Prolonged post-operative bleeding due to an acquired von Willebrand syndrome

S.E. Kinsey, K.O. Ryder and S.J. Machin

Department of Haematology, Middlesex Hospital, Mortimer Street, London, W1, UK.

Summary: Acquired von Willebrand syndrome is a rare cause of post-operative bleeding, and should be considered in all such cases, in spite of previous uneventful surgical challenge.

Introduction

Post-operative bleeding due to a haemorrhagic defect after routine surgical procedures is a well recognized complication and is usually diagnosed by a routine laboratory coagulation screen consisting of a platelet count, prothrombin time, thrombin time and activated partial thromboplastin time.¹ The cause of such abnormalities is then readily recognized and corrected by the administration of vitamin K₁ and relevant blood products such as platelet concentrates, fresh frozen plasma, cryoprecipitate or factor VIII concentrates. However, in elderly patients the possibility of an isolated coagulation factor defect is often not considered in these circumstances. We report the problems experienced in diagnosis and treatment of an unusual acquired haemostatic defect in an elderly man who had prolonged post-operative bleeding after a routine inguinal hernia repair.

Case report

An 81 year old Caucasian man had a routine inguinal hernia repair. On four occasions during the first twenty post-operative days the wound was re-explored to control continual profuse bleeding from the operative site. This resulted in the wound being extended to 32cm in the inguinal region and an orchidectomy being performed due to an expanding scrotal haematoma. After the fourth re-exploration, a coagulation screen revealed a moderately prolonged activated partial thromboplastin time and the patient was then transferred to our hospital for further investigation and management.

Examination on admission revealed an extended surgical scar in the right inguinal region, continually

oozing heavily blood stained fluid with marked associated induration and a large right sided scrotal haematoma. Previous surgery at ages 10 and 42 years had been uneventful with no post-operative bleeding problems. Initial laboratory findings were: haemoglobin concentration 104 g/l, platelet count $658 \times 10^9/l$, prothrombin time 15.5 s (normal range 13–16 s), thrombin time 13.5 s (normal range 12–14 s), activated partial thromboplastin time 60 s (normal range 30–40), template bleeding time > 20 min (normal range 2–10 min) and normal serum biochemistry. Further investigation of the prolonged activated partial thromboplastin time and bleeding time showed: activated partial thromboplastin time repeated with 50% patient's plasma and 50% normal plasma after 10 min incubation, 48 s, factor VIII:C 0.12 IU/ml (normal range 0.5–2.0 IU/ml), factor VIII:vWFag < 0.08 IU/ml (normal range 0.5–2.0 IU/ml), factor VIII:vWF < 0.08 IU/ml (normal range 0.5–2.0 IU/ml), Bethesda inhibitor assay to factor VIII:C negative but to factor VIII:vWF (using a ristocetin co-factor assay) positive at a level of 1.6 units/ml and platelet aggregation responses normal with ADP and collagen but absent with 1.2 mg/ml ristocetin. These results were compatible with a diagnosis of von Willebrand's syndrome with an inhibitor against von Willebrand's factor which was presumably an acquired defect.

To promote wound healing and prevent continual blood loss, treatment was initiated with an infusion of 30 bags of cryoprecipitate. Immediately post-infusion the factor VIII:C level had risen to 0.27 IU/ml but there was no appreciable change in the bleeding time or factor VIII:vWF levels (Table I). In view of these disappointing results and continuing clinical bleeding a 3 litre plasma exchange with human albumin solution and fresh frozen plasma was undertaken followed one hour later by an infusion of 30 bags of cryoprecipitate. This resulted in correction of the abnormal laboratory parameters (Table I) and even-

Correspondence: S.J. Machin, M.R.C. Path.
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Table 1 Changes in haemostatic parameters after initiation of specific replacement

	Presentation	Sample I*	Sample II**	Normal range
Bleeding time (min)	>20	18	12	2–10
APTT (s)	60	48	41	30–40
FVIII:C (IU/ml)	0.12	0.27	3.04	0.5–2.0
FVIII:cWF (IU/ml)	<0.08	<0.08	1.92	0.5–2.0
FVIII:vWFag (IU/ml)	0.08	0.08	0.44	0.5–2.0

*Sample I – 5 min after 30 bags cryoprecipitate

**Sample II – after a 3 litre plasma exchange and 30 bags of cryoprecipitate

APTT = activated partial thromboplastin time; F = factor; C = coagulant; vWFag = von Willebrand Factor (antigen).

tual cessation of bleeding from the old surgical incision.

Factor VIII:vWF levels were maintained above 0.40 IU/ml by 8 hourly infusions of cryoprecipitate and heat treated factor VIII concentrates, and in addition three further plasma exchange procedures were undertaken. During the following 20 days this treatment was continued until the wound was completely healed and the patient fit to be discharged home.

Subsequent investigation revealed an IgG kappa paraprotein of 6.6 g/l with no immune paresis which was considered to be a benign monoclonal paraproteinaemia. This IgG paraprotein was demonstrated to have inhibitory action against factor VIII:vWF functional activity.

Discussion

Acquired von Willebrand's syndrome is an uncommon disorder first reported in 1968,² frequently

associated with systemic lupus erythematosus, lymphoproliferative disorders or isolated IgG paraproteinaemias.³ The diagnosis is usually first suspected by an easy bruising tendency or a prolonged post-operative bleeding episode in an elderly patient who is found to have an isolated prolonged activated partial thromboplastin time and/or bleeding time. Very often the importance of investigating a prolonged activated partial thromboplastin time is overlooked and replacement therapy instigated blindly with fresh frozen plasma. In this patient relevant treatment to arrest prolonged post-operative bleeding required detailed haemostatic studies before a specific therapeutic plan could be initiated and its efficacy monitored. The previous demonstration of an antibody inhibitor to the factor VIII:vWF complex has only recently been recognized.⁴ This enabled effective factor VIII replacement therapy and plasma exchange to be carried out and wound healing to ensue.

References

1. Machin, S.J. Bleeding and coagulation disorders. In: Denham M.F. & Chanarin, I. (eds) *Blood Disorders in the Elderly*. Churchill Livingstone, Edinburgh 1985, pp 132–156.
2. Simone, J.V., Cornet, J.A. & Abildgaard, C.F. Acquired von Willebrand's syndrome in systemic lupus erythematosus. *Blood* 1968, 31: 806–812.
3. Bloom, A.L. The von Willebrand syndrome. *Semin Hematol* 1980, 17: 215–227.
4. Sampson, B.M., Greaves, M., Malia, R.G. & Preston, F.E. Acquired von Willebrand's disease: demonstration of a circulating inhibitor to the Factor VIII complex in four cases. *Br J Haematol* 1983, 54: 233–244.