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Bernard-Soulier Syndrome; Case Study

[1]Dr. Housam Al Madani, [2]Dr. Mai Saud Nazer, [3]Dr. Waad Hassan Alotibi

1. INTRODUCTION

Bernard-Soupier syndrome (BSS) was first known in 1948 by two French hematologists—Jean Bernard and Jean Pierre Soupier. They found out a patient from a consanguineous family with severe bleeding episodes, thrombocytopenia, and very large platelets (5). BSS is a platelet function disorder, transmitted in an autosomal recessive manner. Caused by a defects in the glycoprotein (GP)Ib/IX/V complex (2). These genes stand for a group of linked proteins normally found on the surface of the platelets. (3). Composed of four subunits, GPIbα disulphide-linked to two GPIbαβ subunits, GPIX and GPV in a ratio of 2:4:2:1, respectively (3). its a rare hereditary disorder, (1:1000000) (1).found more frequently in close relatives marriage (6). Present in both males and females (4). Start early with bleeding symptoms, like epistaxis, ecchymosis, meno metrorrhagia, and gingival bleeding (5) Distinguished by a prolonged bleeding time, large platelets, and thrombocytopenia (3). Diagnosed by platelet aggregation studies and flow cytometry (5) BSS cases are often misdiagnosed as idiopathic thrombocytopenic purpura (ITP)(3). In this case report, we present two brothers with causative mutations in GPIbβ.

2. CASE HISTORY

Eleven years old Saudi boy previously healthy until the age of four years old when he started to complain of bleeding from the nose for two days prior to admission . Other systemic review was unremarkable. he was not on any medications. Physical examination is unremarkable.

Laboratory finding were; CBC (HG: 9.3, RBC: 3.39, WBC: 9.7, PLATELET: 17). The patient diagnosed as idiopathic thrombocytopenia. Received IVIG and discharged in good condition after insertion of nasal packs.

In addition, he had multiple admissions due to the same complain epistaxis and low platelet count.

In the current admission, he admitted to pediatric medical ward due to a history of epistaxis and multiple ecchymosis. On examination he was conscious, alert, oriented, not distress. No enlarged lymph nodes were palpable in any part of his body. His abdomen was not distended, and his spleen and liver were not palpable other systemic examination is unremarkable. Laboratory values were as follows; CBC (hg: 12, WBC: 7.5, PLATELET: 11), Blood film; many large and giant platelets seen.

Serologic examinations for Human Immunodeficiency Virus and hepatitis B and C were all negative. Diagnosed clinically as idiopathic thrombocytopenia, received IVIG 1 mg/kg and platelet transfusion. After that the patient develop headache, dizziness, fever, and vomiting for two days . Start on antibiotics as a case of aseptic meningitis.

Later on, His younger brother 5 years old came to the hospital complain of epistaxis, multiple ecchymosis. Other systemic review was unremarkable. His laboratory values were as follows; CBC: (WBC: 7, Hb: 11.8, platelet: 8), Blood film; many large and giant platelets seen. Diagnosed as hereditary thrombocytopenia The doctor arranged appointment for follow up and Genetic analysis for both of them. The result of Molecular genetic analysis of the genes GP1BA, GP1BB, GP9 showed presence of homozygous mutations on GP1BB and both of them had low platelet count, they receive platelet transfusion. Finally they diagnosed as Bernard-Soulier Syndrome (BSS).

Table.1: Mutations Identified and some diseases associated in Patients with BSS

Geen Mutations	Nucleotide Substitutions	Genotype	Initial Diagnosis	References
GPIBα				
mutations	3998-3999delTG	Homozygous	ITP	(7)
41F	4444insT	Compound	ITP	(7)
43M	4464delA	heterozygous		
	4447C>A (TCA>TAA)	Homozygous	ITP	(8)
26F	4464delA			
	4464delA	Homozygous	ITP	(9)
34F		Homozygous		(10)
14F				
GPIBβ				
mutations	777C>T (CGC>TGC)	Heterozygous	GPD	(11)
37F	949C>G(CCG>CGG)	Homozygous	BSS	(12)
6F	991A>G (TAC>TGC)	Compound	ITP	(13)
37F	1050G>C(GCC>CCC)	heterozygous		
	991A>G (TAC>TGC)	Homozygous	BSS	(14)
20F	1096G>A(TGG>TAG)	Homozygous	ITP	
37M	del 22q11.2	Compound	BSS	(15)
1moF	unknown	heterozygous		
GPIX mutations				
39F	1856T>C (TTT>TCT)	Homozygous	ITP	(16)
46F	1910G>A (TGT>TAT)	Homozygous	BSS	(17)
31M	1910G>A (TGT>TAT)	Homozygous	ITP	(17)
46M	1982G>A (TGT>TAT)	Homozygous	ITP	(18)
30F	2076G>A(TGG>TGA)	Homozygous	ITP	(9),(19)
39F	2076G>A(TGG>TGA)	Homozygous	ITP	(20)
44F	2076G>A(TGG>TGA)	Homozygous	ITP	(20)
GPIBβ		Heterozygous	BSS with AML	(21)
mutations	Asn41His	Heterozygous	BSS with Myocardial infarction	(22)
GPIBβ				
mutations				

3. DISCUSSION

Childhood epistaxis is a common complaint that usually abates in adulthood; however, epistaxis can be life threatening when episodes are frequent and accompanied by substantial blood loss **(23)**.

Leukemia, idiopathic thrombocytopenic purpura, and allergic purpura should be included in the differential diagnosis of patients with mucocutaneous hemorrhage. When mucocutaneous hemorrhage is seen in leukemia, it is usually accompanied by thrombocytopenia in the peripheral blood. Patients with idiopathic thrombocytopenic purpura have decreased platelet counts and may have detectable antiplatelet antibodies. Inherited thrombocytopenias were, in the past, considered exceedingly rare. Today the widespread diffusion of electronic cell counters has rendered the identification of these conditions more common, the hereditary nature of the illness may be missed, and patients are subject to misdiagnosis of autoimmune thrombocytopenic purpura and inappropriate therapy, such as steroid treatment and splenectomy. (24-26)

(Table 1)* showed Mutations Identified and some diseases associated in Patients with Bernard-Soulier Syndrome

Their ages ranged from 1 to 70 years. They had platelet counts from 22 to 178 × 10^9/L. The mean value of MPV was 12.6 fL, with a range from 10.4 to 17.2 fL.

In Bernard-Soulier syndrome, thrombocytopenia is associated with morphologically abnormal large platelets and platelet dysfunction.

The clinical manifestation is variable and include purpura , epistaxis , gingival bleeding, menorrhagia, occasional gastrointestinal bleeding, hematoma, or hematuria.

Here, We report on two brothers with Bernard-Soulier syndrome (BSS) who presented with bleeding symptoms. They demonstrated typical BSS feature such as giant platelets, and reduced expression of platelet GPIb/IX receptor. In accordance, the eldest patient's bleeding symptoms were severe and required many platelet transfusions compared to his younger brother and other BSS patients.

4. CONCLUSION

Giant platelets in our patients made us think of Bernard-Soulier syndrome but flow cytometry and gene analysis should confirm the diagnosis. As a conclusion, Bernard–Soulier syndrome should be considered before the patient is diagnosed with immune thrombocytopenia.

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