Transient Thrombasthenia in a Patient with Tuberculosis

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SUMMARY

A 20-year-old Black female presented with menorrhagia and epistaxis. Similar episodes, two years previously, had necessitated blood transfusion. No association with drug ingestion was found and the family history revealed no bleeding diathesis. The patient had a normal platelet count and a prolonged bleeding time. Platelet aggregation, clot retraction and platelet factor 3 release were grossly abnormal. She had axillary tuberculous lymphadenitis and chemotherapy was initiated. Three months later there was no clinical or laboratory evidence of a platelet abnormality. No reason for this transient thrombasthenia, which is unknown to us, was found. Glanzmann's disease is a hereditary thrombasthenia with a similar qualitative platelet defect.

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Thrombasthenia, first described by Glanzmann in 1918,[1] is a congenital, qualitative platelet defect, characterised by a normal platelet count, prolonged bleeding time, defective clot retraction and platelet aggregation.[2] The fundamental abnormality is the failure of the platelets to aggregate with adenosine diphosphate (ADP).

A case is reported in which a transient, apparently acquired but recurrent, qualitative platelet defect, similar to that of thrombasthenia, was found in a patient with tuberculous lymphadenitis.

CASE REPORT

History and Routine Investigations

A 20-year-old Black female was admitted to Pelonomi Hospital on 1 October 1972 with a history of menorrhagia and epistaxis, which had been severe enough to necessitate transfusion with 2 units of blood at the referring hospital. Symptoms attributable to anaemia were prominent. Her past history revealed that in 1970 there had been a similar episode of menorrhagia and epistaxis, also requiring transfusion. Another haemorrhagic incident may also have occurred in 1962. In between these episodes she had noticed neither easy bruising nor excessive bleeding after minor or major trauma. Menstruation had commenced at age 14, periods were regular and lasted for 3 - 4 days, and were regarded as normal by the patient. She had had no previous operations but had given normal birth to a child in 1969. In 1970 (2 years previously) she became blind after bilateral eye infections.

No parental consanguinity or family history of a bleeding diathesis was evident and drug or possible toxin ingestion was denied. Loss of weight (about 7 kg) and anorexia had been noted.

On examination she appeared severely anaemic and somewhat wasted. No purpura or ecchymoses were seen on the skin or mucous membranes and there was no evidence of haemarthrosis. Prominent lymph nodes were palpable in the right axilla, and there was no hepatosplenomegaly. Blindness was due to cataract caused by bilateral iritis and uveitis with extensive posterior synechiae. No local cause for the menorrhagia or the epistaxis was found. Systematic examination otherwise showed nothing abnormal.

Tuberculous lymphadenitis was diagnosed on lymph node biopsy with the demonstration of acid-alcohol-fast bacilli. The Mantoux skin test was strongly positive—20-mm reaction zone with 2 tuberculin units. A chest radiograph was within normal limits. Urine was normal on biochemical and microscopic examination. Blood urea was 19 mg/100 ml, total serum protein 6,2 g/100 ml with 2,9 g albumin and 1,5 g gammaglobulin.

Haematology (3 October 1972): The Hb was 4,0 g/100 ml, haematocrit 13%, red cell count 1,60 × $10^6/\mu l$, MCV 81 fl, MCH 29 pg, MCHC 30%, and reticulocytes 19,9%. The total leucocyte count was 8 200/μl, comprising 52% granulocytes, 1% eosinophils, 45% lymphocytes and 2% monocytes. The platelet count was 315 000/μl. The ESR was 78 mm/h (Westergren). The red corpuscles appeared slightly hypochromic and diffuse polychromasia was prominent. Many large thrombocytes were present. These were regarded as reflecting increased thrombopoiesis.[3] Sternal bone marrow aspirate demonstrated erythroid hyperplasia, with normal iron stores but no sideroblasts; megakaryocytes were normal in number, and morphology and platelet budding were active.

Plasma prothrombin time, partial thromboplastin time with kaolin, thrombin time, reptilase time and factor VIII level were all normal.

Platelet Studies

Venous blood was collected with disposable plastic syringes and mixed with one-tenth volume 3,8% disodium

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TABLE I. RESULTS OF PLATELET FUNCTION TESTS PERFORMED ON THE PATIENT DURING AND AFTER THE HAEMORRHAGIC EPISODE

	Patient			
	12 October 1972	11 April 1973	Normal values	Method reference
Platelet count	220 000/μl	230 000/μl	150 000 - 400 000/μl	5
Bleeding time	>50 min	2,3 min	<11 min	4
Capillary resistance test	Positive	Negative	Negative	12
Platelet adhesiveness to glass	0%	69%	>40%	11
Platelet aggregation				
5 μM ADP	3%	64%	71 ± 25% (± 2 SD)	9, 10
0,5 mg/ml collagen	21%*	81%	70 ± 26%	
5 μM adrenaline	0%	81%	60 ± 30%	
5 μM serotonin	0%	4%	6 ± 3%	
0,1 U/ml thrombin	3%	50%	>20%	
Microscopic examination				
Citrated PRP	Discoid	Discoid	Discoid	2
Citrated PRP plus ADP 5 μM	Spiny; no aggregation	Spiny; aggregation	Spiny; aggregation	2
Citrated PRP plus collagen	Adhesion; no aggregation	Adhesion; aggregation	Adhesion; aggregation	2
Platelet factor 3 availability				
Hardisty	44 sec (control 27 sec)	28 sec (control 29 sec)	Difference <3 sec	7
Spaet	2 sec	11 sec	Shortening of RVV >6 sec	8
Clot retraction				
Whole blood	0%	50%	48 - 64%	6
Citrated PRP	0	++++	++++	2
Citrated PRP plus $MgCl_2$	0	++++	++++	2

* Fall in optical density interpreted as platelet adhesion to collagen and not aggregation (see Fig 1).

citrate in polystyrene tubes. Platelet-rich plasma (PRP) and platelet-poor plasma (PPP) were separated by centrifugation at 100 *g* for 5 minutes and 2 500 *g* for 20 minutes, respectively. Tests were performed as soon as possible after venesection.

Bleeding time was done according to Ivy's method,[4] platelets were counted with a Coulter model FN electronic particle counter,[5] and clot retraction was estimated in whole blood[6] and in citrated PRP in uncoated glass tubes, with and without the addition of 0,05M magnesium chloride.[2]

In vitro observations were made on citrated PRP by phase contrast microscopy at room temperature. The platelets were first observed for spontaneous change in platelet shape and aggregation and then after the addition of approximately 5 μM ADP and 0,5 mg/ml collagen (final concentration). Platelet factor 3 availability was determined by incubation of PRP with kaolin[7] and collagen[8] with assay of platelet coagulant activity released at 20 minutes. Platelet aggregation was measured turbidimetrically[8,9] at 37°C in an EEL aggregometer with continuous stirring (1 000 rpm) of PRP adjusted to 300 000 platelets/μl. Aggregating agents in 0,1-ml volumes were added to 0,9 ml PRP, giving the following final cuvette concentrations: ADP 5 μM, adrenaline 5 μM, serotonin 5 μM, acid-soluble collagen 0,5 mg/ml and thrombin 0,1 units/ml. The maximum decrease in optical density (OD) induced was related to the difference in optical density between PRP and PPP and expressed as percentage platelet aggregation. Platelet adhesion to glass was measured by the rotating-bulb method of Wright.[10]

The results of platelet function tests are summarised in Table I and aggregation curves are depicted in Fig. 1.

Routine tests for platelet haemostatic function (bleeding time, Hess test), *in vitro* platelet adhesion to glass, platelet coagulant activity as measured by platelet factor 3 release, platelet response to aggregating agents and clot retraction were all markedly abnormal at the time of the initial examination in 1972. Especially in view of the non-reactivity of the platelets to ADP, these results were interpreted as being consistent with thrombasthenia. Defective release of platelet coagulant activity is also seen in thrombasthenia.[2,13]

As is evident from the data in Table I, platelet function was completely normal in 1973, paralleling the clinical improvement and general well-being of the patient.

The patient's mother was examined and platelet function was found to be normal. Unfortunately, other family members were not available for investigation.

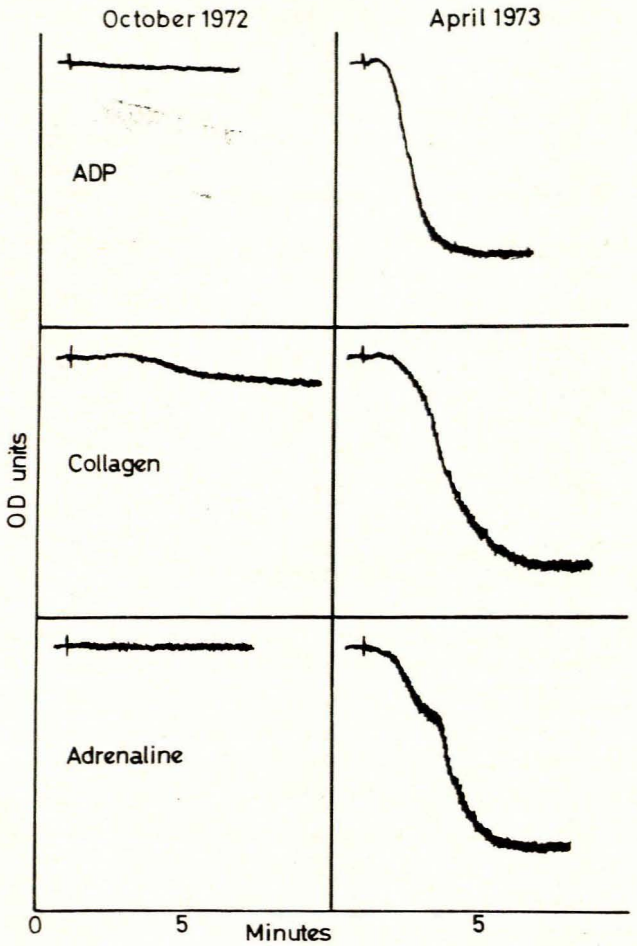

Fig. 1. Platelet aggregation curves during and after the haemorrhagic episode. Arrows indicate at what point aggregating agents were added. Quantitative results are given in Table I.

Course of the Disease

The anaemia was corrected with 5 units of red cell concentrate and haemorrhage arrested by local measures. Treatment with streptomycin 1 g/day, INH 600 mg/day and ethionamide 250 mg every 8 hours was initiated after the diagnosis of tuberculous lymphadenitis had been established. Two weeks after admission she had a further episode of epistaxis which was controlled by local plugging. The vaginal bleeding diminished gradually and examination under anaesthesia and curettage revealed no abnormality. Bleeding ceased about 2 weeks after admission. She then received a further 3 units of packed red cells, and was discharged from hospital.

When she was seen at the Haematology Clinic in April 1973, the gain in body mass and the general well-being of the patient were striking. She had had no further episode of haemorrhage and was menstruating normally. The patient has attended the clinic regularly since then and at no stage has any subjective or objective evidence of a bleeding diathesis been noted.

DISCUSSION

This report describes a transient qualitative thrombasthenic platelet defect in a patient with tuberculous lymphadenitis. In view of the one certain previous haemorrhagic episode and the likelihood of a second similar incident, the present association with tuberculosis may be coincidental. We have also been unable to link any of these episodes with drug or toxin ingestion.

The haemostatic disorder resulting from the thrombasthenia was clearly defined. The fundamental abnormality is the failure of platelets to aggregate with ADP. The patient also had the other functional abnormalities of platelets which characterise thrombasthenia: a normal platelet count, prolonged bleeding time, defective clot retraction and defective aggregation. In this patient the lesion was not congenital, there was no family history, the haemorrhagic tendency was episodic and platelet function returned to normal. These findings clearly distinguish this disease from thrombasthenia.

We are at a loss to explain these findings, but this case report may contribute to the understanding of the haemostatic process involved.

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