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Case report

Recurrent haemoperitoneum in a mild von Willebrand's disease combined with a storage pool deficit

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Haemoperitoneum secondary to haemorrhagic corpus luteum has been described in severe bleeding disorders such as afibrinogenaemia, type 3 von Willebrand's disease and patients under oral anticoagulation. We have studied one patient who presented three episodes of severe bleeding at ovulation, requiring surgery twice, with the diagnosis of mild von Willebrand's disease and mild storage pool deficiency. Mild von Willebrand's disease (associated with other thrombopathies or coagulopathies) should be considered in this pathology, although physicians would prefer to find a severe haemorrhagic disorder as the underlying condition in these cases. *Blood Coagul Fibrinolysis* **12**:207–209 © 2001 Lippincott Williams & Wilkins.

Keywords: recurrent haemoperitoneum, type 1 von Willebrand's disease, storage pool deficiency

Introduction

Haemoperitoneum can occur as a result of the rupture of a bleeding follicle and a few cases have been reported in patients with severe bleeding disorders (e.g. afibrinogenaemia and type 3 von Willebrand's disease [1–3]), but it has also been described with oral anticoagulation [4]. Yet there is only one available report of haemoperitoneum secondary to a haemorrhagic corpus luteum in mild von Willebrand's disease type 1 [5].

We report one patient who presented three episodes of severe bleeding at ovulation, two of them requiring surgery. In this case, two mild haemostatic disorders induced a severe bleeding tendency.

Methods

The bleeding time was measured by the method of Ivy *et al*. [6]. Platelet retention to glass beads was measured by Hellem's test [7]. Blood was taken by venipuncture and collected in polystyrene tubes with 0.11 mol/l trisodium citrate to perform the platelet's test. Platelet adenosine triphosphate (ATP) release was measured by the luciferin luciferase as described by Feinman *et al*. [8]. The agonists used were adenosine diphosphate (2.5 and 5 μmol/l), epinephrine (10 μmol/l), collagen (1 and 8 μg/ml), arachidonic acid (0.5 mmol/l) and ristocetin (1.2 and 0.4 mg/ml). Quinacrine mustard (0.1 mmol/l) was used as the fluorescent marker of dense granule storage. The quantitation of stained platelets was performed by flow cytometry according to Gordon *et al*. [9]. Light-scatter and fluorescence data were obtained at a logarithmic setting. FACscan (Becton-Dickinson, San José, California, USA) data were analysed with the CELL-QUEST analysis software system (Beckton-Dickinson). The normal control (n = 50) for

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mepacrine labelling gave a normal range of 75 ± 15 (mean ± 2SD).

The antigenic level of von Willebrand factor (vWF) was measured according to Laurell [10] and biological activities [ristocetin cofactor (vWF:Rco)] according to Mac Farlane *et al*. [11]. Factor VIII (FVIII) was tested by a one-stage assay [12], and factor XIII subunits were measured by Laurell [10] with polyclonal antibodies (ASSER XIIIa and ASSER XIIIb; STAGO, Asniéres, France).

The results of vWF, vWF:RCo and FVIII were calibrated against the International Reference Preparation for Factor VIII-related Activities in Plasma, National Institute for Biological Standards and Controls, London.

Case report

The case patient was 19 years old when, in 1986, she presented an episode of acute abdominal pain at ovulation time. Haemoperitoneum was found at laparotomy and wedge resection of the left ovary was performed.

The patient was studied in 1987 and a prolonged bleeding time was observed with normal values of FVIII:C, vWF antigen (vWF:Ag) and vWF:RCo (Table 1). A decreased platelet retention to glass beads was found with a diminished platelet ATP release induced by several agonists. The patient had a previous history of minor bleeding episodes (easy bruising, haematomas, epistaxis and gum bleeding) and her mother had presented frequent haematomas in arms and legs. The patient had not taken aspirin or any other antiplatelet drugs. Her blood group is O+.

The mother was studied in 1987 and a prolonged bleeding time, diminished platelet retention and border line vWF:RCo (50%) were found. We ignore her blood group.

With these studies and familial history, mild von Willebrand's disease and mild storage pool disease were suspected but not confirmed.

A new episode of intraperitoneal bleeding was diagnosed by ultrasound a few years later that did not require surgery and the patient was managed using a conservative approach.

In 1996, von Willebrand's disease was diagnosed (FVIII, 50%; vWF:Ag, 32%; vWF:RCo, 48%). A decreased mepacrine labelling measured by flow cytometry was found and ATP release was reduced again, both studies confirming a mild storage pool disease. Other laboratory tests, e.g. fibrinolysis and factor XIII, were normal.

In October 1999, the patient presented acute abdominal pain at ovulation that was not relieved by antispasmodic drugs. She was admitted a few hours later with a hypovolemic shock and a haematocrit of 12%. Haemoperitoneum was confirmed by laparotomy and the right ovary was removed. After the last episode of haemoperitoneum, oral contraceptives were prescribed without recurrence of the peritoneal bleeding and with normalization of the vWF:Ag (92%) and vWF:RCo (64%).

Discussion

Haemoperitoneum secondary to haemorrhagic cor-

Table 1. Laboratory results

	Patient, 2 February 1987	Patient, 25 September 1996	Patient WOC, 30 March 1999	Mother, 18 June 1997	Normal value
Bleeding time [6]	10 min	10 min	ND	7 min 30 s	< 4 min 30 s
Platelet retention (%)	11	11	ND	15	25–70
Prothrombin time (%)	90	90	96	100	70–100
APTT (s)	44	50.5	48	46	< 50
FVIII (%)	120	50	70	65	50–150
vWF:Ag (%)	100	32	92	84	50–100
vWF:RCo (%)	75	48	64	50	50–100
FXIIIa (%)	ND	105%	ND	ND	50–100
ATP release	D	D	ND	ND	Normal
Mepacrine labelling (%)	ND	56	ND	ND	> 60

WOC, With oral contraceptive; APTT, activated partial thromboplastin time; FVIII, factor VIII; vWF:Ag, von Willebrand factor antigen; vWF:RCo, von Willebrand ristocetin cofactor ; FXIIIa, activated factor XIII; ATP, adenosine triphosphate; ND, not done; D, decreased with all agonists.

pus luteum has been described in severe bleeding disorders such as afibrinogenaemia [1], von Willebrand's disease type 3 [2,3] and also in patients under chronic oral anticoagulation [4,5], but only occasionally observed in mild type 1 von Willebrand's disease (vWD) [13]. Our patient has a severe bleeding tendency because she presented three episodes of haemoperitoneum, the first and last (life-threatening) requiring surgery. Considering the high frequency of vWD, it was our first option but infrequent causes for bleeding such as decreased factor XIII subunits were also investigated [12]. She had abnormal tests suggesting vWD since her first study, supported by her familial history; however, we needed more data to confirm it. It seems difficult to admit that mild storage pool deficiency (confirmed by low level of mepacrine) combined with mild type I vWD is the real cause of recurrent haemoperitoneum. Physicians would prefer to find a severe haemorrhagic disorder as the underlying condition in these cases, but mild von Willebrand's disease associated with other mild haemostatic disorders should also be contemplated in this pathology.

There are no reports on administration of desmopressin (DDAVP) in cases of haemoperitoneum not reaching a surgical stage. If recognized early, this could be a way to avoid surgery.

In women of child-bearing age, we are faced with a big challenge when the patient stops oral contraceptives to become pregnant. An infusion of factor VIII concentrate in severe von Willebrand's disease has been suggested in the past [3] as a prophylactic approach but there are no specific guidelines yet for mild von Willebrand's disease. An ultrasound follow-up with the possibility of using DDAVP in case of detecting a bleeding follicle could be an alternative.

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