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MEDICAL MEMORANDA

Multiple Coagulation Abnormalities in a Case of Cryptogenic Splenomegaly

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We describe here a case of cryptogenic splenomegaly of 20 years duration associated with acquired haemorrhagic diathesis. The study of the blood coagulation and fibrinolysis mechanism of this patient showed multiple abnormalities compatible with chronic defibrination syndrome. Splenectomy resulted in complete clinical cure and disappearance of the abnormal findings on laboratory tests.

Case Report

A 57-year-old man was admitted to hospital on 12 September 1972 because of prolonged bleeding after tooth extraction. There was no family history of bleeding or anaemia. He had had malaria when he was 21 and pulmonary tuberculosis when he was 23. Haemorrhagic manifestations began at 36 years when appendectomy was complicated by prolonged bleeding from the operative site. At that time marked splenomegaly was found. Since then he had frequent and severe epistaxes which when he was 42 and 53 necessitated admission into hospital and treatment with blood transfusions. During the second stay in hospital a mild thrombocytopenia (80,000 platelets/mm³) was found. Excessive bleeding, lasting for more than 10 days, resulted from scaling of tartar when he was 40 and tooth extraction when he was 45 and 50.

Five days before admission he had had a tooth extracted. The day before extraction laboratory studies showed: packed cell volume (P.C.V.) 37%, haemoglobin 11.2 g/100 ml, W.B.C. 8,000/mm³ with normal differential, platelets 250,000/mm³, bleeding time 2 min (Duke), and prothrombin time 17 sec (control 13 sec). The tooth extraction was followed by excessive bleeding. On admission he continued to bleed. He was anaemic and a greatly enlarged and firm spleen was palpable 10 cm below the left costal margin. The remainder of the clinical examination showed nothing

abnormal. The laboratory studies on admission showed: P.C.V. 24%, haemoglobin 8.6 g/100 ml, W.B.C. 10,800/mm³ with normal differential, and platelets 80,000/mm³. Serum iron was 25 µg/100 ml, and the total iron binding capacity was 380 µg/100 ml. The peripheral blood smear showed marked hypochromia and the bone marrow smear was normal but without stainable iron. Serum bilirubin was 0.7 mg/100 ml and serum haptoglobins 40 mg/100 ml. The results of the autohaemolysis, Coombs's, and Motulsky's tests were negative, as were results of tests of osmotic fragility (direct and after 24 hours incubation at 37°C) and heat-unstable and alkali-resistant haemoglobin. Haemoglobin electrophoresis was normal. A complete liver function evaluation and serum protein electrophoresis and immunoelectrophoresis showed nothing abnormal. Radiological examination of the bones and gastrointestinal tract, cholecystography, and pyelography also showed nothing abnormal. The spleen, besides its size, was characterized by the x-ray appearance of multiple puctiform foci of calcification (see fig.). The determination of surface radioactivity after administration of autologous red cells labelled with ⁵¹Cr showed splenic sequestration of red cells.

The haemorrhage stopped 11 days after admission. During this period he was treated with local measures and transfusions of

X-ray picture of spleen showing multiple puctiform foci of calcification.

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fresh blood (8 units altogether). On the 12th day in hospital the patient was still anaemic (haemoglobin 9.8 g/100 ml) and was given parenteral iron therapy (2 g), but the anaemia was only partially corrected (table I).

TABLE I—Haematological Findings in Peripheral Blood

	On admission	After Iron Treatment	After Splenectomy
P.C.V. (%)	24	34	48-50
Haemoglobin (g/100 ml)	8.16	11.8	15.2-15.4
Reticulocytes (%)	0.8	1.4	1.5
W.B.C. ($\times 10^3/\text{mm}^3$)	10.8	6.0	12.0-6.0
Differential count	Normal	Normal	Normal
Hypochromia	++	—	—
Anisocytosis	+	+	—
Poikilocytosis	+	+	—

STUDY OF HAEMOSTATIC MECHANISM

The platelet count ranged from 75,000/mm³ to 140,000/mm³. The bleeding time (Ivy), repeatedly measured, was within normal range. The platelet adhesiveness test result, the aggregation by adrenalin, adenosine diphosphate, connective tissue extract and thrombin, the platelet factor-3 availability, and the clot retraction were all normal.

The blood coagulation and fibrinolysis studies showed multiple but mild abnormalities (table II): borderline prolongation of prothrombin time, prolonged partial thromboplastin time, hypofibrinogenaemia, decreased factor V, VIII, and X activity, and increased fibrinogen/fibrin degradation products (F.D.P.). On the other hand, the euglobulin clot lysis time and the plasminogen level were normal.

EFFECT OF SPLENECTOMY

The patient underwent splenectomy in November 1972 with an uneventful postoperative course. Since then he has been in good clinical condition (for the first time for 20 years). The haemoglobin level has been constantly normal and the platelet count has ranged in slightly increased levels (table I). The results of blood coagulation and fibrinolysis tests were repeatedly normal (table II).

SPLEEN HISTOLOGY

The spleen was hard and weighed 1,820 g. There was marked thickening of the capsule up to 0.6 cm. On section the spleen showed multiple, irregularly outlined, yellow-brown, and firm focal areas of 0.1 to 0.9 cm diameter. The vessels of the hilus were dilated with many thrombi. Histologically there was congestion of the red pulp and hyperplasia of the reticular stroma and its cells.

TABLE II—Coagulation and Fibrinolysis Data

	Normal Values	Before Splenectomy				After Splenectomy		
		17-19-9-72*	7-10-72	23-10-72	9-16-11-72	13-12-72	16-3-73	3-5-73
Platelet count ($\times 10^3/\text{mm}^3$)	150-400	80-130	75	120	75	1000	600	620
P.T. (sec; P./C.)		14/13	13/12	14/12	13/12	12/12	11/12	
T.T. (sec; P./C.)		14/12	10/10	13/12	12/10	11/11	12/12	
P.T.T.K. (sec; P./C.)		48-74/40	61/43	59/38	56/39	46/48	40/42	
Fibrinogen (mg/100 ml)	180-350	264	234	128	84-123	420	350	335
Factor V (%)	70-120			64	51	104		
Factor VIII (%)	60-180	42-54		50	51	152	140	130
Factor X (%)	60-180	68		54		95		
A.T.-III (%)	75-125			84		102		100
Euglobulin clot lysis time (min)	120-360	200	210		78			
Plasminogen (units)	2-5				180			
F.D.P. ($\mu\text{g}/\text{ml}$)	8		10		2-5	2-8	2-5	

P.T. = Prothrombin time. P./C. = Patient values/control values. T.T. = Thrombin time. P.T.T.K. = Partial thromboplastin time with kaolin. A.T.-III = Antithrombin-III.

F.D.P. = Fibrinogen/fibrin degradation products.

*After blood transfusions.

The above described foci of connective tissue included calcium and iron pigment micelle-like deposits. The Malpighian bodies were inconspicuous.

Comment

This patient had acquired a bleeding tendency lasting for nearly 20 years, which was successfully treated by splenectomy. The cause of bleeding was not revealed until his last stay in hospital at our unit. Investigation of the haemostatic mechanism then showed multiple blood coagulation abnormalities: decreased platelet count and plasma levels of fibrinogen and factors V, VIII, and X and increased F.D.P. and prolongation of prothrombin time and partial thromboplastin time. Detailed studies of his haemostatic mechanism had not been previously performed, but on one occasion mild thrombocytopenia was found and on another occasion the prothrombin time was prolonged. These findings are compatible with chronic, mild, and partially compensated defibrination syndrome. Increased primary fibrinolysis was excluded since the plasma fibrinolytic activity was normal.

In chronic defibrination the consumption of coagulation factors is slow, resulting in mild clinical manifestations and laboratory disturbances (Frick and McKelvey, 1955; Merskey *et al.*, 1967; Mosesson *et al.*, 1968; Verstraete and Vermeylen, 1968; Straub, 1971). Thrombocytopenia is a rather constant finding, but in our case it could also have been the result of splenic sequestration.

As haemostatic defects were totally corrected by splenectomy the coagulation abnormalities were due in some way to his splenomegaly. We suggest that the spleen in our case behaved like giant haemangioma in Kasebach-Merritt syndrome (Blix and Aas, 1961).

The nature of the patient's splenomegaly was obscure. Laboratory and histological data excluded the existence of an active systemic disease affecting the spleen or a local disease of the organ. The possibility that splenomegaly was due to an infection (possibly malaria) in the past cannot be excluded.

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