Correspondence

Acta haemat. 71: 285–286 (1984)

0001–5792/84/0714–0285 $ 2.75/0

Diagnosis of Heterozygous State for Bernard-Soulier Disease

Bernard-Soulier disease (BSD) is an inherited bleeding disorder characterized by a prolonged bleeding time, with a normal or decreased number of unusually large platelets which fail to aggregate in response to ristocetin. This disease is generally transmitted as an autosomal recessive disorder, but it has also been shown that abnormal platelet morphology is transmitted as an autosomal dominant [1]. In heterozygous BSD patients, giant platelets are found in significantly lesser numbers than in homozygous BSD patients. Heterozygotes of BSD are asymptomatic. Although they have not been well studied, it has been proposed that heterozygous subjects can be identified by their giant platelets [1–3]. More recently, *George* et al. [2] described an abnormal platelet membrane glycoprotein I concentration in 3 heterozygotes from two families with BSD.

In this study we investigated ristocetin-induced platelet aggregation (RIPA) in heterozygous BSD patients to see if it might be helpful for their identification. 12 members from six families of patients with BSD were investigated. 6 of them were mothers, 4 fathers, and 2 were brothers of our patients. Their ages ranged from 6 to 45 years. With the exception of case No. 4, there was a consanguinity between the parents of all our patients. Platelet aggregation studies were

Table I. Ristocetin-induced platelet aggregation in heterozygous subjects with Bernard-Soulier disease

Patients Case No.	Date	Ristocetin-induced aggregation (T_{max}), %[1]		
		mother	father	brother
1	November 20, 1980	45	50	–[2]
	October 22, 1982	26	28	–
	May 11, 1983	55	–	–
2	August 8, 1980	18	13	16
	October 6, 1980	–	36	10
	May 21, 1981	30	60	32
3	December 12, 1980	22	–	–
	January 15, 1981	32	–	–
	April 16, 1981	60	–	–
4	April 26, 1983	18	–	46
	May 6, 1983	38	58	32
5	April 13, 1981	21	–	–
6	February 28, 1980	53	20	–

[1] Normal values: mean ± SD, 73 ± 2.9%; range, 56–90%.
[2] – = Not studied.

performed on a chrono-Log aggregometer (Broomally, Pa., USA) using a model 702 strip chart recorder. RIPA was tested using ristocetin (Lundbeck Co., Copenhagen, Denmark) diluted with normal saline to obtain a final concentration of 1.6 mg/ml. Aggregation curves were evaluated according to the percent aggregation (T_{max}) which indicates the maximum percent change in light transmission of platelet-rich plasma after the addition of ristocetin. As seen in table I, except for the father of case No. 4 all heterozygotes showed decreased RIPA compared to controls. This decreased rate of aggregation by ristocetin could not be corrected with the addition of normal plasma, which is also characteristic for platelets of patients with BSD [4, 5]. When tests were repeated in some heterozygotes on separate occasions, various degrees of reduced or even normal ristocetin-induced platelet response were observed, possibly due to variation in the number of giant platelets in the circulation. Although the platelet response to ristocetin had not been investigated previously, recently *George* et al. [2] reported normal RIPA in their 3 heterozygous BSD patients. However, they did not mention whether they had repeated these tests or not.

In conclusion, the present study shows a further defect related to the platelets in heterozygous BSD. In addition to the measurements of platelet size and distribution and of membrane glycoprotein I concentration, the heterozygous state of BSD is recognizable by the abnormal aggregation response of platelets to ristocetin, which is more practical.

References

1 Cullum, C.; Cooney, D.P.; Schrier, S. L.: Familial thrombocytopenic thrombocytopathy. Br. J. Haemat. *13:* 147–159 (1967).

2 George, J.N.; Reimann, T.A.; Moake, J.L.: Bernard-Soulier disease. A study of four patients and their parents. Br. J. Haemat. *48:* 459–467 (1981).

3 Kanska, B.; Niewiarowski, S.; Ostrowski, L.; Poplawski, A.; Prokopowicz, J.: Macrothrombocytic thrombopathia. Clinical, coagulation and hereditary aspects. Thromb. Diath. haemorrh. *10:* 88–100 (1963).

4 Howard, M.A.; Hutton, R.A.; Hardisty, R.M.: Hereditary giant platelet syndrome. A disorder of a new aspect of platelet function. Br. med. J. *iv:* 586–588 (1973).

5 Weiss, H.J.; Tschopp, T.B.; Baumgartner, H.R.; Sussman, R.I.; Johnson, M.M.; Egan, J.J.: Decreased adhesion of giant (Bernard-Soulier) platelets to subendothelium. Am. J. Med. *57:* 920–925 (1974).

Accepted: July 24, 1984

Gönül Hicsönmez, MD, Fevzi Özkaynak, MD,
Division of Hematology,
Department of Pediatrics,
Hacettepe University,
Ankara (Turkey)