Case report: Use of recombinant von Willebrand factor in a patient with acquired von Willebrand syndrome due to specific IgM-antibodies directed against von Willebrand factor

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Introduction

Acquired von Willebrand Syndrome (avWS) is a rare coagulation disorder which can be associated with IgM-paraproteinaemia. Some patients develop specific antibodies against von Willebrand factor (vWF) that increase its clearance. Recently, recombinant vWF has become available for the treatment of bleedings and prevention of surgical bleedings in patients with inherited von Willebrand`s disease, but experience in patients with avWS is limited. Here we report on an 80-year-old patient who presented with recurrent, severe transurethral bleeding and was diagnosed with avWS and underlying IgM-paraproteinaemia with evidence of a specific antibody against vWF (proven by ELISA). Patient's characteristics and laboratory results at presentation are shown in Table 1. Figure 1 shows results of SDS-agarose-Gel electrophoresis for multimer analysis.

Table 1: Patient characteristics and laboratory results at presentation

Age	80
Gender	male
Underlying disease	Monoclonal IgM-paraproteinaemia
Paraprotein	IgM-kappa
Serum concentration of paraprotein (mg/ml)	94 (40-230)
Platelets /nl	288 (163-337)
APTT(sec)	40 (26-37)
FVIII:C (%)	29 (70-150)
vWF:Ag (%)	27 (57-174)
vWF:Ac (%)	6 (47-173)
Thrombocyte aggregometry (Born) (%)	ADP: 89 (>70) Collagen: 82 (>70) Ristocetin: no activation (>70) Arachidonic acid: 85 (>70)
vWF plasma multimers	Type 2
Anti-vWF	positive
Proposed mechanism	Immunologic clearance

Normal values are shown in brackets.

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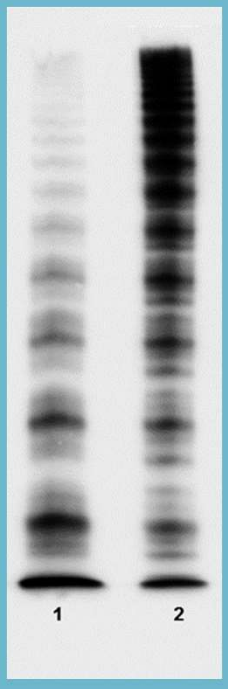
The patient's transurethral bleeding required several transfusions despite local electric coagulation. Hemostyptic treatment was initiated with tranexamic acid and a plasmatic (p) vWF/factor (f) VIII product. The first administration of pvWF/fVIII (40 IE/kg) resulted in an increase of vWF activity from 6% to 52%, but after 4 hours vWF activity decreased to 26% and after 24 hours to 16%. In parallel vWF specific antibody eradication was started with prednisolone (1 mg/kg/day) followed by rituximab (375 mg/m² body surface area, weekly, 4 cycles). Repetitive application of pvWF/fVIII did not sufficiently elevate vWF activity despite increasing doses of pvWF and bleeding reoccurred. Treatment with recombinant vWF (Vonicog alfa) was initiated due to the higher content of high molecular weight multimers. We observed an increased recovery of vWF activity within 2 hours after the first application of Vonicog alfa (42 IE/kg) from 32% to 75%. 12 hours after a second application (42 IE/kg) vWF activity was still 59%. Bleeding stopped after application and did not occur again (even though vWF activity levels were decreasing by time despite higher doses of Vonicog alfa). Due to the insufficient effect of immunosuppressive therapy with prednisolone and rituximab, we initiated a therapy with dexamethasone (20 mg on day 1, 2, 4, 5, 8, 9, 11, 12) and bortezomib (1,3 mg/m² on day 1, 4, 8, 11). After only one cycle of therapy, the IgM-paraproteinaemia disappeared and vWF activity increased to 200%. No adverse events were reported.

Conclusion

Use of recombinant vWF was safe and highly effective in a patient with avWS and underlying IgM-paraproteinaemia with a specific antibody against vWF and might be taken into consideration for treatment of acute bleeding in these patients. Since bleeding stopped after administration of Vonicog alfa despite decreasing vWF levels, it is possible that transient presence of high molecular weight multimers is sufficient to control bleeding in patients with avWS. Further research needs to be done on this topic.

Figure 1: Multimer analysis of patient's plasma at presentation



Multimer analysis (SDS-agarose Gel electrophoresis) of patient's plasma (1) and a normal patient's plasma (2) indicates the loss especially of the high molecular weight multimers in our patient.

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