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Bernard Soulier Syndrome

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Bernard-Soulier (BS) Syndrome is one of the hereditary hemorrhagic disorders(1). Similar to von-Willebrand's disease, there is a defect in platelet adhesion in BS Syndrome. Earlier two siblings with this disorder were reported from India(2). Here we report 4 unrelated patients detected in our laboratory in last 15 years.

Case Reports

Case 1: A 6½-year-old male child presented with history of ecchymoses on different parts of body and bleeding from mucosal surface of lips since one year of age. There was also prolonged bleeding following tooth extraction. At each episode, the bleeding had continued for 12-16 hours. One month back, he had prolonged gastro-intestinal bleeding and two units of whole blood with hematolcele and streptochrome were given. His two female siblings 11 and 8½ years old, had similar hemostatic defect. History of consanguinity was absent.

Case 2: A 2½-year-old male child presented with repeated episodes of excessive bleeding in last one year following history of blunt trauma. Epistaxis occurred once only. Six months back he had prolonged gum bleeding and was controlled with 2 units of whole blood transfusions. His brother (10 years age) was apparently asymptomatic. There was no history of consanguinity.

Case 3: An 18-year-old female, presented with history of gum bleeding since 4 years of age. At menarche she had menorrhagia. It was controlled by combined hormonal pills (Ovral). Other bleeding problems were of mild in nature and did not necessitate any blood transfusion. In the past one year, she had been put on multiple courses (4-6 weeks each) of oral corticosteroid therapy with symptomatic relief. There was no family history of any hemostatic defect or consanguinity.

Case 4: A 7-year-old male child, presented with bleeding for 48 hours from gums following tooth extraction. History of prolonged bleeding on injury was present since 2 years of age. On examination, a small hematoma was present on forehead. She did not need any blood transfusion in the past. There was no family history of excessive bleeding or consanguinity.

Screening tests of coagulation (*Table 1*) were done by standard techniques(3). Platelet factor 3 (PF_3) availability was determined by the method of Hardisty and

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TABLE I—*Screening Tests in Patients of Bernard-Soulier Syndrome*

Tests	Case 1	Case 2	Case 3	Case 4	Control
Bleeding time	9′ 30"	4′ 30"	>15'	>15′	2′–5′
Platelet count ($\times 10^9/1$)	212	106	190	140	150–450
Coagulation time	12′	–	11′ 30"	–	7′–4′
Prothrombin time	12"	12"	13"	14"	11"–14"
Activated partial thromboplastin time	43"	41"	38"	50"	35"–45"
Fibrinogen prothrombin time	9"	8"	11"	9"	9"–11"
Serum prothrombin time	60"	10"	12"	12"	>18"
Prothrombin consumption Index (%)	15	80	91.6	75	<40
Stypven time	16"	20"	20"	14"	14"–18"
Clot stability	normal	normal	normal	normal	normal
Clot retraction (%)	40	–	30	–	>30
Platelet factor 3 (PF_3) availability with ADP (at 20′)	24"	22"	31.5"	25"	14"–18"
PF_3 assay	normal	normal	50%	normal	normal
Factor VIIIc assay	normal	–	–	normal	normal

Hutton(4). Assay of PF_3 was done with repeated frozen and thawed platelet rich plasma(5). Platelet aggregation studies were carried out after Born(6) with aggregometer (Chronolg Corporation, Havertown, USA). Correction of ristocetin aggregation defect by normal plasma was also studied(7).

Discussion

Three of our 4 patients were male and bleeding time was prolonged in 3 patients. Thrombocytopenia was seen in 3 cases and in one, the platelet count was variable. Large platelets were present in the peripheral blood smear in all cases. Screening tests for platelet disorders namely bleeding time, prothrombin consumption index, stypven time and platelet factor 3 (PF_3) availability (at 20') with ADP(8) were abnormal in all 4 cases either singly or in combinations. Platelet aggregation studies were normal with adenosine diphosphate (ADP 1.25 μg/ml), adrenalin (1.25 μg/ml), collagen (1.0 μg/ml) but absent with ristocetin (2 mg/ml).

All our patients had PF_3 availability defect and one (Case 3) had PF_3 deficiency. Lipoprotein rich unit membrane of platelets contain the PF_3(9). The exact mechanisms of availability of this platelet membrane constituent to serve as catalytic surface for acceleration of prothrombin activation is not yet known(10). Association of defective PF_3 availability is considered nonspecific as it may occur with both hereditary and acquired disorders of platelet

function such as thrombasthenia(11), uremia(12) and dysproteinemia(13). It is possible that the poor availability in our cases could be a non-specific phenomenon, however, its deficiency in one of them could be an associated finding hitherto undescribed in cases of BS Syndrome.

Bernard-Soulier Syndrome is characterised by giant platelets with or without associated thrombocytopenia, inability to aggregate with ristocetin with no correction on addition of normal plasma and apparently normal aggregation with ADP(7).

All the cases fulfilled the above criteria. Case 4 had a slight prolonged partial thromboplastin time but normal procoagulant activity of factor VIIIc and non-correctable defect of ristocetin aggregation with normal plasma excluded the possibility of von-Willebrand's disease.

Demonstration of abnormality of membrane glycoproteins Ib, in the platelets(14) is confirmatory and may be reduced in parents and heterozygotes. However, we have not studied this in our patients.

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