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Incidental finding of mixed hemoglobinopathy in pregnant woman - Case report

Achado incidental de hemoglobinopatia mista em uma gestante - Relato de caso

Hallazgo incidental de hemoglobinopatía mixta en una embarazada - Reporte de caso

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Diego Fernando Lopez Muñoz
ORCID: https://orcid.org/0000-0001-6156-1619
Unidad Central del Valle del Cauca, Colombia
E-mail: dflopez@uceva.edu.co
Karol Vanessa Gutierrez-Bonilla
ORCID: https://orcid.org/0009-0000-0229-6018
Unidad Central del Valle del Cauca, Colombia
E-mail: karol.gutierrez01@uceva.edu.co
Juan Camilo Castaño-Ospina
ORCID: https://orcid.org/0009-0001-3130-2613
Unidad Central del Valle del Cauca, Colombia
E-mail: juan.castano03@uceva.edu.co
Cristhian Camilo Velandia-Mosquera
ORCID: https://orcid.org/0009-0007-1074-1055
Unidad Central del Valle del Cauca, Colombia
E-mail: cristhian.velandia01@uceva.edu.co
Valentina Taborda-Ipus
ORCID: https://orcid.org/0009-0002-0578-7925
Unidad Central del Valle del Cauca, Colombia
E-mail: valentina.taborda01@uceva.edu.co
Caterine Eliseth Montezuma-Sanchez
ORCID: https://orcid.org/0009-0007-5339-2289
Universidad Libre, Cali, Colombia
E-mail: caterine.montezuma01@gmail.com
Juan Andrés Galeano-Ruiz
ORCID: https://orcid.org/0009-0004-3851-029X
Unidad Central del Valle del Cauca, Colombia
E-mail: juan.galeano02@uceva.edu.co

Abstract
Microcytic and hypochromic anemic syndromes, beta-thalassemia type are usually underdiagnosed. Due to the similarity of clinical manifestations, the need for complementary studies, and the lack of clinical suspicion. This hinders their timely intervention. This study aimed to show a clinical case of an incidental finding of mixed hemoglobinopathy in a pregnant woman. we present the case of a 25-year-old primigravida patient hospitalized in the context of sepsis of urinary origin, associated with encapsulated bacteria. The hemogram reports low hemoglobin and refractoriness to iron treatment. Ferrokinetic studies were normal, the blood smear revealed a varied poikilocytosis, it was suggested to perform hemoglobin electrophoresis, which reported a mixed hemoglobinopathy as an incidental finding.
Keywords: Beta-thalassemia; Hemoglobin S; Hemoglobinopathies; Electrophoresis; Pregnant woman.

Resumo
As síndromes anêmicas microcíticas e hipocrômicas do tipo beta-talassemia são geralmente subdiagnosticadas. Devido à similaridade das manifestações clínicas, à necessidade de estudos complementares e à falta de suspeita clínica. Isso dificulta a intervenção oportuna. Este estudo teve como objetivo apresentar um caso clínico de achado incidental de hemoglobinopatia mista em gestante. Apresentamos o caso de uma paciente primigesta de 25 anos, hospitalizada em um contexto de sepse de origem urinária, associada a bactérias encapsuladas. O hemograma relatou baixa hemoglobina e refratariedade ao tratamento com ferro. Os estudos ferrocinéticos estavam normais, o esfregaço de sangue revelou uma poiquilocitose variada e foi sugerida a realização de eletroforese de hemoglobina, que relatou uma hemoglobinopatia mista como achado incidental.
Palavras-chave: Beta talassemia; Hemoglobina S; Hemoglobinopatias; Eletroforese; Gestante.

Resumen
Los síndromes anémicos microcíticos e hipocrómicos tipo beta-talasemia suelen estar infra diagnosticados. Por similitud de manifestaciones clínicas, necesidad de estudios complementarios y falta de sospecha clínica. Esto dificulta su intervención oportuna. Este estudio tuvo como objetivo mostrar un caso clínico de hallazgo incidental de

hemoglobinopatía mixta en una mujer embarazada. Presentamos el caso de una paciente primigravida de 25 años hospitalizada en contexto de sepsis de origen urinario, asociada a bacterias encapsuladas. El hemograma reporta hemoglobina baja y refractariedad al tratamiento con hierro. Los estudios ferro cinéticos fueron normales, el frotis sanguíneo reveló una poiquilocitosis variada, se sugirió realizar electroforesis de hemoglobina, que informó una hemoglobinopatía mixta como hallazgo incidental.
Keywords: Beta talasemia; Hemoglobina S; Hemoglobinopatías; Electroforesis; Mujer embarazada.

1. Introduction

Hemoglobin is a globular protein composed of four subunits, each containing a polypeptide chain called globin, of which there are two types, alpha (α) and beta (β). A prosthetic group, called the heme, is composed of a protoporphyrin IX molecule with an iron atom (Fe2+) in the center. Any change in the synthesis of the molecule, either quantitative or qualitative, is associated with hemoglobinopathies.

Sickle cell syndrome HbS/β-thalassemia is a complex hereditary haemoglobinopathy that combines the presence of hemoglobin S (HbS) and beta-thalassemia (β-thalassemia). This in turn is due to more than 200 different mutations in the beta-globin gene (HBB), which can result in a total absence of β-chains (β0-thalassaemia) or partial synthesis (β-thalassemia). On the other hand, HbS is caused by a point mutation in codon 6 of this same beta-globin gene that results in the substitution of glutamic acid for valine (GAG > VAL). This mutation causes the red blood cells to adopt an abnormal 'crescent' shape.

In countries with Afro-descendant populations, such as Colombia, several β-thalassemia mutations have been reported, mainly in the HBB gene. The distribution of these mutations seems to be related to the ethnic composition and historical migratory flows in Latin America. (Vafaei et al., 2022; Carvajal-Alzate, 2019; Gasparini et al., 2016)

The importance of early detection of mixed hemoglobinopathies in pregnant women is highlighted. This allows for appropriate management and prevention of complications. It also contributes to knowledge about genetic variability in specific populations and its impact on maternal and child health.

This study aimed to show a clinical case of an incidental finding of mixed hemoglobinopathy in a pregnant woman.

2. Methodology

The study design is descriptive, qualitative, and case report type (Pereira et al., 2018; Toassi & Petry, 2021), focused on a pregnant woman diagnosed incidentally with mixed hemoglobinopathy.

An informed consent was obtained from the patient for disclosure of her clinical information and the use of images in scientific publications. This study was approved by the ethics committee, ensuring adherence to ethical guidelines, including the Declaration of Helsinki. Data collection was carried out through a retrospective review of the patient's medical history, which included the following aspects: demographic data (age, medical and obstetric history), initial symptoms that led to hematological evaluation, and laboratory results, which included hematological tests, hemoglobin electrophoresis, and other relevant analyses to identify the specific type of hemoglobinopathy. The results were analyzed descriptively to conclude appropriate management and the potential risks for mixed hemoglobinopathy in this context (Kasparek et al., 2021).

3. Case Presentation

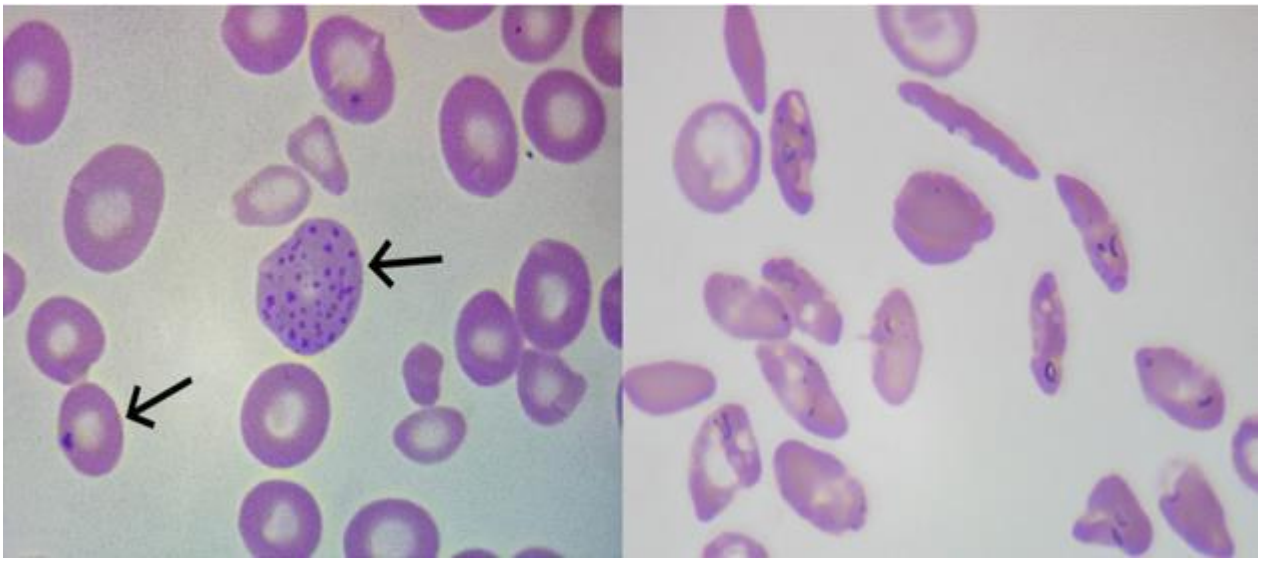
History: 25-year-old primigravida, G1P0, 20 weeks pregnant, 6 days after early ultrasound, consulted for a clinical picture of fever of 38.7°C, associated with pelvic pain, frontal headache, and chills. On physical examination vital signs: BP: 80/50 mmHg, MAP 60mmHg HR: 114 bpm, RR: 29 rpm, SPO2: 98% with FiO2 of 21%, T: 38.1°C, BMI: 22.27 kg/m2. FHR: 170 bpm. The patient was febrile, in regular general condition, with dry mucous membranes, pale conjunctiva, normal uterine

tone at the abdominal level, no uterine dynamics, no evidence of uterine sensitivity or irritability, pain on palpation of the right flank and positive ureteral stitches, at genitourinary level, no cervical changes.

Additional tests: Hemogram HGB 8 g/dL, RBC 3.4x10^6 uL, HCT 25.2%, MCV 74.1 fl, MCH 25.3 pg, MCHC 31.7 g/dL, WBC 18.54x10^3 uL, NEU 15.99 x10^3, LYMPH 1.48 x10^3, MONO 0.87 x10^3, EO 0.0 x10^3, BASO 0.03 x10^3, PLT 203 x10^3. Peripheral blood smear: Red blood cells: Anisocytosis (microcytes 2+), hypochromia 2+, polychromasia +, anisopoikilocytosis, dianocytes ++ and few sickle cells (Figure 1).

Peripheral blood smear. and Acid electrophoresis of hemoglobin. Are now presented:

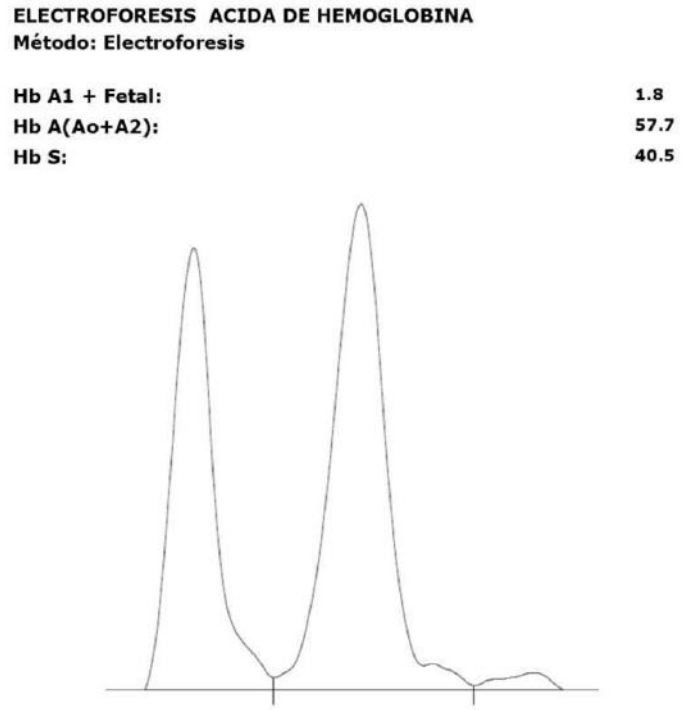
Figure 1 - Peripheral blood smear. Wright's staining.



Description of Figure 1. of the red series marked by poikilocytosis with presence of polychroma, basophilic stippling and sickle cells. Objective 100XC. Motic Images Plus Software. Source: Own Authorship.

Hemoglobin electrophoresis: Hb A1 + Fetal pattern: 1.8%, Hb A (A0+A2): 57.7%, Hb S: 40.5%. (Figure 2) Corresponding to beta-thalassemia minor, with sickle cell trait S. Urine culture: isolation of Klebsiella *pneumoniae* >100,000 CFU/mL. Multisensitive antibiogram.

Figure 2 - Acid electrophoresis of hemoglobin.



Description of Figure 2. Interpretation corresponding to beta-thalassemia minor, with sickle cell trait S. Source: Own source.

Obstetric ultrasound: single fetus in variable situation, placenta anterior, normal amniotic fluid (AF), fetal growth percentile 25-50 for gestational age, without morphostructural alterations.

Renal ultrasound: right kidney with physiological pyelocaliceal dilatation, no evidence of lithiasis.

3.1 Evolution

A diagnosis of severe sepsis of urinary origin was made and the patient was admitted to the obstetric intensive care unit where antibiotic treatment was optimized with Cefuroxime 750 mg IV every 8 hours, support measures, including fluid resuscitation and vasoactive support with Norepinephrine. Given off-target hemoglobin levels and an acute hemolytic pattern due to an infectious process, a transfusion of 2 units of compatible red blood cells and thromboprophylaxis with low molecular weight heparin was performed, given the high thromboembolic risk. She had an adequate clinical evolution with the treatment given, and she was finally discharged with antimicrobial prophylaxis with cephalexin until delivery, Folic Acid 5 mg per day, and multidisciplinary management at high obstetric risk, consultation with hematology, and genetic counseling.

4. Discussion and Final Considerations

Sickle cell beta-thalassemia is a rare recessive genetic disorder that combines hemoglobin S and a partial reduction in beta globin chain synthesis. Clinically, it is characterized by a mild form of sickle cell disease, with symptoms less severe than homozygous sickle cell disease. Diagnosis is based on clinical and hematological findings, with predominant HbS, low HbA and elevated HbA2 and fetal Hb (Sahli et., 2013).

It is worth mentioning that patients with this type of blood dyscrasia are at increased risk of infections by encapsulated bacteria, due to splenic deficiency, alterations in opsonization/phagocytosis, and decreased antibodies.

This type of pregnant woman requires specialized management, frequent check-ups, and fetal monitoring to detect obstetric complications that can increase mortality if not properly managed. Taking precautions reduces the risk of pregnancy complications. Glycaemia monitoring from week 28 every 2 weeks and constant blood pressure control are recommended. Warning signs are vaginal bleeding, abdominal or back pain, requiring immediate evaluation. Placental abruption is an emergency that requires prompt diagnosis and treatment to prevent serious complications and save the life of the mother and child. (Luk'yanenko et al., 2017; Saliva et al., 2016).

Scientific evidence highlights the need to strengthen neonatal screening and genetic counseling programs, which allow early diagnosis, prevention of complications, and improved prognosis of inherited diseases and metabolic disorders. This has a positive individual and public health impact, improving quality of life and reducing healthcare costs, especially in ethnically diverse and resource-limited countries (Bender et al., 2020).

According to Pate and colleagues, a study of pregnant women highlights a significantly higher risk of maternal and infant mortality in pregnancies complicated by haemoglobinopathies. These disorders lead to an increased incidence of adverse outcomes, including previous miscarriage, intrauterine growth restriction (IUGR), postpartum haemorrhage (PPH) and anaemia in affected pregnant women. Neonatal outcomes are also significantly worse, with a higher prevalence of anaemia and low birth weight observed in all types of haemoglobinopathy-related pregnancies. In addition, more severe complications such as hepatic encephalopathy, sepsis, jaundice, perinatal death and fetal acidosis are often seen in pregnancies complicated by sickle cell disease. These findings highlight the critical importance of early diagnosis, vigilant monitoring and tailored management strategies to optimise maternal and fetal health in this high-risk population (Patel 2024).

In their review, Moukalled et al. highlighted the significant risks associated with pregnancy in women with underlying hemoglobinopathies. In sickle cell disease (SCD), perinatal complications are more common, including spontaneous abortion, stillbirth, intrauterine growth restriction, preterm delivery, and low birth weight. These outcomes are largely due to uteroplacental insufficiency caused by placental vascular occlusion, resulting in fetal hypoxia. To optimize maternal and fetal outcomes, management must be multidisciplinary, involving hematologists and high-risk obstetricians. This approach includes prenatal planning, genetic counseling, and careful monitoring of hematologic status. Early intervention is essential to minimize risks and improve the prognosis for both mother and child (Moukalled 2022).

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