SICKLE CELL TRAIT: A CAUSE OF ABDOMINAL PAIN AND PULMONARY EMBOLISM

RASGO DREPANOCÍTICO: UNA CAUSA DE DOLOR ABDOMINAL Y TROMBOEMBOLISMO PULMONAR.

O TRAÇO DREPANOCÍTICO: UMA CAUSA DE DOR ABDOMINAL E TROMBOEMBOLISMO PULMONAR

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El rasgo drepanocítico es una entidad muy poco frecuente en nuestro medio, por lo cual su sospecha diagnóstica es baja. Generalmente los pacientes con dicho trastorno desarrollan sus vidas siendo asintomáticos. Pero existen algunas circunstancias, como la exposición a situaciones de mayor consumo de oxígeno (como actividad física vigorosa) o escenarios de menor concentración de oxígeno (como ascenso a grandes alturas) que pueden actuar como gatillos para el desarrollo de sus manifestaciones clínicas. Se presenta el caso de un paciente al que se le diagnosticó rasgo drepanocítico y cuyas expresiones clínicas comenzaron posteriormente al ascenso a grandes alturas sobre el nivel del mar.

Conceptos clave:

¿Qué se sabe sobre el tema?

- Se estima que existen cerca de 300 millones de personas a nivel mundial con rasgo drepanocítico.
- El rasgo drepanocítico es una rara enfermedad en Argentina, siendo su sospecha diagnóstica muy baja en nuestro medio.
- Los pacientes con rasgo drepanocítico permanecen generalmente asintomáticos durante toda su vida, presentando rara vez crisis vaso-oclusivas, a menos que exista exposición a condiciones extremas de hipoxia o acidosis.

¿Qué aporta este trabajo?

- Se presenta el caso de un paciente con rasgo drepanocito, cuyo diagnóstico se vio retrasado debido a la baja sospecha diagnóstica en nuestro medio.
- El paciente presentado, permaneció asintomático durante toda su vida, hasta que se expuso a elevada altitud sobre el nivel del mar.
- La presentación conjunta de infarto esplénico y tromboembolismo pulmonar se encuentra poco descripta en esta patología.
- Se destaca la importancia de tener en cuenta esta patología, para evitar complicaciones asociadas a la misma como lo son la enfermedad tromboembólica o infarto esplénico que pueden llegar a comprometer la vida de los pacientes.

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Resumen:

Introducción: El rasgo drepanocítico es una rara enfermedad en Argentina. Se trata de un trastorno heterocigoto en el cual los individuos portan la mutación del gen de Hemoglobina S (HbS) en uno de los dos alelos de los genes de beta-globina, siendo el otro normal. Estos pacientes no presentan las manifestaciones clínicas típicas de la anemia de células falciformes. Sin embargo, bajo ciertas circunstancias, pueden desarrollarse algunas de las manifestaciones propias de la enfermedad.
Métodos: Hombre de 39 años que se presentó con un cuadro de dolor abdominal persistente luego de un viaje a una ciudad ubicada a elevada altitud sobre el nivel del mar. Fue sometido a procedimiento de laparotomía sin arribar a un diagnóstico certero. Posteriormente a ello, el paciente desarrolló un cuadro de infarto esplénico y tromboembolismo pulmonar.
Resultados: El test de sickling fue positivo y se identificó HbS en el estudio de electroforesis. En este contexto se arribó al diagnóstico de rasgo drepanocítico. Asimismo, se observó un estudio de anticoagulante lúpico fuertemente positivo.
Conclusión: La presentación de rasgo drepanocítico como dolor abdominal y tromboembolismo pulmonar en pacientes adultos luego de exposición a grandes altitudes es un diagnóstico raramente sospechado.

Palabras clave: rasgo drepanocítico; infarto del bazo; embolia pulmonar; inhibidor de coagulación del lupus.

Abstract:

Introduction: Sickle cell trait (SCT) is a rare and underdiagnosed disorder in the Argentinian population. In this condition, individuals carry the mutation of the HbS gene in one of the two beta-globin genes. In general, SCT does not present with the typical manifestations of sickle cell anemia. However, under certain circumstances, some clinical characteristics of the disease may develop.
Methods: We discussed the case of a 39-Year old man who presented with persistent abdominal pain of unknown origin after traveling to a high-altitude place. He underwent laparotomy without a definite diagnosis. After that, the patient developed signs of splenic infarction and pulmonary thromboembolism that were confirmed by computed tomography.
Results: A sickling test was positive, and a hemoglobin electrophoresis revealed an abnormal fraction at the HbS level. In this context a diagnosis of SCT was made. Additional, tests revealed a strongly positive lupus anticoagulant.
Conclusion: SCT presentation as abdominal pain and thromboembolic disease in adult patients after exposure to high altitudes is a rarely suspected diagnosis.

Keywords: sickle cell trait; splenic infarction; pulmonary embolism; lupus coagulation inhibitor.

Resumo

Introdução: O traço drepanocítico é uma doença pouco frequente na Argentina. Trata-se de um transtorno heterozigoto no qual os indivíduos carregam a mutação do gene da Hemoglobina S (HbS) em um dos dois alelos dos genes da beta-globina, sendo o outro normal. Estes pacientes não apresentam as manifestações clínicas típicas da anemia falciforme. No entanto, em determinadas circunstâncias, eles podem desenvolver algumas das manifestações da doença.
Métodos: Apresentamos o caso de um homem de 39 anos de idade, que mostrava um quadro de dor abdominal persistente depois de uma viagem a uma cidade situada a grande altitude acima do nível do mar. Ele foi submetido a procedimento de laparotomia sem chegar a um diagnóstico preciso. Posteriormente, o paciente desenvolveu um quadro de infarto esplênico e tromboembolismo pulmonar.
Resultados: O teste de sickling foi positivo e o gene HbS foi identificado no exame de eletroforese. Neste contexto estabeleceu-se o diagnóstico de traço drepanocítico. Analisou-se também um exame de anticoagulante lúpico fortemente positivo efetuado no mesmo paciente.
Conclusão: A manifestação do traço drepanocítico em forma de dor abdominal e tromboembolismo pulmonar em pacientes adultos depois de exposição a grandes altitudes é um diagnóstico raramente suspeito.

Palavras-chave: traço falciforme; infarto do baço; embolia pulmonar; inibidor de coagulação do lúpus.

Introduction

Sickle cell disorder (SCD) is an autosomal recessive disorder that affects the beta-globin chain synthesis of hemoglobin, thus producing hemoglobin S (HbS). This abnormality causes a decrease in the erythrocyte membrane elasticity and deformation capability leading to microvascular occlusion and hemolysis.[1] Its prevalence is higher in the African and Indian population, whereas it is unusual in the rest of the world.[2]

SCD refers to a group of pathologies characterized by a "sickle mutation" of the beta-globin chain which can configure different spectra of the disorder depending on the characteristics of the other globin chain (either normal or mutated). The homozygous variant is called sickle cell disease. Within the remaining spectra, the sickle cell trait (SCT), in which individuals carry the mutation of the HbS gene in one of the two beta-globin genes, being the other normal.[3] These patients usually remain asymptomatic, and they rarely experience vaso-occlusive crises unless they are exposed to certain conditions.[4]

We discussed the case of a patient with SCT that presented with abdominal pain and pulmonary embolism.

Methods

A 39-Year old man with abdominal pain that had started two weeks before was admitted to our hospital due to an episode of upper gastrointestinal bleeding and acute pulmonary infiltrates. The patient had started experiencing abdominal pain two weeks ago, after traveling to the city of La Quiaca, Argentina (3,442 m above the sea level). Upon arrival to that city, he experienced intense diffuse abdominal pain, nausea and vomiting. He had no fever, diarrhea, or other relevant symptoms.

The patient worked in the transportation sector in Córdoba, Argentina. He had a history of allergic rhinitis, and he did not report drug allergies. He had undergone a rhinoplasty and a hand orthopedic surgery. He did not smoke tobacco, drink alcohol, or use illicit drugs. His brother has a history of deep vein thrombosis.

Initially he was evaluated in a hospital of La Quiaca. Due the persistence of abdominal pain and the absence of significant findings in a thoraco-abdominal computed tomography scans (CT), an exploratory laparotomy was carried out. The procedure revealed scarce free abdominal fluid and slight swelling of the appendix, whereby an appendectomy was performed. The patient received high doses of non-steroidal anti-inflammatory drugs (NSAIDs) and due to persistent abdominal pain in postoperative period it was decided to transfer him to a hospital in his native city.

Upon admission to the hometown hospital, the patient showed high inflammation parameters, hemoglobin of 8.6 g/dL, and a new thoraco-abdominal CT revealed a slight splenomegaly with infarction signs and pulmonary infiltrate in right lung base. Broad-spectrum antimicrobial treatment was indicated (with vancomycin, piperacillin-tazobactam and amikacin), without microbial isolation. On the third hospital day, he had an episode of melena with hemodynamic decompensation, for which reason he is referred to our hospital.

Upon admission to our hospital, the patient had mild dyspnea at rest, pain in the upper right half of abdomen and right-sided pleuritic chest pain. On examination the patient had tachycardia and orthostatic hypotension, the temperature was 38.9°C, and the oxygen saturation 85% while he was breathing ambient air. Abdominal examination revealed pain on upper hemiabdomen region without guarding. Thorax examination revealed bilateral crackles. The remainder of the examination was normal.

Laboratory analysis showed an hemoglobin of 6.8 g/dL, white blood cells of 18,700/uL (79% segmented neutrophils), platelets count of 462,000/uL, creatinine of 0.99 mg/L, total bilirubin 0.36 mg/dL, aspartate aminotransferase 60 IU/L (NV<37 U/L), alanine aminotransferase 77 IU/L (NV<41 U/L), gamma-glutamyl transferase 59 U/L (NV<49 U/L), alkaline phosphatase 64 UI/L (NV: 40-130 U/L), lactate dehydrogenase 644 UI/L (NV: 236-460 U/L), C-reactive protein 9.48 mg/dL (NR: <0.6 mg/dL), and procalcitonin 0.13 ng/mL (NR: <0.55 ng/mL). Urinary sediment showed no alterations. HIV, Hepatitis B virus, Hepatitis C virus and VDRL serology were negative as well as blood culture. An upper gastrointestinal endoscopy was performed, where two duodenal Forrest III ulcers were observed. Treatment with proton-pump inhibitors was initiated. The patient refused to receive transfusion of blood products, so fluid therapy, intravenous iron and erythropoietin were administered.

A CT pulmonary angiography was performed, that showed pulmonary infiltrates with "reversed halo sign" and bilateral thromboembolism in the lower lung lobes. A Contrast-enhanced abdominal CT revealed splenomegaly with splenic infarction without evidence of artery obstruction. A transthoracic echocardiography was normal.

The patient was evaluated by a multidisciplinary team of specialists in vascular medicine, internal medicine, hematology and gastroenterology. Due to the absence of active bleeding with low risk of recurrence, and the diagnosis of thromboembolic disease, it was decided together with the patient to start anticoagulant therapy. Low dose enoxaparin (0.5 mg/kg/daily) was initiated, and progressively increased to 1 mg/kg twice-daily.

Due to the thromboembolism associated with abdominal pain and splenic infarction, which occurred after visiting a high-altitude place, SCD was suspected. A Sickling test was positive, and the hemoglobin electrophoresis revealed an abnormal fraction at HbS level, with normal hemoglobin A2 (HbA2). In this context a diagnosis of SCT was made. Additional tests revealed a strongly positive lupus anticoagulant (tested on two occasions within 8 weeks), Antinuclear antibodies, extractable nuclear antigens, IgG and IgM anticardiolipin antibodies, and anti-beta 2 glycoprotein antibodies were negative.

The patient had good clinical progress, without further episodes of clinically-evident gastrointestinal bleeding, and improved the abdominal pain. The hemoglobin values increased gradually to normal values and the patient was suggested to continue anticoagulant therapy indefinitely. Following the diagnosis of SCT, a family health history evaluation was performed, which showed the presence of SCT in the patient's father.

Discussion

SCT is a rare disorder in our population, being usually underdiagnosed. In America, SCD screening programs are implemented only in the United States, Brazil and Costa Rica.[5] There are different methods for the diagnosis of SCD, among which the most relevant are the sickling test and the identification of HbS by electrophoresis. Sickling tests are based on the ability of HbS to form deoxygenated HbS polymers at low oxygen pressures, resulting in erythrocyte deformation (sickle cell), which can be observed under a light microscope. The appearance of sickle cells indicates the presence of HbS. The electrophoresis allows for the differentiation of HbS from the rest of hemoglobines. In adults, the method of choice for HbS determination is High Performance Liquid Chromatography (HPLC).[6]

In general, SCT does not present with the typical manifestations of sickle cell anemia. However, under certain circumstances, some clinical characteristics of the disease may develop.[4,7] These occur as a result of increased adhesion of sickled cells to the vascular endothelium, which triggers hemostatic mechanisms and ischemic tissue damage due to microvascular occlusion.[1] The potential triggers are infections, hypoxia, acidosis, dehydration, physiologically stressful situations, alcohol intake, pregnancy and low temperatures.[8] Similarly, there have been reports of hypoxia-induced sickle cell crises caused by exposure to high altitudes.[9,10] When a sickle cell crisis occurs, the organs most often involved are the brain, the kidneys, the bones, the spleen, the retina, the lungs and the male external genitalia.[7]

Abdominal pain crises are one of most common reasons for seeking medical attention among SCD patients, occurring in up to 50% of them. Its clinical signs may be very different, ranging from nonspecific discomfort to severe life-threatening manifestations. Often, patients undergo surgical procedures before a SCD diagnosis is made.[8,11] Splenic infarction is a very frequent cause of abdominal pain in these patients, and there have been cases reported in people who ascended over 2,300 meters above the sea level.[12] Likewise, reports of splenic infarction at altitudes below 1,500 m in patients who generally present other conditions that exacerbate hypoxia or adaptation to this.[13] Treatment of a painful vaso-occlusive crisis is generally supportive and consists of pain medication, hydration and rest.

Sickle cell disease has been associated with an increased risk of venous thromboembolism compared with the normal population.[4,11,14] To a lesser extent than SCD, SCT patients have also been associated with an increased risk of pulmonary embolism, but not of deep vein thrombosis.[1] HbS polymerization could cause a cell dehydration which added to its repeated conformational changes, would lead to a rigid

erythrocyte membranes with loss of phospholipid asymmetry and externalization of phosphatidylserine.

These alterations would cause vasoconstriction, activation of phagocytosis and the coagulation cascade.[1,4,7,14] In addition, structural changes in red blood cell membrane have been associated with the development of antiphospholipid antibodies, mainly targeted to phosphatidylserine and lupus anticoagulant, showing higher titers in patients with the homozygous variant.[7,14] The treatment for acute thromboembolic disease in SCD patients is anticoagulation, and should be based on the same clinical guidelines established for the general population. Specific clinical trials for the treatment of venous thromboembolism in SCD patients have not been yet developed.[15]

SCT presentation as abdominal pain and thromboembolic disease in adult patients after exposure to high altitudes is a rarely suspected diagnosis. We highlight the importance of considering this disease when there is no certain diagnosis in patients with the clinical manifestations previously described.

Limitaciones de responsabilidad
La responsabilidad del trabajo es sólo de los autores

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Participación de los autores
Todos los autores hemos participado en la concepción del diseño, recolección de la información y elaboración del manuscrito, haciéndose públicamente responsables de su contenido y aprobando su versión final.

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