CLINICAL CASE: FATAL MULTI-ORGAN LEFT VENTRICULAR EMBOLISM IN A PATIENT WITH BETA THALASSEMIA MAJOR UNDERGOING ENDOVASCULAR TREATMENT FOR STENOSIS OF THE SUB-RENAL ABDOMINAL AORTA

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ABSTRACT

Introduction*: Beta thalassemia major is a hereditary anemia secondary to deficient production of the beta-globins in structurally normal hemoglobin, with a consequent precocious destruction of red globules present in the circulation. Coagulation and cardiac complications due to the accumulation of iron are the main causes of death in these patients.*

Clinical case: *The authors present a case of cardiac iron overload complicated by fatal multi-organ embolism due to a left ventricular thrombus in a beta-thalassemia major patient.*

Discussion*: The presence of chronic hypercoagulability related to pro-thrombotic anomalies in beta-thalassemia major patients may be complicated by thrombolytic embolism events. On the basis of our experience, we believe that to prevent rapid deterioration of the patient to fatal multi-organ embolism secondary to thrombolytic detachment it's advisable to perform systemic thrombolysis rather than surgery for a single occlusion which precludes the use of thrombolytic agents.*

Key words*: beta-thalassemia; echocardiography; thrombophilia, multi-organ failure, ferrochelate treatment.*

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Introduction

Beta thalassemia major is a hereditary anemia secondary to deficient production of the beta-globins in structurally normal hemoglobin, with a consequent precocious destruction of red globules present in the circulation[1]. The clinical picture is characterized by severe anemia, associated with both ineffective erythropoiesis and hemolysis, splenomegaly, bone modifications secondary to erythopoietic expansion and iron overload[1]. The latter accumulates in numerous parenchyma (including the heart, liver, and endocrine glands), and is the major cause of the high rate of morbidity and mortality in this disease. Cardiac complications from the accumulation of iron are the leading cause of death in these patients[2,3]. In addition, the higher than normal incidence of thrombus-embolic events and the presence of pro-thrombus anomalies of hemostasis have led to the recognition of the existence of a chronic state of hypercoagulability in thalassemia patients[4].

Clinical Case

The study was conducted on a group of 20 In June 2015 a 56-year-old man came to the emergency room of our hospital experiencing shortness of breath, palpitations, and chest pain for two days. The patient history revealed insulin-dependent diabetes mellitus, arterial hypertension being treated with olmesartan 40mg 1cp/day, and beta thalassemia major (for which he underwent a splenectomy at age 25). The patient had been transfused regularly since age 6, with an average hemoglobin value of 10g/dl; however, the clinical documenta-

tion presented revealed reduced compliance to ferrochelate treatment. The patient was conscious in the emergency room, and well-oriented in space and time (GCS 15). A chest exam revealed a reduced vesicular murmur in all pulmonary fields during breathing, and Sp02 97% in ambient air. The ECG revealed sinus rhythm with widespread anomalies of the ventricular repolarization. The ECG also revealed normal dimensions of the left ventricle, mild systolic dysfunction (injection fraction 47%), with conserved diastolic function, normal arterial pulmonary pressure (27mmHg), and an absence of pericardial effusion. Myocardial necrosis enzymes were normal, as were inflammation indices.

In contrast, serum ferritin was particularly high (10,065ng/mg). A standard chest x-ray demonstrated a normal cardio-thoracic ratio. Hence, a diagnosis of moderate heart failure secondary to left ventricular systolic dysfunction was proposed, due to cardiac iron overload in a thalassemia patient. The patient was then admitted to the Cardiology department of our hospital, and on the second day the patient complained of a sudden and intense pain in the iliac fossa and the left side. An ultrasound and CT of the abdomen were performed, and revealed hepatic iron overload and hydro-abdomen. The chest CT also revealed the presence of an apical thrombus of the left ventricle that was not present on the admission ECG, and was confirmed by a new ECG immediately after the CT scan, which showed the presence of a peduncolated and mobile thrombus adhering to the apex of the left ventricle.

Anticoagulant therapy was then started by administering low molecular weight Heparin 5000, combined with Warfarin 1 cp/day, until reaching an INR value over 2, followed by oral anticoagulant alone[5,6]. About 24 hours after the thrombus episode in the left ventricle, a generalized abdominal pain suddenly appeared in the lower limbs (which were cold to the touch, and peripheral pulse was absent), and associated signs of shock. An urgent cardiac U.S. revealed a disappearance of the apical thrombus previously observed. An angio CT revealed an occlusion of sub-renal abdominal aorta with a bilateral extension at the common iliac arteries. So the patient underwent urgent percutaneous endovascular treatment with placement of an endoprosthesis. Immediately after the operation multi-organ failure occurred due to systemic embolism until the death of the patient.

Discussion

Transfusion therapy improved the patient's prognosis significantly, reducing both the hepatic-splenomegaly from extra-marrow erythropoiesis and the bone deformations due to abnormal hematopoiesis marrow. The iron overload due to the continued transfusions and increased intestinal absorption could not be completely eliminated and was the main cause of morbidity and mortality in this patient[1]. Iron deposits develop in many organs causing tissue damage and reduced capacity for catalysis of free radicals[10]. The serum ferritin level is the most used indicator to evaluate iron deposits; however, that lab value is only approximate and becomes unreliable in the presence of hepatic insufficiency[1].

Cardiac events secondary to iron overload are the main cause of death in thalassemia patients[2,3]. Heart failure due to iron overload usually develops in patients with less than optimal ferrochelate therapy and multiple endocrine pathology. The clinical course of heart failure is extremely variable, from sudden death in patients with insufficient chelating therapy to sporadic cases in which optimization of chelating therapy causes a regression of cardiomyopathy[7].

In addition, the existence of pro-thrombotic anomalies of hemostasis in these patients (low levels of C and S protein, endothelial activation and platelets, high levels of thrombin-antithrombin III), have led to recognition of the existence of a chronic state of hypercoagulability, more serious in

splenectomized subjects. This condition correlates with a higher than normal incidence of thromoembolic events, that principally consist of cerebral ischemia, deep vein thrombosis, and pulmonary embolism[4,5]. In our patient anti-coagulant prophylaxis before the operation and after anti-thrombolytic therapy as indicated in guidelines[8], was not sufficient to prevent systemic embolism. Hence, we believe that in beta-thalassemia patients it's advisable to perform short-term systemic thrombolytic therapy with a cutaneous plasminogen activator rather than surgery for a single occlusion that can preclude the use of thrombolytic agents.

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