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Cardiac and thrombotic complications in the peripartum period of a patient affected by beta-thalassemia intermedia: An unusual case

Giulio Binaghi a,*, Damiana Congia a, Carlo Dessi b, Gildo Matta c, Daniele Pasqualuccia a, Emanuela Serra a, Maurizio Porcu a

a Department of Cardiology, G. Brotzu Hospital, Cagliari, Italy
b Thalassemic DH, Microcitemico Hospital, Cagliari, Italy
c Department of Radiology, G. Brotzu Hospital, Cagliari, Italy

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Beta-Thalassemia (β-T) is a hereditary blood disorder due to reduced or absent β-globin chain synthesis, resulting in chronic hemolysis, ineffective erythropoiesis and iron overload. Its complications include hypercoagulability and organ damage. β-T Intermedia (β-TI) is a term used to define homozygotes or compound heterozygotes individuals, in whom the clinical severity of the disease is between the generally asymptomatic condition (β-T trait) and the severe manifestations of β-T major (β-TM) [1]. Differently from β-TM, individuals affected by β-TI have milder anaemia and only occasionally need blood transfusions, but may present iron overload and thrombotic complications, particularly after splenectomy. Advances in the management of β-T have improved the expectancy and quality of life of these patients, with a consequent increase in their reproductive potential.

Our case concerns a 33-year-old woman affected by β-TI, HCV positive, splenectomized at the age of 25-year-old and treated with regular blood transfusions since four years, who came to our observation during the labour of her first twin-pregnancy consequent of in-vitro fertilization.

In the previous years she underwent an inconstant iron-chelation treatment (ICT) with subcutaneous infusion of deferoxamine, because of poor compliance.

The only cardiovascular magnetic resonance (MR), performed six years before, was normal, with a T2* showing no myocardial iron overload (37.2 ms, normal values > 20 ms). ECG and echocardiography performed at the beginning of the pregnancy were normal.

Deferoxamine was early suspended for the teratogenic risk and the rate of transfusions was increased to a bi-weekly regimen, for an augmented consumption of haemoglobin during the pregnancy; so the patient intensified cardiological evaluations, resulted normal. At 33 weeks, because of foetal distress, a caesarean section was performed with good result for the newborns. During the procedure the mother presented a transient, but severe hypotension with clinical signs of heart failure. Echocardiography evidenced a left ventricle systolic dysfunction (EF: 25%) due to diffuse hypokinesia. Laboratory tests showed an elevated BNP (3,790 pg/ml), an acceptable haemoglobin value (10,0 g/dl) and a very high ferritin level (10,264 ng/ml, normal values: 10–291). Renal and hepatic functions were normal. After intravenous diuretic treatment, the patient had a prompt clinical and hemodynamic improvement and an oral therapy with a low-dose of bisoprolol, ramipril and spironolactone was started after few days.

A combined ICT was immediately commenced with intravenous deferoxamine and oral deferiprone.

In the following days, she presented recurrent episodes of supra-ventricular tachycardia with hemodynamic instability, successfully treated with amiodarone. Because of persistent abdominal pain, a CT scan was performed, showing a bilateral thrombosis of ovarian veins, despite a prophylactic treatment with subcutaneous enoxaparine. For that reason, intravenous non-fractioned heparin was begun, followed by oral warfarin dosed by PT-INR (target 2.0–3.0). The cardiac MR, performed seven days after the delivery, confirmed the diffuse hypokinesia with a reduced EF (40%) and showed dilatation of left ventricle (EDVI: 110 ml/m2). At T2* evaluation, an iron overload was detected both in the heart (10.2 ms) and the liver (0.2 ms; normal values > 6 ms). No myocardial fibrosis or oedema was detected after gadolinium infusion.

On day 22 the patient was discharged at home with a stable hemodynamic status. At that time a significant reduction of ferritin level was noted (4,497 ng/ml). Ten days later, because of the difficulty to reach a stable therapeutic PT-INR with persistence of the ovarian veins thrombosis, we decided to switch from warfarin to rivaroxaban. At 3-month follow-up the patient was stable, with no symptoms even during efforts and abdominal ultrasonography revealed the resolution of ovarian...
thrombosis. Echocardiography showed a normal EF (55%), despite cardiac MR, repeated at month eight, confirmed a persistent severe iron overload (T2*: 9.46 ms).

Nowadays a pregnancy in thalassemic patients is not so rare, in fact several reports have demonstrated as a multidisciplinary approach provides a high rate of success [2,3].

However, even if assisted reproductive techniques are often necessary, in β-TI the prevalence of full-term favourable pregnancies ranges from 77% to 82% and twins account for about 9% of all newborns [2,3,4,5]. In this particular subset of women, thromboembolic complications have been reported with frequent rate [6], despite more recent observation seems not confirm this risk in patients prophylactically treated [3]. The rate of cardiac complications during pregnancy in BT is uncommon, as only 4 cases were detected in a recent observation of 129 thalassemic pregnancies. In this series, peripartum left ventricular dysfunction was found in only 2 women (1.5%) [7]. A direct toxic effect of iron infiltration on cardiomyocytes is considered to be the main cause of hypokinetic cardiomyopathy in thalassemic patient and it is the probable aetiology of the acute ventricular dysfunction in our case, due to a previous insufficient ICT associated to the intensification of blood transfusions and to pregnancy-related haemodynamic changes. Nevertheless, a myocarditis was considered as possible alternative cause, because of the incidence of viral infections among β-T patients is higher than in general population related to the impairment of immune competence and to the iron overload [8]. A myocardial biopsy was not performed, however the hypothesis of a myocarditis is weak, as the cardiac MR, executed early, did not show fibrosis or oedema. A concomitant peripartum cardiomyopathy cannot be excluded, but in our opinion this hypothesis seems to be rather unlikely. Furthermore, the patient developed a deep venous thrombosis despite an adequate prophylaxis. The incapacity to achieve a stable therapeutic PT-INR brought to a shift towards a direct oral anticoagulant, rivaroxaban. Although the data of its use in puerperium are still poor (0.3–0.6% of the whole population enrolled in the EINSTEIN trial) [9] and no previous treatment in thalassemic patients are described; to our knowledge, this is the first case reported. In conclusion, even if acute heart failure is a rare complication during pregnancy in β-TI women, a close cardiologic assessment and follow-up can reduce its rate. Before planning a pregnancy, it needs quantify accurately the risk at baseline assessing systolic and diastolic function, as well as cardiac iron infiltration. During the pregnancy and in the peripartum period regular cardiologic checks must be part of the multidisciplinary evaluation.

Conflict of Interest

The authors have no conflict of interest.

References