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Case Report

Successful Labor Management with ROTEM in a Woman with a Newly Diagnosed Dysfibrinogenemia

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Abstract

Dysfibrinogenemia is a rare coagulation disorder, which is characterized by an abnormal fibrinogen function. Several literature studies reported that women with dysfibrinogenemia might have a great risk of pregnancy and labor complications as well as post-partum thrombosis. In this case report, we focus on the usefulness of ROTEM® in assisting physicians with important information about whether replacement therapy with fibrinogen concentrates is needed in a woman with a newly diagnosed dysfibrinogenemia admitted to hospital for a labor induction.

Keywords: Dysfibrinogenemia; Pregnancy; Thromboelastometry

Introduction

Diseases affecting fibrinogen may be acquired or inherited. Quantitative disorders affect the quantity of fibrinogen (afibrinogenemia, hypofibrinogenemia), while qualitative disorders affect the quality of circulating fibrinogen (dysfibrinogenemia). In dysfibrinogenemia, an autosomal dominant disease, fibrin coagulation tests are variably or infinitely prolonged and fibrinogen antigen levels are normal with a lower functional fibrinogen level. This congenital fibrinogen disease is a rare coagulation disorder whose clinical manifestations can be variable [1]. Over half of patients with dysfibrinogenemia usually do not experience any clinical complications and bleeding occurs in around 25% of patients with a usually a mild presentation. Major hemorrhage is rarely spontaneous and usually associated to delivery, injury or surgery [2]. Dysfibrinogenemia, in approximately 20% of patients, can also be associated to thrombotic complications which can also occur in the postpartum [3,4]. The absences of randomized controlled studies and the great heterogeneity of dysfibrinogenemia clinical manifestations, make management of pregnancy very difficult suggesting an individualized management of pregnancy and delivery in accordance to the fibrinogen level and personal and family history of bleeding and thrombosis [5]. Despite the important efforts to better identify this disease, unique data on its clinical management are still scarce. The absences of randomized controlled studies and the great heterogeneity of dysfibrinogenaemia clinical manifestations, make management of pregnancy very difficult suggesting an individualized management of pregnancy and delivery in accordance to the fibrinogen level and personal and family history of bleeding and thrombosis [5]. Identifying risk factors for postpartum hemorrhage, together with baseline testing may provide physicians with important information about whether fibrinogen replacement therapy should to be used before obstetric complications occur, especially in patients who are otherwise asymptomatic in daily life [6]. We think that together with baseline testing, rotational thromboelastometry (ROTEM) could permit to better assess the patient phenotype and therefore the treatment. This device displays the coagulation process from initiation of clot formation until fibrinolysis and specific reference ranges for the ROTEM thromboelastometry during pregnancy and delivery have been suggested to be able to diagnose coagulopathies and consequently to take precautions during the course of pregnancy [7]. Here, we reported a case of an asymptomatic pregnant patient diagnosed with dysfibrinogenemia just before her labor induction, whose clinical management was helped by ROTEM use.

Case Presentation

A 23yrs old female at her first pregnancy, was admitted to our Hospital in May 2019 at 38+4 weeks of gestation for a normal obstetric control, which revealed an oligohydramnios requiring a labor induction in term pregnancy. Her previous obstetric medical history was negative and routine laboratory exams were normal (prothrombin time, activated prothrombin time, INR, hepatorenal function, coagulation factor VIII, IX and fibrin degradation products), with the exception of functional fibrinogen level which was 44 mg/dl and thrombin time which was prolonged (31sec, normal 14-21 sec). The fibrinogen antigen level could not be evaluated because not available in our hospital. Because standard clotting test (SCT) were normal and the patient never mentioned previous bleeding episodes and/or spontaneous abortions we oriented our diagnosis toward dysfibrinogenemia. In severe hypofibrinogenemia SCT are variably prolonged according to circulating fibrinogen level and usually associated to pregnancy problems and previous spontaneous or associated to delivery or trauma hemorrhages. Because of this low fibrinogen value, fears about bleeding complication associated

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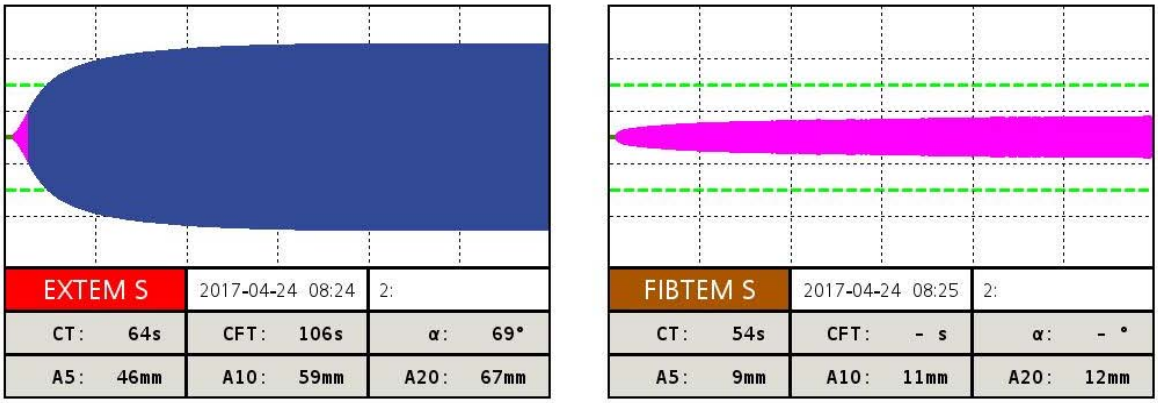

Figure 1: Thromboelastometry trace (EXTEM and FIBTEM tests) representing the coagulation status of the pregnant patient at the beginning of labor.

with childbirth raised doubts on the need to administer fibrinogen concentrates to correct plasma fibrinogen concentration. Due to the limited sensitivity of coagulation assays in the case of very low fibrinogen levels (e.g., <0.5g/L), which makes challenging to distinguish dysfibrinogenemia from severe hypofibrinogenemia [5] we decided to use thromboelastometry (ROTEM™, TEM Innovations, Munich, Germany) to provide additional information on the clot strength before labor induction (Figure 1). The ROTEM test showed normal values: CTEXTEM: 64sec (n.r: 31-63 sec), MCFEXTEM: 68mm (n.r: 42-78 mm); CTFIBTEM: 54 (n.r: 31-79 s) MCFFIBTEM: 13mm (n.r: 12-45 mm) [7] suggesting not to administer fibrinogen concentrate during labor except for bleeding complication or in case of cesarean. The process of delivery, childbirth and post-partum were uneventful and no bleeding episodes or thromboembolic event were recorded. No low molecular weight heparin (LMWH) was used as thromboprophylaxis since the patient never reported a positive personal or family history for thrombosis.

Discussion

Dysfibrinogenemia is a very challenging disorder and there are no firm guidelines on treatment for pregnant patients with this disease. Dysfibrinogenemia can present with highly heterogeneous clinical presentations and patients with similar fibrinogen level measured by Clauss assay may or may not present obstetric complications (spontaneous abortion, placental abruption, post-partum thrombosis and hemorrhage). The indications for dysfibrinogenemia management during pregnancy are scarce and mainly come from case reports in women with reported obstetric complication [8,9]. In those cases, the suggested functional fibrinogen target level to be achieved in order to prevent bleeding and fetal loss was more than 1.0g/L, and a defined fibrinogen concentrate administration was usually suggested to maintain this level [10]. The great variability in the clinical manifestations of dysfibrinogenemia together with the fact that in our case the patient was at her first uneventful pregnancy and that she did not report any previous surgical operations or major trauma made the clinical management of the delivery based to her personal history difficult to perform. In this specific condition, we think it could be of great importance to rely on trustworthy information useful for overcoming the limits of Clauss assay or the absence of fibrinogen antigen levels measurement especially in urgent setting. Rotation Thromboelastometry, a device assessing global haemostatic and fibrinolytic function [11] can potentially provide an additional and rapid method for determining functional fibrinogen and for guiding, if necessary, the prophylaxis treatments in pregnant patients before obstetric complications happen. In particular, we analyzed MCF Fibtem measured with ROTEM, which specifically detects the function of fibrinogen by abolishing platelet function, finding it practically within the normal range. Fibrinogen function, similarly studied with thromboelastography has been demonstrated to have a better prognostic value in predicting the obstetric complication occurrence than other thromboelastography parameters, further underlining the critical role of maternal normal functional fibrinogen for the successful outcome of a pregnancy [12]. In this paper, Zhou et al. have demonstrated that max amplitude measured by functional fibrinogen thrombelastography might predict, better than other parameters, the occurrence of obstetric complications, providing physicians important information to decide whether fibrinogen replacement therapy is suggested. In literature, it has been stated that thromboleastography may be able to discriminate as well between hypo and dysfibrinogenemia [13]. Notwithstanding fibrinogen administration is not been associated to thrombotic complications, the small size of the studies on its use in pregnant women with fibrinogen diseases, has not eliminated all doubts on its safety or efficacy [14]. Because of that, prophylactic administration of fibrinogen concentrate must be tailored and the potential risk of thrombosis weighed against the likely benefits of treatment: thrombosis has been reported in approximately 20% of patients with dysfibrinogenemia [2]. The patient negative obstetric clinical history, the absence of previous spontaneous abortions or bleeding episodes, together with a normal ROTEM test made us decide not to administer a preventive treatment with fibrinogen concentrates giving us the chance to individualize the treatment weighing the potential risk of thrombosis against the possible benefits of treatment. The point of care, rotational thromboelastometry, played an important role in the optimal management of a pregnant patient with fibrinogen disturbances probably avoiding an unnecessary treatment.

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