Case Report

Dialysis without heparin in a patient with combined hereditary deficit in coagulation factor V and protein C

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Introduction

Factor V hereditary deficiency or Orwen parahaemophilia is an uncommon disease [1] usually transmitted as autosomal recessive trait that manifests clinically only in individuals who inherit the defective gene from both parents [2], however, other modes of inheritance have been described [3]. Variants with abnormal non-functional factor V protein have also been described [4]. Factor V, besides expressing procoagulant properties after its activation by thrombin, also plays an important role in the anticoagulant system as a co-factor to activated protein C [5]. Clinically, factor V deficiency causes haemorrhagic manifestations which vary from one family to another but are usually mild. It rarely causes bleeding in affected neonates but has been associated with congenital abnormalities [3]. Bleeding time, prothrombin time and clotting time are prolonged.

Protein C deficiency is inherited as an autosomal dominant trait characterized clinically by recurrent thrombosis. It exists in two different types: type I deficiency is identified by a simultaneous decrease in both functional and antigenic levels of protein C [6]; type II deficiency, which is rarer, is characterized by a depressed functional protein C level, but a normal, or slightly subnormal, immunological protein C level [7].

We report the rare association of familial combined deficits of coagulation factors V and protein C, without clinical manifestations of bleeding disorders or thrombophilia, in a patient with end-stage renal disease. The sole manifestation of this coagulopathy was the absence of heparin requirement during treatment with hemodialysis.

Case

A 34-year-old Saudi female was referred to our centre with a diagnosis of renal failure and pregnancy. She was well until 2 days prior to admission, when she developed nausea and blood-streaked vomiting. She was gravida 8, para 7; all children were alive and well and had never presented with haemorrhagic manifestations. She had no previous medical or surgical history. She had no family history of bleeding disorder or renal problems, except for one niece who was known to have abnormal coagulation, but this abnormality did not cause any clinical problems. Her husband is not a relative. Her mother and father were first cousins.

Investigations showed the following positive findings: urea 29 mmol/l, creatinine 621 μmol/l, uric acid 609 mmol/l. Twenty-four-hour urine collection showed a urinary creatinine of 8.32 mmol (creatinine clearance 9.3 ml/min or 0.15 ml/s) and a urinary protein of 3.5 g. Abdominal ultrasound showed a 9.7 × 4.1 cm right kidney with increased echopattern and poor cortico-medullary differentiation. The left kidney was absent. A single active viable fetus was seen with polyhydramnios.

Routine coagulation screen showed prolonged prothrombine time (26.4 s, control 12.6 s) and prolonged partial thromboplastin time (54 s, control 29.0 s). Bleeding time was normal. Fibrinogen was 1.05 g/l and the platelet count was 1.0 × 10⁴ l/but fibrinogen-degradation-product test was negative. Coagulation factors V and C protein percentage activity were <10% and 20% respectively (normal range 65–130% and 70–130% respectively). All other coagulation factor levels were normal.

Coagulation and coagulation factors assays were performed on the family including the patient’s parents, husband and eight children. The husband’s results were normal. The parents had a slight increase in prothrombin and thromboplastin times and low normal levels of factors V and protein C. All children had a slightly increased or normal prothrombin time and thromboplastin time, but all had low levels of factors V and C protein activity (between 64 and 30% and between 65 and 20% respectively).

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All other coagulation factors, levels were normal. Intravenous rehydration led to a decrease in urea level. Nausea and vomiting subsided subsequently. Fetal monitoring was performed daily until spontaneous delivery occurred at 36 weeks of pregnancy. Just prior to delivery, the patient was given 3 units of fresh-frozen plasma in anticipation of bleeding complications. She had a normal vaginal delivery without abnormal bleeding. The baby was premature but normal. After delivery, she received vitamin K1 parenterally, and her coagulation profile remained abnormal.

One month after delivery, her renal function deteriorated further. A central dialysis line was inserted, an arteriovenous fistula was constructed in the left wrist and she was started on regular treatment with haemodialysis. The above procedures were performed without plasma infusion and were not complicated with abnormal bleeding. Over the next 18 months of haemodialysis she did not require regular heparin during treatment.

The coagulation profile, as well as all the factors’ assays, remained abnormal, when repeated over the 18 months. The patient is still doing well.

Methods

Coagulation factors II, V, VII and X assays were performed using Ortho Factor Deficient Plasma. Prothrombin time was performed using Ortho Brain Thromboplastin. Activated partial thromboplastin time was performed using Thrombosil I Activated PTT Reagent. Fibrinogen determination was performed using Thrombin (Human) Fibrinindex. All the above reagents were supplied by Ortho Diagnostic Systems Inc. (Raritan, NJ, USA). The procedures followed the manufacturer’s instructions.

Clotting assays for protein C and protein S activity were performed using Staclot Protein C and Staclot Protein S reagents (Diagnostica Stago, Asnieres-Sur-Seine, France), the procedures used were those of the manufacturer. The normal range for protein C was 70–130% and for protein S was 65–140%.

Discussion

Although the husband and patient were not closely related, most of the family in this case belonged to the same tribe. Transmission of variant factor V and protein C in this family seems to be autosomal dominant affecting both male and female offspring. This family did not seem to be affected clinically by either haemorrhagic manifestations or thrombosis, and there were no abortions or fetal abnormalities. We postulate that the effect of the deficit of factor V (haemorrhagic tendency) was offset by the deficit of protein C (thrombotic tendency). Clinically, the only manifestation of this prolonged coagulability was that dialysis could be carried out without the administration of heparin. The fact that the patient reported having a niece with a known and undefined coagulation defect, but who was clinically normal, argues against the possibility of a new mutation(s) and suggests for an established familial disorder. The co-inheritance of factor V and Protein C deficiency is rare but may certainly occur by chance.

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References


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