ELSEVIER

Blood 142 (2023) 5424–5425

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

311.DISORDERS OF PLATELET NUMBER OR FUNCTION: CLINICAL AND EPIDEMIOLOGICAL

Some Patients with Suspected Thrombocytopathy Actually Have Ehlers-Danlos Syndrome; Clinical and Prognostic Implications

Nuria Pujol-Moix, MD PhD[1], *Roberto Castro-Seco, MD*[2], *Isabel-Socorro Caparrós-Miranda, MD*[3], *Mònica Fernandez-Benages, MD*[4]

[1] Medicine Department, Universitat Autònoma de Barcelona, Barcelona, Spain
[2] Ophtalmology Dapertment, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
[3] Hematology Department, Hospital Universitario Virgen de la Victoria, Málaga, Spain
[4] Pathology Department, Hospital Universitari de Bellvitge, Barcelona, Spain

Thrombocytopathy is the most likely diagnosis for patients with easy bruising and/or mucous bleeding and normal platelet counts. However, in a small proportion of these patients, all hemostatic tests are normal and the right diagnosis is actually Ehlers-Danlos syndrome (EDS). EDS is a heterogeneous group of genetic connective tissue disorders, characterized by joint hypermobility, skin and vascular fragility, and tissue friability; the most recent classification describes 13 clinical subtypes of EDS with mutations in 19 different genes *(Malfait et al. Am J Med Genet C Semin Med Genet. 2017;175:8)*. Besides joint hypermobility, cutaneous-mucosal bleeding of variable intensity is observed in the majority of patients. In the vascular subtype of EDS, arterial aneurysms, dissections and ruptures of arteries and arteriovenous fistulas are detected as manifestations of vascular fragility; less frequently, such vascular pathologies can also appear in other types of EDS *(Malfait. Matrix Biol 2018;71-72:380)*.

Based on our experience on patients with suspected thrombocytopathy but finally diagnosed of EDS, our objective is to attract the attention of hematologists to the possible diagnosis of EDS for patients with cutaneous-mucosal bleeding without any platelet or coagulation abnormality. This will lead to the adoption of the necessary measures to confirm diagnosis and to prevent complications, sometimes serious, of EDS.

We studied 8 patients, all women, with cutaneous-mucosal bleeding referred to our consultation as suspected thrombocytopathies. The main characteristics of the patients are shown in Table 1. Platelet counts, platelet function, and coagulation tests were normal in all cases. However, the evaluation of their articular mobility showed generalized hypermobility with the Beighton score *(Beighton. Ann Rheum Dis 1973;32:413)*. Two of the patients (cases 3 and 4) presented carotid-cavernous fistulas that led to loss of vision on the corresponding side. Case 3 was a 6-year-old girl with mild cutaneous bleeding and no other clinical manifestations. His mother, with a mild hemorrhagic tendency and no other symptoms, had died at the age of 35 from a massive peritoneal hemorrhage secondary to spontaneous rupture of the spleen; the observation of marked tissue fragility, at surgery and at necropsy, established the diagnosis of EDS. The girl's clinical bleeding, together with normal hemostatic tests and family history, suggested the diagnosis of EDS. This patient developed well, but, at the age of 18, a right carotid-cavernous fistula was diagnosed. Case 4 was a 51-year-old woman with a history of bronchial asthma, duodenal ulcer, gallstones, shoulder dislocations and bleeding tendency. At the age of 45, she had suffered a left carotid-cavernous fistula. Because the results of all hemostasis tests were normal, an exploration of her joint mobility was performed resulting in a positive Beighton score. This suggested the diagnosis of EDS. At the age of 55, we were informed that the patient had died, in another center, from massive bleeding in a surgical intervention for colon diverticula.

Although it is not frequent, there is the possibility that a patient with bleeding and without hemostatic abnormalities suffers from EDS which, in our experience, can lead to serious vascular complications, even in patients with mild symptomatology. We recommend in these patients to perform a test as simple as the Beighton score. If the result indicates a possible EDS, we suggest referring the patient to all the necessary specialists to confirm the diagnosis and carry out proper patient care and prevention of complications. Moreover, bearing in mind the frequency of carotid-cavernous fistulas with orbital involvement in our case series, we suggest the patient should be informed about the ophthalmologic symptoms of this vascular complication *(Fay et al. Clin Neuroradiol 2021;31:165)*. The most characteristic symptom is the anteroposterior displacement of the eyeball with each heartbeat. Other findings are proptosis, difficulty in making eye movements, chemosis, and conjunctival-scleral hyperemia with vascular tortuosity (Fig. 1). The ophthalmologist may also find venous tortuosity in the fundus, intraocular

hypertension, with or without associated glaucoma, and enlargement of the superior ophthalmic vein on imaging tests. The recommended treatment is embolization of the fistula.

Disclosures No relevant conflicts of interest to declare.

Table 1. Main characteristics of the patients

Case	Age at diagnosis	Bleeding	Beighton Score*	Other manifestations	Family
1	22	EB	8	no	mother with undiagnosed bleeding tendency
2	21	EB	9	no	mother with undiagnosed bleeding tendency
3	6	EB	9	no	mother with EDS
4	51	EBH, Ep, SB(3/7)	9	shoulder dislocations, back pain, 5 abortions	women in the family with undiagnosed bleeding tendency
5	41	EB, Ep, MB	9	shoulder dislocations, 1 abortion	no
6	34	EBH, MB	9	no	no
7	29	EBH, SB(1/2)	8	no	mother with undiagnosed bleeding tendency
8	34	EB, SB(1/1), OB(1/1)	9	myopia magna	no

All patients had a normal-looking face and no skin hyperextension

Bleeding: EB = easy bruising; EBH = easy bruising and hematomas due to minimal trauma; Ep = epistaxis; MB = menstrual bleeding; SB = surgical bleeding(number of interventions with excessive bleeding/total number of interventions); OB = obstetrical bleeding(number of deliveries with excessive bleeding/total number of deliveries)
*Beighton score of generalized joint hypermobility results from scoring the hypermobility of various pre-established joints; maximum value 9, positive value > 5

Figure 1. Carotid-cavernous fistula with orbital involvement. Right eye with proptosis, conjunctival hyperemia and chemosis, and conjunctival-scleral vascular tortuosity

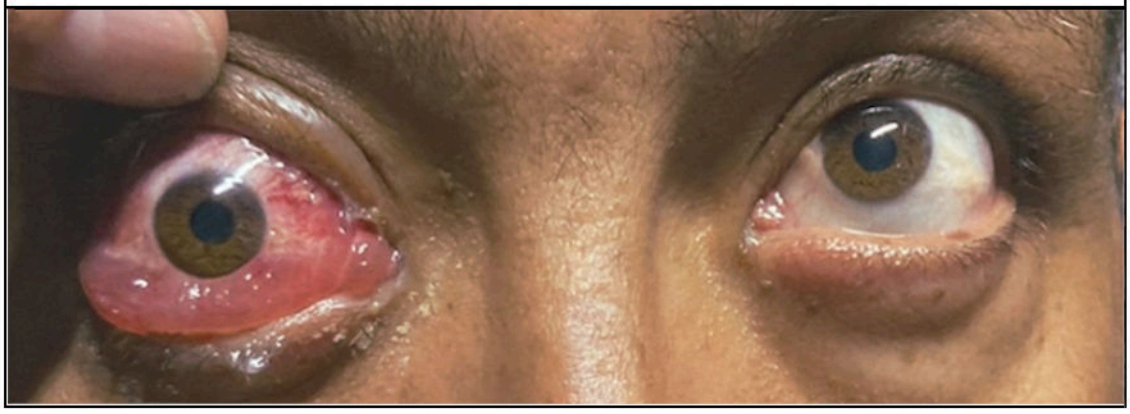

Figure 1

https://doi.org/10.1182/blood-2023-177863