Successful pregnancy after pulmonary embolism and heparin-induced thrombocytopenia - case report

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Summary

The authors present the case of a nulliparous 34-year-old patient. At the tenth week of gestation, she developed phlebothrombosis of veins of the right leg and massive pulmonary embolism. After thrombolytic and heparin therapy she developed rethrombosis and heparin-induced thrombocytopenia type II. Lepirudin was introduced in therapy and in the 12th week of gestation acenocumarol was added. After the 34th week, she received danaparoid sodium. After a week, by cesarean section, a healthy and mature female was delivered.

Key words: Pregnancy; Heparin-induced thrombocytopenia; Pulmonary embolism.

Introduction

Pulmonary embolism is the leading cause of maternal mortality during pregnancy and labor. Incidence is one per 1,000 - 3,000 deliveries. Heparin-induced thrombocytopenia is a life-threatening condition with mortality rate of 29%. In 0.5%-3% of cases, it is caused by venous thromboembolism in pregnancy. The question the authors had to answer was: what to do and how to help this patient who developed heparin-induced thrombocytopenia during therapy of massive pulmonary embolism at ten weeks gestation?

Materials and Methods

The authors present the case of a 34-year-old patient, primipara. At the tenth week of pregnancy, she developed phlebothrombosis of femoral popliteal and crural veins of the right leg and massive pulmonary embolism. She received thrombolytic therapy with tissue plasminogen activator and intravenous heparin therapy; at the beginning she showed clinical signs of improvement, but also developed rethrombosis, proved by Doppler scan of veins of lower extremities, and heparin-induced thrombocytopenia type II (platelet count was 46,000 per ml) which was proved by laboratory tests. Immediately lepirudin was added to the therapy by intravenous infusion and it resulted in clinical and hematological improvement. In her 12th week of pregnancy, oral anticoagulant therapy was started with acenocumarol, controlled by international normalized ratio (INR) (between 1.5 and 2.5). Careful monitoring of fetus was applied, with ultrasound and Doppler assessments. Complete biochemical fetal noninvasive screening testing was performed as well nuchal tanslucency (NT), double and triple screen) with normal results. Resistance indexes in umbilical and cerebral fetal circulation were within normal values. After the 34th week, danaparoid sodium 750 IU subcutaneously every 12 hours was introduced in therapy with control of anti- Xa levels in maternal blood. At the end of the 35th week, cesarean section was performed. The last dose of danaparoid was administered six hours before surgery and continued six hours after. The newborn was healthy with birth weight of 2,700 g and Apgar score of 9. Intensive neonatal care unit was not necessary. For two weeks after delivery the mother received danaparoid sodium twice a day; four days after surgery acenocumarol was introduced in therapy again. After 13 days, therapy with danaparoid was terminated and continuous oral anticoagulant therapy maintained. Lactation was regular. The postoperative course was carefully monitored and was normal. The patient was discharged after 14 days from hospital with ultrasound and laboratory results within the normal range. Follow up of the child in following three years showed normal mental and physical development.

This review shows how important proper and prompt diagnose of phlebothrombosis is during pregnancy. Otherwise pulmonary embolism is frequently a consequence. This severe and life-threatening situation needs anticoagulation therapy with heparin. Some patients are at risk of developing heparin-induced thrombocytopenia, which additionally complicates an already difficult situation. Danaparoid is the medication of choice in these cases. It is subcutaneously administrated, with low side-effects. During second-trimester pregnancy, oral anticoagulant therapy is a safe option. From available literature the authors see similar experiences, although the number of patients treated in this manner is not large, number of complications is greater, but the present authors had no maternal and fetal complications. This is certainly a result of cooperative team work. Lindhoff-Last *et al*. reviewed the use of danaparoid in 51 pregnancies of 49 patients identified in literature between 1981 and 2004. All patients had developed heparin intolerance (32 due to heparin-induced thrombocytopenia, 19 mainly due to heparin-induced skin rashes), and had a current and/or past history of thromboembolic complications. The initial danaparoid dose regimens ranged from 1,000 to 7,500

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U/day administered subcutaneously or intravenously. The median duration of danaparoid use was ten weeks. Danaparoid was used until delivery of a healthy infant in 37 pregnancies. In the remaining 14 pregnancies, it was stopped earlier, because anticoagulant treatment was no longer required (3/14) or an adverse event led to a treatment discontinuation (11/14). Four maternal bleeding events were recorded during pregnancy, delivery or postpartum, two of them were fatal due to placental problems. Three fetal deaths were recorded, all associated with maternal complications antedating danaparoid use [1]. Schindewolf *et al*. found a suitable alternative anticoagulant when heparin-induced thrombocytopenia type II (HIT II) or allergic skin reactions occur. Their results showed that 40/59 pregnancies were carried to term under use of danaparoid and resulted in the delivery of a healthy infant. In 16/19 pregnancies, danaparoid was stopped due to a major adverse event. Five patients showed bleeding complications, seven fetal losses were documented, but there was no association with the use of danaparoid. In 31/59 (52.5%) pregnancies, adverse events were documented, 14/31 (45.2%) could be attributed to danaparoid. Anti-X activity was not detected in five fetal cord blood samples and in four maternal breast-milk samples [2]. Myers *et al*. described a case where danaparoid was used prophylactically in a high-risk twin pregnancy following the development of heparin-allergy while on prophylactic dalteparin. Danaparoid was substituted for dalteparin at 20 weeks of pregnancy following the development of a severe skin reaction while on low molecular weight heparin. Although there was no significant fall in platelet count, an aggregation assay for heparin-induced thrombocytopenia was positive. The skin lesions rapidly resolved following the change to subcutaneous danaparoid. Delivery was through emergency cesarian section at 35 weeks under a general anesthesia, as a dose of danaparoid had been given six hours prior to delivery. A sample of breast milk showed no anti-X activated factor activity. Danaparoid was continued post-delivery until the patient was fully warfarinized [3].

Danaparoid, which has low cross-reactivity for heparin-dependent antibodies and no known teratogenic effects, was used successfully to treat the patient, who developed heparin-induced thrombocytopenia during pregnancy [4, 5]. Danaparoid may be the treatment of choice for this difficult clinical situation in which there are limited therapeutic options.

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