Acquired von Willebrand’s Disease Associated with Gastrointestinal Angiodysplasia and Monoclonal Gammopathy

Sir,

Acquired von Willebrand’s Disease (AVWD) is a rare bleeding disorder, usually occurs in elderly patients. We would like to present case with recurrent gastrointestinal bleeding diagnosed to have AVWD with inhibitors.

A 63 years male presented with a history of recurrent episodes of lower gastrointestinal bleeding for three years. He had also a history of occasional epistaxis and skin bleeds for last 3 months. Repeated endoscopic gastrointestinal examinations demonstrated the presence of multiple angiodysplastic lesions in the descending and sigmoid colon. Family history revealed no members with known bleeding disorders. On examination, he was pale and there were few scattered generalized petechiae. Other physical findings were unremarkable. Hemogram showed Hb of 7.4gm /dl, TLC of $6.4 \times 10^9$/ L, platelet count of $230 \times 10^9$/ L. Peripheral smear examination showed microcytic hypochromic anemia with no abnormal cells. Initial coagulation screening revealed a normal prothrombin time (PT); a prolonged activated partial thromboplastin time (APTT) and a prolonged Ivy bleeding time. At presentation, FVIII procoagulant activity (20%), vWF antigen levels (22%), and ristocetin cofactor activity (13%) were markedly reduced. The ratio of VWF:RCo : VWF:Ag was less than 0.7. Multimeric analysis revealed loss of high molecular weight (HMWM) and intermediate molecular weight multimers. An in-vitro Inhibitor against vWF of the patient’s plasma was demonstrated. A final diagnosis of AVWD – subtype 2A with inhibitors to VWF was made. The patient’s bleeding episodes were initially managed with cryoprecipitate replacement and desmopressin therapy to which he showed an adequate response in terms of his clinical situation and his haemostatic parameters. Patient was subsequently started on steroid therapy (60 mg./day) as a measure of immunosuppression. He continued to have bleeding episodes without any significant improvement. Patient was then managed with plasmapheresis followed by intravenous immunoglobulins (20g/day for 5 days) to which he showed an adequate response in terms of his clinical situation and his haemostatic parameters. After 2 months patient was planned for hemicolectomy, but before surgery he had massive inferior myocardial infarction and died.

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However most of these conditions are associated with protein C deficiency. Priapism is an unusual manifestation of warfarin-induced skin necrosis.

A 46 years male was presented with a history of pain and swelling of the left lower limb for 1-week duration. Doppler ultrasonography showed thrombosis of left peroneal and femoral vein. Patient was managed with...
conventional heparin for first 3 days, subsequently switched over to oral anticoagulant i.e. warfarin at a dose of 4 mg per day. One day following the warfarin therapy, patient developed pain and swelling of the penis as well as retention of urine. On examination, penis was swollen and there were multiple purple bullae with serous exudates over the penis. Hemogram, blood biochemistry was within normal limits. His prothrombin time was 28.2 seconds (control 11-13 seconds). Warfarin was withdrawn and conventional heparin started. Vitamin K and fresh frozen plasma were also administered. Patient was catheterized for retention of urine. As patient did not improve in 48 hours, an opinion of urologist was taken and wound debridement along with cavernous shunt was carried out. Patient improved after 2 days. Thrombophilia screening showed normal level of protein S and antithrombin III. Protein C level was 32% suggesting protein C deficiency. Screening of the family members revealed his sister had also protein C deficiency. After 2 weeks of heparin therapy, warfarin was restarted with a low dose i.e. 1 mg / day, without a loading dose along with heparin. Warfarin was gradually increased to 4 mg/day over a period of fifteen days and heparin was discontinued. Patient was discharged from the hospital on warfarin (4mg / day) and is on follow up.

Warfarin-induced skin necrosis is a rare side effect of the drug and is estimated to occur in only 0.01-0.1% of patients taking the drug.1 The etiology of warfarin induced skin necrosis is obscure and is thought to occur from a transient imbalance in the procoagulant and anticoagulant pathways leading to small vessel thrombosis and subsequent dermal necrosis.1 Areas rich in subcutaneous fatty tissues are typically involved, particularly the breasts, thighs and buttocks.1,2 Warfarin induced penile necrosis with priapism is rare. Only few cases have been reported in literature.2,3 The condition must be differentiated from cellulitis. Amputation of the penis should be avoided, since necrosis usually is limited to superficial tissues.1-3 Many of these patients have protein C deficiency. Acute management includes vitamin K and plasma supplementations as well as parenteral anticoagulant until necrotic lesions have healed. In some patients it may be possible to restart warfarin, but needs to be done slowly.2 Our patient recovered with conservative management and warfarin was successfully re-instituted without further complication. Clinicians and urologist should be aware of this condition to make correct diagnosis and initiate appropriate therapy so that the patient could be spared of unnecessary penile amputation.

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REFERENCES

Leptospirosis in Chennai - Changing Clinical Profile

Sir,

In a recent article, M Jayakumar et al from Chennai have stated that acute renal failure (ARF) due to leptospirosis in Chennai has significantly declined from 31% in 1987–91 to 7.5% in 1995–2004. Of the 120 cases of leptospiral ARF during the period 1987–91, the highest number of 45 cases were reported in 1990.1 Since 1992, there has been a decline in leptospiral ARF cases and during a 10 years period from 1995-2004, only 84 cases were reported.

Our experience also suggests that though severe leptospirosis has declined, mild leptospirosis has increased. In a study of 57 cases in 1990-91, Jaundice occurred in 84% and renal failure occurred in 72%. Serogroup Automnalis was the most common serogroup encountered. 26 patients were dialysed and two patients died.2 In a recent study of 106 cases of leptospirosis from North Chennai, Jaundice occurred in 17.8% and renal failure occurred in 10.3% showing a decline in complications. Fever, headache and myalgia were the common presentations. Only 2 patients were dialysed and there were no deaths. Contaminated environment (95%) and rainfall (50%) were the important epidemiological risk factors. Icterohemorrhagiae was the most common serogroup and Autonium was not detected.

The reasons for decline of severe leptospirosis suggested were greater awareness of the disease, availability of better diagnostic facilities and widespread use of antibiotics. In addition, serogroup Automnalis, a virulent serogroup causing severe leptospirosis has also declined since 1995. The seropositive prevalence rate in Chennai was 32.9% in 1993. The increase in mild leptospirosis suggests that the environmental risk factors (Infected rodents and domestic animals, contaminated environment and rainfall) play an important role in the persistence and spread of the disease. Intensive surveillance for early detection of mild leptospirosis with appropriate therapy would definitely play an important role in reducing the incidence of severe leptospirosis.

Since diagnostic tests become positive only after 5 days, it would be appropriate to start empiric therapy in suspect cases of leptospirosis with Doxycycline or other appropriate antibiotics.