642-47.
3. Talpaz M, Spitzer G, Hittelman W, Kantarjian H, Gutterman J. Changes in granulocyte-monocyte colony-forming cells among leukocyte-interferon-treated chronic myelogenous leukemia patients. Exp Hematol 1986; 14:668-71.
4. Santucci MA, Soligo D, Pileri S, Zuffa E, Testoni N, Tura S. Interferon-alpha effects on stromal compartment of normal and chronic myeloid leukemia hematopoiesis. Leuk Lymphoma 1993; 11(Suppl.1): 113-8.
5. Ellis TM, McKenzie RS, Simms PE, Helfrich BA, Fischer RI. Induction of human lymphokine-activated killer cells by IFN-alpha and IFN-gamma. J Immunol 1989; 143: 4282-6.
6. Tomás JF, López-Lorenzo JL, Requena MJ, et al. Absence of influence of prior treatment with interferon on the outcome of allogeneic bone marrow transplantation for chronic myeloid leukemia. Bone Marrow Transplant 1998; 22:47-51.
7. Zuffa E, Bandini G, Bonini A, et al. Prior treatment with alpha-interferon does not adversely affect the outcome of allogeneic BMT in chronic phase chronic myeloid leukemia. Haematologica 1998; 83:231-6.
8. Beelen DW, Graeven U, Elmaagacli AH, et al. Prolonged administration of interferon-alpha in patients with chronic-phase Philadelphia chromosome-positive chronic myelogenous leukemia before allogeneic bone marrow transplantation may adversely affect transplant outcome. Blood 1995; 85:2981-90.
9. Muñoz A, Bureo E, Ortega JJ, et al. Treatment of Ph1-positive chronic myelogenous leukemia in children: comparison between allogeneic bone marrow transplantation and conventional chemotherapy. Spanish Working Party for BMT in Children (GETMON). Haematologica 1998; 83:981-4.
10. Anonymous. Potential clinical implications of early diagnosis of chronic myeloid leukemia. Haematologica 1999; 84:289-90.

Prophylactic use of desmopressin in surgery of six patients with symptomatic heterozygous factor XI deficiency

From January 1998 to March 1999, we followed 6 symptomatic heterozygous factor XI (FXI) deficient patients undergoing surgery. There were 4 males and 2 females. Their mean age was 39.8 years (range 6-67 years). Three of the 6 patients were members of the same family. The investigation of additional coagulation abnormalities (e.g. bleeding time, platelet aggregation, other clotting factors levels and von Willebrand factor level) was negative in all 6 patients. This report shows that desmopressin can be used successfully to prevent surgical bleeding in these patients.

Sir,

Patient #1 was a 56-year old female undergoing endoscopic cholecystectomy. Her mother had died at the age of 61 of a post-cholecystectomy hemorrhage. The patient had suffered severe bleeding, which required multiple blood transfusions, after a tonsillectomy at the age of 10. She had had 2 pregnancies, 1 with severe post-partum hemorrhage. At the age of 42 the patient underwent a total hysterectomy and was successfully treated with fresh frozen plasma in order to avoid hemorrhagic complications.

Patient #2, a 65-year old male, the first patient's brother, was transfused aged 60 because of hemorrhagic complications after a prostatectomy.

Patient #3, a 29-year old male, the second patient's son, had received blood transfusions for haemorrhagic complications following splenectomy after road accident trauma. Patients #2 and #3 were scheduled for arthroscopic reconstruction of knee ligaments.

Patient #4, a 67-year old nulliparous female, was to undergo right leg saphenectomy. This patient had suffered from menorrhagia and reported bleeding complications during left leg saphenectomy 2 years previously.

Patient #5, a 6-year old male child, had received blood transfusions at the age of 3, for post-tonsillectomy hemorrhage: he was hypospadic and needed reconstruction of his urethra.

Patient #6, a 16-year old male, suffered from excessive and prolonged bleeding after two dental extractions. He was undergoing hydrocele surgery.

Before surgery, each patient was tested for the response to a subcutaneously injected dose of 0.3 µg/kg of DDAVP. In all patients the desmopressin injection led to normalization of the APTT, a slight increase in FXI activity (mean 12.0 U/dL; range 9-14 U/dL), a marked increase in FVIII:C (mean 147.8 U/dL; range 132-162 U/dL), vWF:Ag (mean 89.3 U/dL; range 68-123 U/dL) and vWF:Ricof (mean

Table 1. Hemostatic parameters before and 60 minutes after subcutaneous DDAVP injection.

Patients	*Before DDAVP*					*60 minutes after DDAVP*				
	APTT (ratio)	*FXI:C (U/dL)*	*FVIII:C (U/dL)*	*vWF:Ag (U/dL)*	*vWF:RiCof (U/dL)*	*APTT (ratio)*	*FXI:C (U/dL)*	*FVIII:C (U/dL)*	*vWF:Ag (U/dL)*	*vWF:RiCof (U/dL)*
Patient #1	1.34	32	104	89	130	1.08	46	260	180	210
Patient #2	1.25	42	130	96	102	1.08	54	275	190	190
Patient #3	1.28	40	87	107	118	1.11	52	249	230	210
Patient #4	1.19	45	117	107	107	0.91	54	270	175	210
Patient #5	1.35	36	117	104	110	1.11	50	256	188	205
Patient #6	1.32	34	108	94	104	1.07	45	240	170	175

Normal range: APTT = 0.8-1.15 (ratio); FXI:C = 60-140 U/dL; FVIII:C 50-150 U/dL; vWF:Ag = 60-150 U/dL; vWF:RiCof = 50-145 U/dL.

74.8 U/dL; range 71-103 U/dL) levels (Table 1).

In patient #1 we utilized desmopressin (0.3 µg/kg s.c. starting 60 min before the operation) 12 hourly on the day of the operation, then once daily until day +4. We gave DDAVP once daily (0.3 µg/kg s.c.) for 5 days to the remaining patients, starting on the day of the operation. All patients received tranexamic acid (10 mg/kg thrice daily i.v. for 5 days). Serum electrolytes were monitored regularly.

DDAVP therapy was well tolerated and no hemorrhagic complications occurred during or after surgery.

FXI deficiency is a rare inherited coagulation disorder characterized by rarity of spontaneous bleeding but the risk of severe hemorrhagic complications after trauma or surgery. There is often little direct correlation between the tendency to bleed and the severity of the disease itself, so it is extremely difficult to predict hemorrhagic complications after surgery in patients with mild disease.[1-3]

Currently available therapeutic products for the treatment of bleeding in FXI deficient patients include fresh frozen plasma and virus-inactivated FXI concentrates: the former may carry blood-borne viruses, the latter, although the first choice treatment in patients with severe FXI deficiency, should be used cautiously because of its thrombotic risk.[4-6]

Recent reports indicate that DDAVP has been used successfully to prevent surgical bleeding in FXI defective patients.[7,8] Our case reports confirm these findings: we first tested and then utilized subcutaneous desmopressin in symptomatic heterozygous FXI deficient patients undergoing surgery. No hemorrhagic complications occurred peri-operatively.

It remains to be clarified how DDAVP acts in such patients: the administration of DDAVP causes a slight increase in FXI activity and a marked increase in FVIII/vWF levels with normalization of APTT. Even though the observed APTT normalization is probably linked to the marked increase in FVIII:C, the slight but significant increase in FXI activity may contribute to the hemostatic efficacy of DDAVP in such patients.

Spurious increases of FXI:C in functional assays due to concomitant, DDAVP-dependent increases of FVIII:C are rather unlikely as Castaman *et al.*[7] have previously demonstrated parallel degrees of increase in both FXI:C and FXI:Ag after administration of DDAVP.

However, although the mechanism by which DDAVP increases FXI levels is still not clear, our data suggest that this drug is effective in preventing surgical bleeding in patients with mild factor XI deficiency.

Massimo Franchini, Marzia de Gironcoli, Giuseppe Lippi, Franco Manzato,* Giuseppe Aprili, Giorgio Gandini*

*Servizio di Immunoematologia e Trasfusione - Centro Emofilia, Azienda Ospedaliera di Verona, and *Istituto di Chimica e Microscopia Clinica, Università di Verona, Italy*

Key words

Factor XI deficiency, desmopressin, hemophilia.

Acknowledgments

The authors thank Mrs. Anne Immovilli for her language supervision and Mrs. Daniela Alberti for her technical support.

Correspondence

Massimo Franchini, Servizio di Immunoematologia e Trasfusione, Centro Emofilia, Ospedale Policlinico, via Delle Menegone 1, 37134 Verona, Italy.

Phone: international +39.045.8074321 – Fax: international +39.045.8074626.

References

1. Bolton-Maggs PHB, Young Wan-Yin B, Mc Graw AH, et al. Inheritance and bleeding in factor XI deficiency. Br J Haematol 1988; 69:521-8.
2. Smith JK. Factor XI deficiency and its management. Haemophilia 1996; 2:128-36.
3. Bolton-Maggs PHB. Factor XI deficiency. Baillére's Clin Haematol 1996; 9:355-68.
4. Mannucci PM, Bauer KA, Santagostino E, et al. Activation of coagulation cascade of a factor XI concentrate in congenitally deficient patients. Blood 1994; 84:1314-9.
5. Bolton-Maggs PHB, Colvin BT, Satchi G, et al. Thrombogenic potential of factor XI concentrate Lancet 1994; 344:748-9.
6. Richards EM, Makris MM, Cooper P, Preston FE. In vivo coagulation activation following infusion of highly purified factor XI concentrate. Br J Haematol 1997; 96:293-7.
7. Castaman G, Ruggeri M, Rodeghiero F. Clinical usefulness of desmopressin for prevention of surgical bleeding in patients with symptomatic heterozygous factor XI deficiency. Br J Haematol 1996; 94:168-70.
8. Bauduer F, Bendriss P, Freyburger G, Ducout L, Marti B. Use of desmopressin for prophylaxis of surgical bleeding in factor XI-deficient patients. Acta Haematol 1998; 99:52-3.

Comparison between radial immunodiffusion and flow cytometry techniques for detecting antiplatelet antibodies

The aim of our work was to compare radial immunodiffusion (RI) (in use for years) versus flow cytometry (FC) (a new technique). The discrepancies of the results in our patient population indicate that both techniques are valuable tools to understand the pathogenesis of thrombocytopenia.

Sir,

To evaluate the clinical use of RI and FC for detecting antiplatelet antibodies, we analyzed platelet samples from 39 patients. The samples were grouped according to the etiology of the thrombocytopenia into: group A (n=12): immune thrombocytopenic purpura (ITP) (Table 1), group B (n=19): conditions associated to bone marrow failure or malignancy (Table 2) and group C (n=8): unexplained mild thrombocytopenia.

Surface platelet associated IgG (PAIgG) was assayed by FC using the procedure described by Lin *et al.*[1] and total (PAIgG) by RI using the procedure described by Morse *et al*.[2] We observed significant positive correlations between both methods when all 39 cases were examined (r=0.44, *p*=0.006). The main contribution to this significant positive correlation was given by group A results (r=0.8, *p*=0.0018).