Fibrinogen Marburg
A New Genetic Variant of Fibrinogen

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Summary

A new case of congenital dysfibrinogenemia has been discovered in a 20 year old woman, who suffered from a severe postpartal hemorrhage after the delivery of her first child, followed by episodes of thrombosis. Coagulation studies revealed a prolongation of thrombin time, reptilase time was immeasurable. Thromboplastin time and partial thromboplastin time were slightly prolonged.

Low fibrinogen levels were obtained by techniques, which depend on the coagulation velocity following addition of thrombin, while immunological procedures gave slightly diminished values of fibrinogen. Patient’s fibrinogen had a moderate inhibitory effect on the fibrin formation in normal plasma. However, inhibitors of the fibrinogen – fibrin conversion could not be detected. Coagulation factors were normal, fibrinolysis as well. The cause of the coagulation disorder was found to be a defect of the fibrinogen molecule, leading to an abnormal fibrin polymerization of patient’s fibrin monomers. The release of the fibrinopeptides in the paper electrophoresis was normal. The defect of the fibrinogen molecule did not protect from thrombotic complications.

The same defect could be found in the lower scale in patient’s father, 4 of her 7 brothers and sisters, and her son.

Zusammenfassung


Eingegangen am 1. 9. 1975
Wiedereingang am 27. 7. 1976
nicht vor thrombotischen Komplikationen. In geringem Ausmaß ließ sich diese Störung bei dem Vater der Patientin, bei dem Sohn und bei vier von sieben Geschwistern nachweisen.

Key words: Dysfibrinogenemia, fibrinogen, fibrin monomer aggregation, fibrinopeptides

In recent years more and more molecular variants of the different coagulation factors were detected [12, 13, 14]. This, for example, is reported from prothrombin and the coagulation factors VII, VIII, IX, X. So it could be shown, that in many cases not a deficiency of a coagulation factor, but an abnormal defective protein was synthesized [21, 25, 26, 30].

For abnormal fibrinogen Ménaché collected 22 families, which were described in medical literature [37]. More cases were presented recently [1, 2, 8, 9, 11]. Some showed bleeding tendency, others thrombotic tendency, most of them had none of the clinical symptoms.

In this publication we describe a woman who had a severe hemorrhage followed by repeated thrombotic events. We found that an abnormality in the formation of fibrin was the reason for this disorder.

Case Report

The patient was a twenty year old woman, who had no tendency to bleed, only a disposition to obtain minor hematoma. Menstrual flux was normal. But a perilous bleeding happened after the delivery of her first child. Because of placenta praevia the delivery had to be finished by caesarian section. A short time after this event a profusely uterine hemorrhage occurred, therefore a hysterectomy was performed. The patient received 2000 ml fresh blood during the operation. On the seventh postoperative day a pulmonary embolism happened, therefore the patient was treated with phenprocoumon.

Embolism occurred repetitiously and the patient developed a deep pelvic thrombosis, although Thrombotest had shown good values. While the patient was recovering, another pelvic thrombosis happened on the 36th postoperative day, a third one after the patient's dismissal. These occurrences required the examination of her coagulation mechanism.

The family history showed no disturbance of coagulation. The father is alive and well, the mother died from apoplexia after a long period of hypertension. She had eight deliveries without complications. The patient's brother and sisters are well. No consanguinity in the ascendency is known.

Materials and Methods

Nine volumes of venous blood were collected into one volume of tri-sodium citrate 3.8% (0.1 m). Plateletpoor plasma was separated by centrifugation at 3000 g at 4°C for 10 min and used immediately or frozen at -25°C.

Coagulation and fibrinolytic studies of the proposita and her family were performed with the following techniques: bleeding time (Ivy [27]), prothrombin time, thrombin time, partial thromboplastin time, factor II, V, X were measured using reagents and plasma available from Behringwerke (Marburg, Germany), factors VIII, IX from General Diagnostics Division (Warner Lampert Co., Morros Plains, N.J.). Reptilase and thrombin-coagulase reagents from Boehringer Mannheim (Germany) were used.