

## A case of factor V deficiency presenting as menorrhagia

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### SUMMARY

**Factor V deficiency is a rare hereditary disorder. We report a patient with factor V deficiency who presented with menorrhagia and pelvic haematoma. The Haematology Department at the Royal Brisbane Hospital performed the definitive factor assays leading to the diagnosis. The challenges of her management were obtaining adequate supplies of factor V and her socioeconomic circumstances. The main future challenge will be the supervision of her pregnancies.**

### Case Report

The patient was a 26-year-old unmarried woman from the remote Trobriand Islands of Papua New Guinea (PNG). From her infancy she had shown a tendency to easy bruising. She had two sisters, both of whom had a bleeding tendency and also frequently developed episodes of menorrhagia. There was no history of bleeding disorders in the rest of the family. Since menarche at the age of 16 years, her menstruations had always been prolonged and heavy, at the end of which she became listless, weak and tired.

In July 1990, she was admitted to the Port Moresby General Hospital (PMGH) with a diagnosis of ruptured ectopic pregnancy but at laparotomy, apart from a haematoma, the pelvic organs were normal. 800 ml of blood was evacuated from the pelvic haematoma. The haemoglobin then was 6.1 g/dl; platelet count was 157,000 per  $\mu$ l; the prothrombin time (PT) and activated partial thromboplastin time (APTT) were prolonged to 44 and 99 seconds respectively. Renal and liver function tests were normal. The anaemia was corrected by packed cell blood transfusion after which she absconded from hospital.

She was referred from the provincial hospital with menorrhagia and was admitted to PMGH on 3 March 1993. General examination was unremarkable. There was a 14-week-size, firm, nonmobile mass arising from the pelvis. The rest of the abdominal examination was normal. Pelvic examination revealed a mass in the pouch of Douglas which had pushed a normal-size uterus anteriorly.

### Investigations and results on admission

#### *Haematology*

Haemoglobin level was 10.9 g/dl, white cell count 6000/ $\mu$ l.

#### *Coagulation profile*

APTT was 120 seconds, PT 40 seconds, fibrin degradation products (FDP) moderately positive in 1:5 dilution (72  $\mu$ g/l) and platelet count 190,000/ $\mu$ l.

#### *Other investigations*

The renal and liver function tests were normal. Pelvic ultrasound revealed a multiloculated mass in the pelvis measuring 10

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x 20 cm with multiple areas of fluid interspersed with echogenic areas consistent with haematoma. Both ovaries and uterus were normal.

### Management

From the history, examination and preliminary tests, vascular and platelet disorders were largely ruled out and therefore a coagulation defect was thought the most likely cause of her problem. Results of specific coagulation factor assays conducted by the Royal Brisbane Hospital Haematology Department were as shown in Table 1.

Consequently a firm diagnosis of factor V deficiency was made. She was given fresh frozen plasma (FFP) at a dose of 15 ml/kg body weight. Clotting time, PT and APTT were performed before and 10 minutes after infusion of FFP. There was a considerable degree of improvement in the test results: PT was respectively 53 and 18 seconds before and after the FFP infusion; APTT was respectively 129 and 55 seconds before and after the infusion.

For the menorrhagia, she was started on depot medroxy progesterone acetate (Depo-provera) 150 mg every three months. She was discharged from hospital on 30 April 1993 and advised to come back every 3 months for Depo-provera injections.

### Progress and follow-up

On 28 May 1993 she was readmitted with severe menorrhagia and a further pelvic collection. Her haemoglobin was 5.1 g/dl. She was transfused with 3 units of packed cells and

3 units of fresh frozen plasma. Treatment was commenced with 10 mg of norethisterone (Primolut N) tablets tds. Within 48 hours of admission the bleeding had ceased and she was discharged to continue the norethisterone for 14 days, and advised to come back for review after 3 months. The Depo-provera was continued at a higher dose of 300 mg. She has since not had any more episodes of menorrhagia. She was advised to live in Port Moresby where supplies of FFP would be relatively more easily available.

### Discussion

Factor V deficiency is a rare hereditary condition. It was first reported by Owren in 1947 and is associated with a mild to moderate bleeding disorder. It is an incomplete autosomal recessive condition and is usually symptomatic only in the homozygous state. Occasionally, one may encounter a patient with acquired antibodies to factor V who has a negative family history. Mucocutaneous bleeding and haematomas are the most common symptoms and signs; haemarthroses are rare. Women with this disorder frequently have menorrhagia, as was demonstrated in our patient. Both the PT and APTT are prolonged, usually prompting specific factor assays (1).

Bleeding can be controlled using freshly prepared FFP, the only current source of factor V. Normal haemostasis is achieved with levels above 15 ml/kg; the plasma is given frequently in small infusions so as to avoid circulatory overload. Although the gene directing the synthesis of factor V has been sequenced, recombinant therapeutic products are not currently available (1).

**TABLE 1**

COAGULATION FACTOR ASSAYS IN THE PATIENT

Factor	Test result	Normal range (U/ml)
II	0.92	0.5-1.5
V	0.03	0.5-1.5
VII	1.04	0.5-1.5
VIII:C	0.72	0.5-1.5
IX	0.72	0.5-1.5
X	0.88	0.5-1.5

Even though the PT is markedly prolonged, some patients do not have major haemorrhagic symptoms. In rare instances, antibodies to factor V arise in patients with congenital absence of factor V. This latter group of patients show a lot of symptoms but can usually be managed with the infusion of fresh platelets that contain normal platelet factor V (1). Several families with combined deficiency of both factor V and factor VIII have been reported (2). They usually show fewer symptoms than patients with haemophilia A, but therapy requires the use of FFP (3).

Few cases of factor V deficiency in the practice of obstetrics and gynaecology have been reported in the literature. Ueno et al. in 1991 discussed a patient with combined deficiency of factor V and VIII who presented with genital bleeding. When she became pregnant 4 years later her factor VIII:C activity rose from 12% to 70% but the factor V level remained low. She was delivered by caesarean section under replacement therapy with factor VIII concentrates and FFP. There was no excessive bleeding (4).

Patients with factor V deficiency usually present with menorrhagia but pelvic haematoma formation is rather rare. The haematoma could be either from retrograde menorrhagia or due to bleeding from the ovaries after rupture of the follicles at ovulation.

We would have liked to investigate the other members of the family but logistics did not allow it. These logistic problems had an impact on her treatment. She simply had to stay in Port Moresby in order that she could avail herself of treatment facilities which were unavailable in Alotau, the provincial capital. Even at the PMGH supplies of FFP cannot always be guaranteed.

Future pregnancies and their management were discussed with her. She would need close antenatal, intrapartum and postpartum monitoring. As has been reported by several workers, the mother and her infant are both at risk. These risks include maternal as well as neonatal haemorrhage. FFP and packed cells should be made available for transfusion at a moment's notice. A neonatologist should also be present at delivery for assessment of the baby's coagulation status (5,6).

Suppressing the endometrial activity was an important part of the management. We found that 300 mg of Depo-provera every three months was required to effect this. If her reproductive capacity is not an issue, endometrial ablation would be an alternative treatment if medical suppression of the endometrium with Depo-provera, Danazol or gonadotrophin release hormone (GnRH) agonists are not successful. Hysterectomy could address the menstrual problems after she has finished her family. Surgery can be managed safely with FFP.

Whilst menorrhagia is more likely to be associated with abnormalities of the reproductive system, blood dyscrasias account for about 20% of menorrhagia of adolescent females. These disorders include idiopathic thrombocytopenic purpura (ITP), von Willebrand's disease and deficiencies of factors II, VII and XI (7). Although less common, ovulatory menorrhagia may also be an early manifestation of acute leukaemia. Liver and renal diseases may also cause menorrhagia which is usually correctable with hormone therapy (8).

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