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PRS GLOBAL OPEN

VIEWPOINT

Hemostasis and Type 1 Neurofibromatosis

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It has long been known that patients with neurofibromatosis type 1 (NF1) have a propensity to bleed, in particular during neurofibromas surgery.[1] The massive bleeding in NF1 is largely responsible for the high disease mortality. Thus, minor surgical interventions may become a real challenge, even for experienced surgeons.

Bleeding is the result of both an increased vascular fragility and primary hemostasis disorders.[2] Despite this finding, direct studies of hemostasis in NF1 patients are essentially lacking, but necessary. Then, we tried to assess primary hemostasis in a cohort of NF1 patients who underwent surgical intervention in our plastic surgery department, between January 2012 and January 2014.

In our study of 135 patients, we found an elevated activated partial thromboplastin time (APTT) in 13 patients. Further analyses of these patients revealed 2 von Willebrand disease (VWD), 1 reduction in factor XI, 2 reductions in factor XII, and 1 in von Willebrand factor (VWF) (Table 1). Other blood parameters, including platelet count, prothrombin time, thrombin time and fibrinogen, were normal in all subjects.

VWD is an inherited bleeding disorder resulting in impaired concentration, structure, or function of VWF. The prevalence of all forms of VWD is of about 1% in the general population. Our study showed similar rates (1.4%).

In 1983, Prieto Veiga et al.[3] have described an association between NF1 and VWD. A common embryologic alteration in the mesenchyme has been suggested as the pathogenic mechanism. In 1995, Rasko et al.[2] have studied hemostasis in a cohort of 28 NF1 patients and suggested that a plasma factor, present in a significant proportion of NF1 patients, could interfere with the ability of collagen to interact with other proteins such as VWF and the platelet collagen receptor.

In our study, the APTT was elevated in 13 patients. The APTT allows exploring an entire set of coagulation factors. However, one limitation of this test is that the result is an average of these clotting factors levels. Thus, it would be preferable to use a more reliable test that can detect hemostasis disorders, including the presence of VWD.

Table 1. Coagulation Analysis for the Patients with Abnormal APTT

Patient	Age (y)	APTT	F8	VWFa	F9	F11	F12
1	33	1.24	104	—	95	97	100
2	28	1.21	98	—	90	100	110
3	23	1.33	100	—	97	93	100
4	18	1.30	57	57	80	98	56
5	45	1.37	27	32	98	95	100
6	56	1.42	19	24	100	98	99
7	20	1.36	103	—	89	100	48
8	26	1.38	60	53	90	97	40
9	32	1.30	100	—	95	34	98
10	46	1.27	90	—	90	100	95
11	19	1.26	97	—	99	100	93
12	30	1.35	100	—	99	95	100
13	31	1.41	108	—	96	97	97

APTT results in this table are given in ratio patient/control. Coagulation factor results are given in percentage.
APTT, activated partial thromboplastin time; VWF, von Willebrand factor

The PFA-100 (Siemens Healthcare, Marburg, Germany) is a relatively new tool for the investigation of primary hemostasis.[4] Properly used, it can be considered a worthwhile addition to hemostasis laboratories involved in the identification of primary hemostatic disorders and in the diagnosis or therapeutic monitoring of VWD.

Our results did not show abnormally high levels of hemostasis abnormalities in this cohort of NF1 patients. However, the results of only 13 patients were verified in our hospital with PFA-100 dosage.

Although previous studies have shown no correlation between hemostasis abnormalities and intraoperative bleeding severity, it would still appear precautionary to assess hemostasis in NF1 patients, in particular in those undergoing surgery.

According to us, it would be preferable to perform this evaluation in a hospital setting, with PFA-100 analysis, in all NF1 patients before surgery. The results of this pilot study will allow us to suggest this assessment to all NF1 patients followed in our hospital and to estimate the prevalence of bleeding disorders in a larger sample of patients with this condition.

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Plast Reconstr Surg Glob Open 2017;5:e1414; doi:10.1097/GOX.0000000000001414; Published online 26 July 2017.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.

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