D-dimer levels as a predicting factor for DIC following single twin death: a case report and review of the literature

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Summary

Background: Intrauterine death of one twin in the second or third trimester occurs in about 1% of all twin pregnancies. The retention in utero of the dead fetus may be associated with maternal disseminated intravascular coagulation. *Case:* We present the case of a diamniotic monochorionic pregnancy with intrauterine death of the first twin at 24 weeks. The pregnancy reached 33 weeks. In our case although all coagulation factors were within normal limits, D-dimer levels were significantly high, without any evidence though of any clotting problems to the mother. *Conclusion:* The role of D-dimers is practically unknown in multiple pregnancies. It seems that the interpretation of elevated D-dimer levels is still of limited value for prediction or prognosis of thromboembolic complications of multiple pregnancies.

Key words: D-dimers; Twin pregnancy; DIC; Intrauterine death.

Introduction

Intrauterine death of one twin in the second or third trimester occurs in about 1% of all twin pregnancies [1]. In monochorionic twins the most common cause for this complication is the twin to twin transfusion syndrome (TTS). Intrauterine death of a fetus in a monochorionic pregnancy may be associated with adverse outcome for the co-twin. The risk of death or neurological handicap in such cases is at least 30% to the surviving twin due to hypotension, vascular occlusion due to thrombi or hemorrhage resulting from coagulation disorders [1]. The interval between the occurrence of intrauterine death and organ damage varies and cerebral complications can even predate fetal demise. The death of one twin in utero will usually stimulate uterine activity and most pregnancies will deliver within three weeks, usually resulting in prematurity and compounding problems in the surviving co-twin [2]. Retention in utero of a dead fetus may lead to maternal disseminated intravascular coagulation (DIC). The thromboplastin-like material released from the necrotic fetal tissue may activate the maternal coagulation system, resulting in hemostatic failure.

Prior to 34 weeks of gestation most centers would advocate administration of antenatal steroids, tocolysis and conservative management with continuous fetal monitoring until 34 weeks. The evidence is not clear regarding the best mode of delivery and if it affects the outcome of the surviving twin [3, 4].

We present the case of a diamniotic monochorionic pregnancy with intrauterine death of the first twin at 24 months plus three weeks. Pregnancy reached 33 weeks and the patient delivered normally. Clotting parameters and especially D-dimer levels were monitored in order to predict DIC of the mother.

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Case Report

A 34-year-old para 1 woman with a diamniotic monochorionic twin pregnancy was referred at 24 weeks and three days to the emergency clinic of our department with the diagnosis of intrauterine death of one twin. She had no past medical history. Her first pregnancy was uncomplicated and she delivered vaginally at 39 weeks. According to her medical records the detailed ultrasound (US) scan at 23 weeks showed severe twin-to-twin transfusion syndrome (TTS), with the donor twin weighing 220 g with absent end-diastolic flow, and the recipient twin weighing 380 g with normal Doppler studies. On examination the intrauterine death of the one twin (twin B) was confirmed and the remaining twin (twin A) showed normal cardiac activity, cephalic presentation, normal amniotic fluid and growth (490 g) and normal Doppler studies of umbilical artery and ductus venosus. A more detailed scan revealed enlargement of the heart without any structural defects, occupying half of the chest cavity, which was attributed to the TTS. The blood work-up results upon admission were reassuring apart from D-dimer levels (Hb: 10.6 g/dl, WBC: 9.8 10^3/μl, PLT: 331 10^3/μl, INR: 0.9, PT: 9.7 sec, aPTT: 28 sec, fibrinogen: 451 and D-dimer: 7702 μg/l). The patient was subsequently admitted to the high dependency unit and was started on enoxheparine (40 mg s.c. daily). Thorough information was given to the parents about the possible risks for the remaining fetus and the maternal well-being due to the risk of DIC. Clotting status and full blood count were checked every three days. No significant changes were observed during hospitalization apart from D-dimer levels gradually falling to plateau at 2440-2550 μg/l at 28 weeks of gestation (Table 1). Betamethazone (24 mg IM divided in two doses) was administered within 24 hours from admission. Detailed US scans were performed weekly to assess fetal status and wellbeing. Fetal growth, cardiac activity, fetal movements, amniotic fluid and Doppler studies were normal. The pregnancy reached 33+0 weeks before spontaneous contractions started during the night and despite intravenous tocolysis (ritrodine) administration, the patient delivered vaginally within three hours a live male infant weighing 1,810 g with Apgar scores of 6 at 1 min and 8 at five min. The infant was admitted to the neonatal intensive care unit for observation. The mother's post-

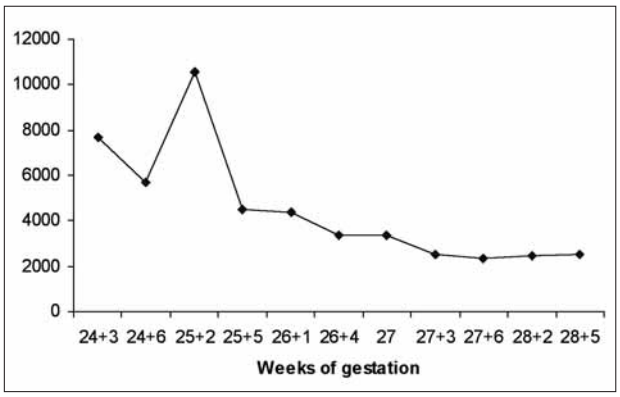

Figure 1. — D-dimer levels.

partum hospitalization was uneventful and the infant was discharged after 12 days. The infant showed no obvious clinical signs of neurological problems, although head circumference was smaller than the 3rd centille. US scan of the brain was not satisfactory due to the small anterior fontanelle. Subsequent brain magnetic resonance imaging (MRI) showed calcifications and enlargement of the right and left ventricles. Follow-up appointments were arranged by the neonatologists for further evaluation of the infant.

Discussion

Intrauterine fetal death leads to a gradual depletion of maternal coagulation factors. Thromboplastic substances are released into maternal circulation and may trigger DIC, which occurs in about one-third of patients who retain a dead fetus in utero for longer than four to five weeks [5].

Increased D-dimer levels indicate increased fibrinolysis following fibrin formation. D-dimer assays are used to measure fibrin degradation products and they have been a useful marker for the early diagnosis of DIC and thromboembolism [6]. D-dimer is formed by plasmin-mediated proteolysis of cross-linked fibrin. D-dimer levels have been found to increase significantly in normal pregnant women in comparison to non pregnant women [7-9]. This can be attributed to the physiological hemostatic balance displacement towards hypercoagulability. In multiple gestations this imbalance in hemostasis is even more exaggerated [10]. The physiological alterations associated with multiple gestations, initiated by placental and fetal production of proteins and steroids, can be another reason for the increased levels of D-dimer occurring. Bar *et al*. showed that D-dimer levels in 49 women with normal twin pregnancies were significantly higher than in women with singleton pregnancies [11]. Morikawa *et al*. studied 48 normal singleton and twin pregnancies and concluded that there was a progressive increase in prenatal D-dimer levels, which is consistently higher in women with twin pregnancies [10]. Enhanced coagulation-fibrinolysis activity that normally occurs during late gestation is more exaggerated in women with twin pregnancies [12, 13].

In the present case, although all coagulation factors were within normal limits, D-dimer levels were significantly increased, without occurrence of clotting problems (DIC) in the mother. The clinical significance and etiology of increased D-dimer levels in normal singleton pregnancies is unclear and practically unknown in multiple pregnancies. It seems that the interpretation of elevated D-dimer levels is still of limited value for prediction or prognosis of thromboembolic complications of multiple pregnancies.

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