CORRESPONDENCE

ACQUIRED VON WILLEBRAND'S DISEASE IN THE MYELOPROLIFERATIVE SYNDROME

To the Editor:

We read with great interest the article of Budde et al in the November 1984 issue of *Blood* concerning two patients with myeloproliferative disorders who developed an acquired form of von Willebrand's disease following splenectomy.[1] This report confirms and extends our previous observations.[2] As in the study of Budde et al, we investigated post-splenectomy hemorrhage in a patient with myeloproliferative disease which occurred at a time of rising platelet counts. While we did not perform multimer analysis of the von Willebrand protein in the patient's plasma, the discrepancy between ristocetin cofactor activity (2.5%) and factor VIII-related antigen (60%) suggested the diagnosis of variant von Willebrand's disease. Our patient, too, responded to factor VIII (cryoprecipitate) infusion. Subsequent to this episode, the hemostatic abnormality disappeared spontaneously. An antibody against the von Willebrand protein was ruled out. Prompted by this observation, we prospectively investigated patients with the myeloproliferative syndrome known to us at that time, including ristocetin cofactor determinations. Subnormal ristocetin cofactor activity was found in five of nine patients with polycythemia vera and in one of 12 patients with chronic myeloid leukemia.[2]

Since then, we have regularly been investigating the factor VIII/von Willebrand factor system in every patient with the myeloproliferative syndrome when considering antithrombotic treatment, biopsy, or surgery. As a result, considerable fluctuation of measured ristocetin cofactor activities was found during repeated examinations of the same patient. Recently, another severe bleeding episode attributable to acquired von Willebrand's disease was detected in a patient with polycythemia vera at the time of thrombocytosis following splenectomy, presenting with a ristocetin cofactor activity of <2% and an antigen value of 115%.

From our own observations and the recent study of Budde et al, one must conclude that "acquired defects of the VIIIR:WF system are, in addition to the well known functional abnormalities of blood platelets, quite common in myeloproliferative disorders, especially polycythemia vera, and must be reckoned with before surgery in particular."[2] The etiology of this type of acquired von Willebrand's disease remains mysterious.

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To the Editor:

We have read with interest the report of Budde et al[1] on "Acquired von Willebrand's Disease in the Myeloproliferative Syndrome." The authors described a decrease of VIIIR:RCOF levels, lack of larger von Willebrand multimers, and an alteration of multimeric triplet in two thrombocythemic patients with bleeding symptoms.

Several biochemical and metabolic platelet abnormalities have been described in myeloproliferative disease (MPD),[2,3] but a clear relationship between platelet features and thrombohemorrhagic complications is still not well established.[4] We have also studied factor VIII-related properties in 24 patients with increased platelet number. Twenty-one were affected by primary thrombocytosis: eight had polycythemia vera (PV) (mean platelet count ± SD, 1,111 ± 990 × 10^9 platelets per liter), 13 had essential thrombocythemia (ET) (1,296 ± 626 platelets × 10^9 per liter), and three had secondary thrombocytosis (ST) (869 ± 217 platelets × 10^9 per liter).

Histories of hemorrhages and thrombosis were recorded (28% thrombosis, 52% hemorrhages), but at the time of study, only two patients were symptomatic with bleeding symptoms. Normal values of VIII:C and VIIIR:Ag were found in all patients studied. On the contrary, a significant decrease ($P < .05$) of VIIIR:RCOF, related to the lack of larger vWF multimers, was found in 57% of the MPD patients. The mean VIIIR:RCOF value in patients with abnormal results was 43% ± 13% (range, 18% to 52%) and the mean value of larger vWF multimers (expressed as the percentage of normal densitometric scan) was 39% ± 12% (range, 31% to 56%). The incidence of vWF abnormalities was 70% in ET patients and 38% in PV patients. A normal vWF pattern was observed in the three patients with ST.

A significant correlation ($P < .03$) was found between platelet count and the levels both of VIIIR:RCOF and vWF multimeric pattern in PV patients, while the significance was lacking in patients with ET. These features and the normal vWF composition presented by ST patients suggest that the abnormality was not induced simply by high platelet number. This agrees with the partial improvement in vWF multimeric pattern obtained by Budde through the lowering of the platelet count.[1] However, the lowest level of VIIIR:RCOF and the greatest loss of larger multimers (both less than 30% of normal) were observed in two patients who presented a platelet number higher than 2,500 × 10^9 per liter and bleeding symptoms at the time of the study. The relationship between the vWF picture and bleeding diathesis in MPD was confirmed by the observation that 75% of the asymptomatic patients with the decrease of larger vWF multimers and of VIIIR:RCOF had bleeding history, while only 22% of