rupture may also be due to trauma such as sneezing, rough coitus or blunt abdominal injury. The overgrowth of the fungus *T. glabrata* is an interesting complication in our case. It seems that in this patient the fungus caused a local infection, since repeated attempts to culture it from the blood failed. The problem of *T. glabra* fungaemia has recently been reviewed by Block et al. This organism may be found as a commensal in the body and has pathogenic potential.

In view of our inability to document a fungaemia in the patient, antifungal treatment was withheld and there was spontaneous recovery.

**REFERENCES**


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**Von Willebrand's disease in pregnancy**

**A case report**

O. SADAN, P. MacPHAIL, A. B. KOLLER, G. J. HOFMEYR

**Summary**

A 30-year-old woman with von Willebrand's disease completed her third pregnancy uneventfully. She was infused during labour with fresh frozen plasma and cryoprecipitate. This is in keeping with the good outcome reported in the literature when management is appropriate and surveillance is maintained.

Von Willebrand's disease is a bleeding disorder caused by an autosomally inherited qualitative and/or quantitative abnormality of the von Willebrand factor (VWF), a portion of the factor VIII complex (Table I). Abnormalities of this factor, responsible for the adherence of platelets to damaged endothelium, result in prolonged bleeding time. In von Willebrand's disease platelet dysfunction may be associated with a reduced level of factor VIII:C, which acts as a co-factor in the coagulation cascade. This may result in bleeding similar to that seen in classic haemophilia.

In order to highlight recent advances in the understanding of this disorder a case report and review of the relevant English-language literature is presented.

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**TABLE I. NOMENCLATURE OF THE FACTOR VIII/VWF COMPLEX**

| VIII:C | The protein co-factor involved in the intrinsic activation of factor X and which corrects the coagulation abnormality in haemophilia A |
| VIII:C Ag | The antigenic expression of VIII:C |
| VWF | The large protein with a multimeric structure involved in the adherence of platelets and which corrects the bleeding time in von Willebrand's disease |
| VIII R:Ag | The antigenic expression of the VWF |
| VIII R:R Co | Ristocetin co-factor; a property of VWF which promotes platelet agglutination in the presence of the antibiotic ristocetin |
| Factor VIII complex | The form in which VIII:C and VWF normally circulate in the plasma; sometimes referred to as the factor VIII/VWF complex |

**Case report**

The patient, a 30-year-old white woman, attended the antenatal clinic of Johannesburg Hospital at 7 weeks’ gestation. Von Willebrand’s disease had been diagnosed at the age of 13 years when her bleeding time was prolonged (less than 30 min), factor VIII:C activity was 23%, factor VIII R:Ag was 24% and the ristocetin co-factor (VIII R: RCo) was 25%. A family history suggestive of an autosomal dominant inheritance was present. Fresh frozen plasma (FFP) and cryoprecipitate were infused during her previous labours. Healthy infants weighing 2 800 g and 3 300 g were delivered spontaneously and blood loss was measured at 250 ml and 300 ml respectively.

The antenatal course of the present pregnancy was uneventful. Factor VIII:C activity rose to 70% with a normal partial thromboplastin time but bleeding time remained prolonged with a VIII R:Ag
Discussion

Von Willebrand's disease is a bleeding disorder with a complex haemostatic defect. A prolonged bleeding time due to abnormal platelet function is a consistent finding and may be accompanied by a coagulation defect resulting from decreased factor VIII procoagulant (VIII:C) activity. These abnormalities arise from qualitative and/or quantitative abnormalities of the VWF, a large multimeric glycoprotein necessary for the adherence of platelets to damaged endothelium, and complexed with the factor VIII:C in the circulation.1,2 Recently, discovery of aberrations in the multimeric structure of the von Willebrand protein has permitted classification of the disease into seven subtypes (IA-B; IIA-D; III).3 These abnormalities are inherited as either dominant or recessive traits and phenotypic expression varies greatly both between and within individual cases.4

The diagnosis depends on the demonstration of abnormal platelet function with a prolonged bleeding time and abnormal ristocetin-induced platelet aggregation, as well as abnormally low levels of VIII:C and the antigen associated with the VWF (VIII R:Ag).5,6 Von Willebrand's disease often presents in early childhood, usually with mucous membrane bleeding (e.g. epistaxis). Excessive bruising, bleeding after dental extractions and menorrhagia are common. Patients with very low levels of VIII:C may experience bleeding indicative of defective coagulation, such as haemarthrosis. In pregnancy factor VIII activity rises slightly in the first trimester but remains steady until the middle of the third trimester, after which it may rise sharply to peak at term. These changes are unlikely in patients with initial factor VIII levels less than 30%, who will need factor VIII replacement during delivery.5,7 All patients with von Willebrand's disease have a high risk of bleeding during spontaneous abortion in early pregnancy.6,8

The spontaneous rise in factor VIII activity during pregnancy may obviate the need for replacement therapy at delivery. Krishnamurthy and Miotti9,10 reported a successful caesarean section without factor VIII cover in a patient with von Willebrand's disease who had normal levels of factor VIII:C and VIII R:Ag but a prolonged bleeding time. In a review of 17 cases in the English-language literature up to 1972 Noller et al.11 pointed out that only 5 patients had serious bleeding problems. Of these, 1 developed intrapartum haemorrhage. In 3 patients the levels of the VWF at delivery were low. Factor VIII:C activity and the bleeding time should be monitored during pregnancy. If these remain abnormal it is advisable to raise the level of the factor VIII:C above 30% before delivery or 60% before operation and maintain it at or above this level during the first week of the puerperium, or postoperatively.12 Infusion of preparations containing the large multimers of VWF will restore the bleeding time to normal for 8 - 12 hours and elevate the level of factor VIII:C. The latter will continue to rise for 12 - 24 hours after infusion and may obviate the need for further infusion. Only FFP and cryoprecipitate, either single donor 'wet' preparations or frozen dried preparations from small donor pools, contain these multimers. Factor VIII concentrates used in the treatment of classic haemophilia do not contain large multimers of VWF and are not suitable for the treatment of von Willebrand's disease. Cryoprecipitate should be used in preference to FFP since a smaller volume is needed. A single dose of FFP or cryoprecipitate of between 30 and 50 U of VIII:C/kg is usually sufficient and should be infused once the first stage of labour is established.

After the third stage, the danger of bleeding due to the platelet disorder is considerably less, provided adequate contraction of the uterus is maintained. Replacement therapy in the week following delivery should be governed by the level of factor VIII:C and the occurrence of bleeding. In some types (I and II) of von Willebrand's disease an infusion of 1-deamino-8-d-arginine vasopressin (DDAVP) may correct the abnormal VIII:C activity and in type I the bleeding time as well,13,14 but its use in pregnancy is not advised. Firstly, response is limited to type I and some forms of type II. Secondly, it is likely that patients who respond to DDAVP will show spontaneous improvement in VIII:C activity during pregnancy and lastly DDAVP should be avoided in conditions such as child-birth where primary haemostasis cannot be assured by mechanical means, and where bleeding might be excessive.15 Oestrogen therapy has also been reported to result in less bleeding than expected in surgical procedures.15

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