinal cephalic left dorsum, fetal heart rate: 150 beats per minute, uterine height 30cm. On vaginal palpation, cervix posterior long, soft, closed without transvaginal leakage. Symmetrical extremities without edema. Alert and oriented to person, place, time, and event.

The patient presented a complete blood count (CBC), Hemoglobin (HB) 6,7gr/dl, hematocrit (HCT): 22%, White blood cells (WBC): 8.800 mm3, segmented 62%, platelets (PLT): 130.000 mm3, HIV negative, VDRL not reactive, blood type Rh O+. The patient is admitted with the diagnoses of:

- Simple preterm pregnancy of 34.5 weeks,
- Thalassemia major
- Chronic arterial hypertension
- Severe anemia,

with the plan of hospitalization, maternal fetal monitoring, pulmonary maturation inducers. In view of improvement and in stable clinical conditions with HB: 10.5gr/dl, the patient is discharged.

Subsequently the patient came back with the following labs: HB: 6 g/dl, HCT: 20%, PLT: 90,000 mm3, PT (prothrombin time): 13.2 TPT (thromboplastin time): 39.6 and jaundice. Due to the results obtained in the laboratories, it was decided to terminate the pregnancy by cesarean section due to high risk of maternal complications.

Prior to and during the surgery, the patient received a total of 7 globular concentrates, obteining a live female newborn, weighing 1700gr, size 38cm, APGAR of 8 points at the first minute and 9 points at 5 minutes, normal delivery. Then, bilateral salpingectomy was performed, showing citrine liquid with icteric dye of approximately 300cc and a large spleen, hemostasis was verified and a right intrauterine drain was left, culminating without complications.

In the immediate postoperative period the patient did not evolve satisfactorily, reporting HB: 4.20 grams/dl, HTO: 14%, PLT: 109,000 mm3. The generalized weakness, dizziness and headache were accentuated with icteric staining of the skin and mucous membranes, so a unit of globular concentrate was performed. Then blood chemistry was requested and showed creatinine: 1 mg/dl, uric acid: 8.80 mg/dl, aspartate amino transferase (AST): 227 U/I (0 - 32), alanine amino transferase (ALT) 140 U/I, total bilirubin: 8.46 mg/dl, direct bilirubin: 7.49 mg/dl, indirect bilirubin: 0.98 mg/dl, lactate dehydrogenase (LDH) 512 U/L, alkaline phosphatase 410 U/L.

She was evaluated by hematology who recommended to continue with globular concentrates and transfusion until reaching the minimum of 7g/dl of HB, treatment that could not be completed due to the report of 4+ crossmatching blood test. After that, an interconsultation with surgery was made to evaluate the possibility of splenectomy, a procedure that, due to the hemodynamic status of the patient was performed as an emergency through exploratory laparotomy, finding:

- Enlarged Spleen of Approx. 30cm in Size.
- Splenic Hilum with 3 Vascular Diamentum within Normal Limits.
- The Rest of the Intra-Abdominal Organs were within normal Limits.

Therefore she was evaluated by the ICU-A service who reported alveolar hemorrhage and hematuria. On physical examination BP: 60/40 mmHg HR: 130 RR: 38 febrile with 39 degrees, anisocoria, right pupil 6cm and left pupil 2cm reactive, generalized mucosal skin pallor, hemorrhage through the oral cavity, poor respiratory perfusion, use of accessory muscles, connected to mechanical ventilation, tachycardic heart sounds without murmurs. Ventilatory parameters are adjusted FIO2 60% RR30. The patient died the same day due to hypovolemic shock and disseminated intravascular coagulation (DIC).

Discussion

The major cause of death in thalassemics is iron overload. The life expectancy of a person will depend on the type of disease and the quality of treatment. In cases with beta thalassemia minor, life expectancy is normal; in those with intermediate thalassemia there may be some variation and in those with beta thalassemia major there is a lower probability of life expectancy. Failure due to heart failure has been reported in these cases between 20 and 30 years of age, resulting in death. There are also cases of mortality in adolescence or early youth [1,2].

In the same order and direction it is uncommon for Thalassemia major to represent a problem for the obstetrician, since the iron overload associated with this pathology usually causes lack of pubertal growth and delayed sexual development. These patients are often infertile and anovulatory, and present with hypogonadotrophic hypogonadism due to hemosiderin deposition in the hypothalamus and pituitary. Iron deposited in the anterior pituitary is the main cause of alterations in sexual maturity; reported in 50% of the affected individuals with this condition [4,5].

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Thalassemia major is not only dangerous for the fetus, which generally dies, but also for the mother, who may suffer significant sequelae [1]. Pregnancy is a state of hypercoagulability with increased platelet activity and consumption which, when combined with the hemodilution that occurs, leads to a slightly lower platelet count compared to a non-pregnant woman. This mild

thrombocytopenia is usually asymptomatic and is not manifest in all seasons. Profound changes in hemostasis have been observed in patients with B thalassemia major, intermediate or minor, the presence of a higher than normal incidence in patients with thalassemia intermedia, and the existence of prothrombotic hemostatic abnormalities in most patients, have led to the recognition of the existence of a hypercoagulable state in these patients [4,5,6].

Thrombosis is typically a complicated episode with temporary activation of hemostasis. These thrombi may contribute to pulmonary hypertension, low lung capacity, hypoxemia, and diffusion defects associated with right pulmonary failure and to the high frequency of cerebral ischemic brain lesions associated with asymptomatic brain damage detected on magnetic resonance imaging. A wide range of laboratory tests have provided strong evidence for the existence of a chronic hypercoagulable state in thalassemia, particularly in splenectomized patients [1,4]. However, in this case, the patient was not splenectomized at an early age so there were no thrombus-related complications. This agrees with what was reported by Gregorio Evans M (2003) in the presentation of a case of thalassemic anemia in pregnancy, explaining the thrombosis of lower extremities that required amputations, and the encephalic vascular accident that sequels the patient and that patient was splenectomized in infancy.

In pregnancy, severe anemias with hemoglobin below 6 g/dL have been associated with reduced amniotic fluid volume, fetal cerebral vasodilatation, abnormal heart rate patterns, prematurity, spontaneous abortion, low birth weight and fetal death. Thalassemia major is not only dangerous for the fetus, which usually dies, but also for the mother, who can be severely affected [4,6]. The patient in question, despite the scientific evidence of the risk of fetal death, did not present complications, however, the mother was left with sequelae that cost her life some time after delivery, due to hypovolemic shock consistent with the pathophysiology she presented.

Pregnancies have been described in this group of patients with fetal loss, which gives us evidence that the diagnosis of thalassemic anemia does imply a risk of stillbirth as a result, because pregnancy can precipitate heart failure [4].

Conclusion

Pregnant women with thalassemia anemia diagnosis present a high risk of stillbirth and complications for the mother, a risk that is not only supported by the literature but also by the reported case. The state of hypercoagulability, alloimmunization, and iron overload represent complications that explain the risk of death, thus responding to the objective of the study. Given the limited number of cases presented in gyneco-obstetric clinical practice, understanding this unusual situation is crucial to improve therapeutic approaches, thereby increasing the morbidity of both the mother and fetus; which could involve early termination of pregnancy to safeguard the life of the fetus or reducing the pregnancy rate in these patients through contraceptive methods.

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