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Successful pregnancy outcome in a patient with both congenital hypofibrinogenemia and protein S deficiency

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Congenital hypofibrinogenemia is a rare disorder with autosomal dominant inheritance, manifested in females by menorrhagia, recurrent abortion, and placental abruption.[1] Protein S deficiency is associated with deep vein thrombosis, placental infarction, and preeclampsia.[2] We present a patient with both disorders.

Case

The patient was a 31-year-old woman, gravida 5, para 0–0–4–0, with a medical history of deep vein thrombosis and pulmonary embolus at age 18 while taking oral contraceptives. The woman was diagnosed as having protein S deficiency and low titers of anticardiolipin antibodies. After an elective termination, the woman conceived three times and was placed on subcutaneous heparin each time, yet suffered spontaneous abortions with normal karyotypes. Her third pregnancy was complicated by deep vein thrombosis. Testing persistently revealed a fibrinogen level of 70 mg/dL. Subsequently, the patient's father was noted to have a fibrinogen level of 125 mg/dL. After another conception and before referral, the patient was prescribed heparin, low-dose aspirin, and progesterone suppositories. We modified her treatment to include fresh frozen plasma transfusions, 1–2 U every 2 weeks, to maintain her fibrinogen at greater than 150 mg/dL. Unfractionated heparin was discontinued and low-molecular-weight heparin was begun; aspirin was discontinued. At 38 weeks' gestation, labor was electively induced and low-molecular-weight heparin was continued. The fetal heart rate was nonreassuring, and a male fetus was delivered in good condition via a low transverse incision. Both the operation and postoperative course were uneventful. Of interest, the neonate's fibrinogen level was 66 mg/dL.

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Comment

Transfusions of fresh frozen plasma not only raised and maintained the patient's fibrinogen level, but also provided some protein S, thereby decreasing her heparin requirements. We believe that low-molecular-weight heparin minimized the risk of abruption. This type of heparin has been used extensively in Europe, and data suggest that it is at least as effective as unfractionated heparin. Enoxaprin (Clexane; Rhone-Poulenc Rorer, France) does not cross the placenta and contains the antithrombin III binding site but, unlike unfractionated heparin, does not produce factor IIA (thrombin) inhibition. As such, the partial thromboplastin time is not altered.[3]

The autosomal dominant hypofibrinogenemia apparently was inherited from the patient's father and likewise passed on to the neonate. The protein S deficiency was probably inherited from the patient's mother. In short, this patient had an impaired ability both to make appropriate fibrin clots and, paradoxically, to inhibit their inappropriate formation. Given the patient's clinically insignificant anticardiolipin antibody level, there was no true indication for aspirin therapy.[4]

References

1. Hasselback R, Marion RB, Thomas JW. Congenital hypofibrinogenemia in five members of a family. Can Med Assoc J 1963;88:19–22.
2. Mercer B, Garner P. Thrombophlebitis. In: Gleicher N, ed. Principles and practice of medical therapy in pregnancy. 2nd ed. Norwalk, Connecticut: Appleton & Lange, 1992:1292.
3. Dulitzki M, Pauzner R, Langevitz P, Pras M, Many A, Schiff E. Low molecular weight heparin during pregnancy and delivery: Preliminary experience with 41 pregnancies. Obstet Gynecol 1996;87:380–3.
4. Lockwood CJ, Rand JH. The immunobiology and obstetrical consequences of antiphospholipid antibodies. Obstet Gynecol Surv 1994;81:432–41.

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