

Case Report

Recurrent thromboembolism after splenectomy in a patient with complex hemoglobin disease: a case report



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Introduction

Some hematological diseases can benefit from splenectomy for either diagnosis or treatment. When dealing with patients with thalassemia, splenectomy is a common therapeutic option, particularly indicated when the patient has increased transfusion demand, symptomatic splenomegaly or any signs of poor health, leucopenia, and thrombocytopenia.¹ However, splenectomy can lead to thromboembolic events, particularly in splenectomized patients with thalassemia intermedia.^{1,2} Thromboembolic complications in splenectomized patients with complex hemoglobin diseases are seldom reported due to the rarity of these conditions. We therefore report a case of a woman with hemoglobin (Hb) C/β⁰-thalassemia and recurrent venous thromboembolism after splenectomy. The patient and all family members signed a consent form.

Case report

A forty-year-old woman was referred to the hematology clinic with mild microcytic hypochromic anemia and thrombocytosis. Her blood film revealed anisocytosis, poikilocytosis, microcytosis, hypochromia, stomatocytes, target cells, erythroblasts and macroplatelets (Figure 1).

She reported a family history of thalassemia and a personal history of splenectomy in 2001 due to a painful splenomegaly. She denied transfusion-dependency. In 2002, she suffered a pulmonary embolism, which recurred in 2003. In 2004, she had a deep venous thrombosis of her right lower limb. This had occurred three days after a laparoscopic tubal sterilization procedure, when warfarin was suspended for four days before surgery. All thromboembolic events were objectively confirmed.

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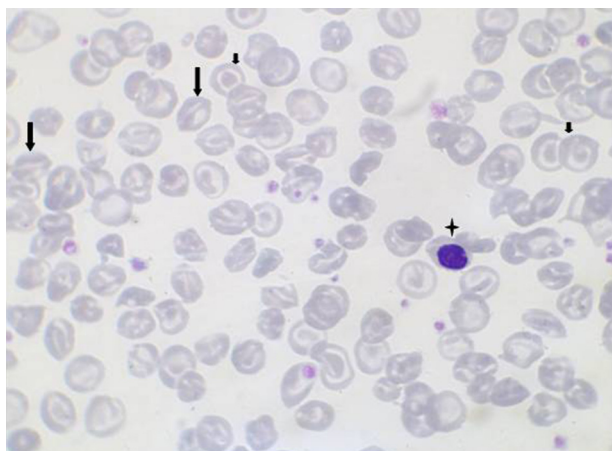


Figure 1 – Blood film of the proband. Blood film showing anisocytosis, poikilocytosis, microcytosis, hypochromia, stomatocytes (arrows), target cells (small arrows), erythroblasts (cross) and macroplatelets.

In 2005, a Doppler echocardiography revealed pulmonary hypertension with an estimated pulmonary pressure of 53 mmHg. Finally, in 2007, she was diagnosed with congestive heart failure (New York Heart Association III/IV). Thrombophilia screening was performed, revealing absence of the prothrombotic mutations: factor V Leiden and prothrombin G20210A. Antiphospholipid antibodies were also absent. She is under anticoagulation with warfarin indefinitely and since then she has not presented any thromboembolic event.

DNA analysis revealed a compound heterozygosity for Hb C (HBB: c.19G>A)/ β^0 -thalassemia (HBB: c.118C>T). A family study was carried out (Figure 2). Her father was heterozygous for HBB: c.19G>A (I-1 – Figure 2). He was asymptomatic with unremarkable blood count and film. Her mother (I-2 – Figure 2)

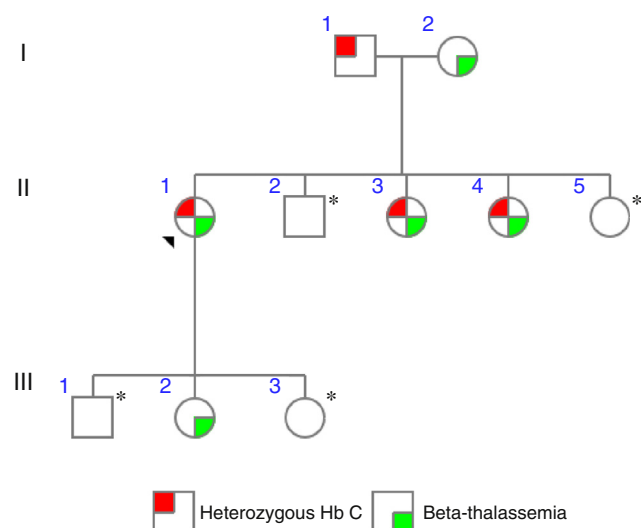


Figure 2 – Pedigree of the family. Molecular genetic analyses were performed for six family members. The arrowhead indicates the proband (II-1). * Indicates members in whom blood was not collected. The mutation causing heterozygous β^0 -thalassemia was CD39 (HBB: c.118C>T).

and one of her daughters (III-2 – Figure 2) were heterozygous for HBB:c.118C>T. Like the proband, two sisters also carried HbC/ β^0 -thalassemia (II-3 and II-4 – Figure 2). They reported transfusions only during labor, but denied splenectomy and never had a thromboembolic event. Their blood count showed mild microcytic hypochromic anemia.

Discussion

Thalassemia itself, especially β -thalassemia intermedia, is a well-known cause of a hypercoagulable state due to abnormalities involving platelets, red blood cells (RBC), endothelial cells and thrombin activation.^{3,4,5} Other hemostatic changes may include alterations in the levels of procoagulant or anticoagulant factors, and/or chronic activation of endothelial cells, or white blood cells.⁴ Splenectomy may also increase the risk of thrombosis.^{1,2}

Patients with β -thalassemia have chronic platelet activation, increased platelet aggregation, expression of CD26P and CD63 and shortened platelet life span related to enhanced consumption.⁵ Moreover, there are major RBC alterations due to the formation and precipitation of hemichromes, presence of reactive oxygen species and an increased thrombin generation related to the expression of procoagulant negatively-charged phospholipids on the RBC surface.² Indeed, loss of the hemocatheretic function of the spleen leads to an increased number of abnormal circulating RBCs, which are capable of generating thrombin.⁶ This explains why the lack of regular transfusions increases the risk of thrombosis.⁵

The patient reported herein had three thromboembolic events, two unprovoked pulmonary embolisms and a provoked deep venous thrombosis. Splenectomized patients with thalassemia with high RBC counts, thrombocytosis, pulmonary hypertension and transfusion naivety are at higher risk to develop thromboembolic events.¹ This patient had all these risk factors. Due to the occurrence of recurrent thrombosis and to the described risk factors for thrombosis, a long-term secondary prophylaxis with warfarin was recommended with a target international normalized ratio (INR) between 2 and 3. This was highly effective, as she has not had any thrombotic events since.

One important question while attending patients with thalassemia and high thrombotic risk is how to manage them while in high-risk situations for thrombosis such as before splenectomy, immobilization and hospitalization? Since high quality evidence for recommending thromboprophylaxis is lacking, we manage patients with thalassemia similar to the general population. Therefore, further studies on this issue are warranted.

Conclusion

We conclude that splenectomy triggered the thromboembolic events in this patient, who already had a hypercoagulable state due to Hb C/ β^0 -thalassemia. This is supported by the occurrence of three thromboembolic events after splenectomy and the absent history of thrombosis in her two sisters who carry the same genetic defect, but were not splenectomized. Clinicians should be aware of the high risk of thrombosis

in patients with hemoglobin diseases before they indicate splenectomy.

Conflicts of interest

The authors declare no conflicts of interest.

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