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Acquired Type I von Willebrand's Disease in a Patient with Essential Thrombocytosis

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Both thrombotic and haemorrhagic complications may occur in patients with myeloproliferative disease (MPD) [3, 4, 8], often as an expression of different steps of the same condition. Furthermore, no strict correlation between clinical manifestations and increased platelet number 'per se' is seen, suggesting the presence of qualitative platelet defects in addition to the simple enhancement of platelet count. Recently, a possible explanation for the haemorrhagic events seen in MPD was supplied by the description of an acquired von Willebrand's disease (vWd) associated with the increased platelet number [1, 2, 5]. An abnormal factor VIII pattern characterized by a decreased factor VIII ristocetin co-factor (VIII:RCoF) and a disappearance of circulating higher-molecular weight multimers with normal factor VIII-related antigen (VIII:Ag) and factor VIII coagulant (VIII:C) was observed. All patients studied showed a pattern similar to type IIB vWd even though no hyperresponsiveness to ristocetin was found [7]. We have recently studied a young patient with essential thrombocytosis who shows an apparently acquired type I vWd. The patient is a 9-year-old girl who was asymptomatic at the time of study, with a platelet count of 1200×10^9 platelets/l. She presented a prolonged bleeding time (7 min 30 s vs. a normal one of less than 6 min) an abnormal partial thromboplastin time (PTT = 46.6 s vs. a normal one of 36 s) together with a normal ristocetin platelet aggregation (RIPA). All the components of factor VIII complex were decreased (see table I), with a major reduction for VIII:RCoF value (17%). In addition, all multimeric components of the von Willebrand factor were represented even though reduced as confirmed by SDS-agarose gel electrophoresis and autoradiography. This pattern is similar to a mild form of vWd, the only difference from it being a normal RIPA. It is interesting to note that, also in this patient as already observed in MPD patients with type IIB like vWd, RIPA doesn't seem to be affected by the abnormal plasmatic pattern of vWd. No significative differences in factor VIII assay and multimeric pattern were found using an antiproteolytic cocktail containing EDTA (6 mM), Leupeptin (200 µg/ml) and n-ethylmaleimide (5 mM), thus excluding a possible in vitro consumption or an artifactual disappearance of von Willebrand's factor during the blood sample manipulation [6]. The family study failed to demonstrate the presence of other members with a tendency of bleeding and factor VIII abnormality, confirming the acquired

nature of the reported pattern. The observation of an acquired type I vWd in a patient with essential thrombocythosis in addition to the already described acquired type IIb-like forms and the lack of correlation between platelet count and factor VIII decrease in other essential thrombocythosis patients studied by us [5], suggests the presence of a marked heterogeneity in platelet abnormalities in this disease. Therefore, the abnormal pattern of factor VIII cannot be explained only on the basis of an increased platelet count in MPD. It is worth noting that a correlation between these two parameters is present, on the contrary, in polycythemia vera [5].

Table I. Factor VIII-related properties in the proposita and in her parents as compared with normal values

Subjects	PTTs	RIPA 1.5mg/ %	VIII R: RCoF %	VIII R: Ag %	VIII: C %
Proposita	46.6	86.6	17	25	34
Mother	35.5	79.1	113	118	132
Father	33.9	75.2	121	135	136
Normal	30-40	70-110	60-	60-	60-

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