VON WILLEBRAND DISEASE
BE OR NOT TO BE, THAT IS THE QUESTION

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OBJECTIVES

Bleeding disorders can be challenging to evaluate. Recent research has highlighted the clinical variability in bleeding symptom expression among defined bleeding problems. Moreover, risks for many bleeding disorders are unknown. Von Willebrand disease (vWD) is the most common inherited bleeding disorder, but variable severity and several classification types mean that diagnosis is often not straightforward.

The authors intend to present the case of a patient with important hemorrhagic diathesis, whose diagnostic clarification has been very challenging.

METHODS

Female, 30 years old, easy bruises, mainly after pregnancy two years before, diagnosis of vWD studied abroad. Hemogram, coagulation screening tests, determination of von Willebrand factor (VWF) and factor VIII levels (HemosIL® Reagents), multimers analysis, molecular study (PCR/Direct Sequencing and Capillary Electrophoresis in 3130 Genetic Analyzer), platelet aggregation (PPA-100 and aggreometry, Multiply ® Analyzer) and thrombin generation (TG) studies (CAT – Calibrated Automated Thrombogram, by Stago) were done. Study of parents and sister.

RESULTS

Bleeding score (BS) 11/3 to +45 (easy and severe bruising, wounds, dental extractions and menorrhagia), blood group 0, one eutocic delivery, no previous surgery. Medicated with paroxetine, for depression.

VWF levels (antigenic and functional) border-line, not less than 30% (3 samples), normal multimeric distribution (2 samples), molecular analysis showed two heterozygotic missense mutations in exon 28 (c.4508 T>C, p.Leu1503Pro and c.4517 C>T, p.Ser1506Leu), referenced in association with vWD type 2A and a splicing mutation in exon 30, not described. Reduced TG.

No deficits of clinically important factors, no dysfibrinogenemia, normal platelets number and aggregation studies without changes. Mother’s BS 11/3 to 45, father and sister’s BS not relevant. Parents (2 samples) and sister (1 sample) normal measurements, molecular study is ongoing.

CONCLUSIONS

This patient has a bleeding disorder, presenting severe complaints and a positive family history. Platelet disorders and common coagulation factors deficiencies were excluded. We consider that the patient does not meet the criteria for the diagnosis of vWD, in light of the current classification.

The reduced endogenous thrombin potential and peak of TG results found in CAT, reflect a low thrombin concentration, probably due to an abnormal secondary haemostasis (it was performed in PPP). Other rare bleeding disorders need to be screened.

REFERENCES

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