

- ²² Holmberg L, Lecander I, Persson B, Åstedt B. An inhibitor from placenta specifically binds urokinase and inhibits plasminogen activator released from ovarian carcinoma in tissue culture. *Biochim Biophys Acta* 1978;**544**:128-37.
- ²³ Murano G. The "Hageman" connection: Interrelationships of blood coagulation, fibrino(geno)lysis, kinin generation and complement activation. *Am J Hematol* 1978;**4**:409-17.
- ²⁴ Aoki N. Preparation of plasminogen activator from vascular trees of human cadavers. *J Biochem* 1974;**75**:731-41.
- ²⁵ Binder BR, Spragg J, Austen KF. Purification and characterization of human vascular plasminogen activator derived from blood vessel perfusates. *J Biol Chem* 1979;**254**:1998-2003.
- ²⁶ Aasted B. Purification and characterization of human vascular plasminogen activator. *Biochim Biophys Acta* 1980;**621**:241-54.
- ²⁷ Vetterlein D, Young PL, Bell TE, Roblin R. Immunological characterization of multiple molecular weight forms of human cell plasminogen activators. *J Biol Chem* 1979;**254**:575-8.
- ²⁸ Roblin R, Young PL. Dexamethasone regulation of plasminogen activator in embryonic and tumor-derived human cells. *Cancer Res* 1980;**40**:2706-13.
- ²⁹ Åstedt B. No cross reaction between circulating plasminogen activator and urokinase. *Thromb Res* 1979;**14**:535-9.
- ³⁰ Nilsson IM, Isacson S. New aspects of the pathogenesis of thrombo-embolism. *Progr Surg* 1973;**11**:46-68.

Requests for reprints to: Dr H Ljungnér, Department for Coagulation Disorders, University Hospital, S Förstadsgatan 101, S-214 01 Malmö, Sweden.

The August 1983 issue

THE AUGUST 1983 ISSUE CONTAINS THE FOLLOWING PAPERS

Review article

Formaldehyde in pathology departments RP CLARK

A data processing system adapted to the special needs of the emergency laboratory D NEUMEIER, H SATOR, GE RINDFLEISCH, M KNEDEL

Computer programs in cytology reporting and record keeping KV SWETTENHAM, CD NICKOLS, CL BERRY

The synovium and synovial fluid in multicentric reticulohistiocytosis—a light microscopic, electron microscopic and cytochemical analysis of one case AJ FREEMONT, CJP JONES, J DENTON

Changes in the Paneth cell population of human small intestine assessed by image analysis of the secretory granule area MARGARET E ELMES, J GWYN JONES, MR STANTON

Blood group antigens in the normal and neoplastic bladder epithelium SUSAN J THORPE, P ABEL, G SLAVIN, TEN FEIZI

Demonstration of light chain monotypia in B cell non-Hodgkin's lymphomas using unfixed freeze-dried and formalin-fixed trypsinised paraffin sections Z NEMES, V THOMÁZY, G SZEIFERT

Calcium pyrophosphate dihydrate (CPPD) deposition in ochronotic arthropathy J McCLURE, PS SMITH, AMANDA A GRAMP

Use of the cryostat section in electron microscopy P NORRIS, DWR GRIFFITHS

Increased transfer of iron to the fetus after total dose infusion of iron dextran during pregnancy D BINGHAM, MM KHALAF, G WALTERS, JT WHICHER

Differential effect of detergents on the alkaline denaturation of haemoglobin in maternal and fetal blood, with particular reference to Triton X-100 CG DUCK-CHONG

Analysis of the complexity of the multimeric structure of factor VIII related antigen/von Willebrand protein using a modified electrophoretic technique MS ENAYAT, FGH HILL

Faecal carriage rate of *Aeromonas hydrophila* SALLY E MILLERSHIP, SR CURNOW, B CHATTOPADHYAY
The value of screening blood donors for antibody to hepatitis B core antigen AC ARCHER, BJ COHEN, PP MORTIMER

A miniaturised and simplified technique for typing and subtyping herpes simplex virus JM DARVILLE

Growth hormone and malignancy GS ANDREWS

Angiotensin-converting enzyme and its clinical significance — a review PR STUDDY, RUTH LAPWORTH, R BIRD

Quality assessment of blood glucose monitors in use outside the hospital laboratory RF DRUCKER, DRR WILLIAMS, CP PRICE

Technical method

A new bone marrow aspiration needle to overcome the sampling errors inherent in the technique of bone marrow aspiration A ISLAM

Letters to the Editor

Book reviews

Some new titles

Notice

Copies are still available and may be obtained from the PUBLISHING MANAGER, BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON WC1H 9JR. Price £5.00, including postage.

epinephrine and collagen induced aggregation remained unaffected. However, ristocetin induced aggregation was reduced to a level comparable to the patient's pre-treatment findings at concentrations of 0.15 ml but not at concentrations of 0.05 ml and 0.01 ml (Fig. 2(4)).

Discussion

Only three patients have been reported with an IgA pyroglobulin.⁷⁻⁹ In contrast to our patient all had multiple myeloma, two of whom had the hyperviscosity syndrome. This is the first report of an IgA pyroglobulin in association with a lymphoma. An interesting feature of our patient was her purpura. As her coagulation screen, platelet count and factor assays were normal, it was felt this may have been due to abnormal platelet aggregation. The patient had absent second phase aggregation with adrenalin and markedly decreased aggregation with ristocetin. The abnormality of platelet aggregation induced by adrenalin may occur in normal individuals,¹⁰ and the fact that it persisted after treatment suggests that it is probably a normal variant. In contrast, the ristocetin induced aggregation was probably directly related to her illness as it was reversed with treatment. We propose that it was related to the presence of the IgA pyroglobulin. This is suggested by the studies in which her IgA fraction was isolated and added to normal platelets, producing impaired ristocetin induced aggregation.

The bleeding tendency associated with paraproteinaemia is complex. Abnormalities of the coagulation,¹¹ or fibrinolytic¹² systems may be involved but defects of platelet function,¹³⁻¹⁵ and hyperviscosity,⁸ may be more important. In particular, defects of ristocetin induced aggregation may play a significant role by coating the surface of both platelets and connective tissue

and thereby blocking their interactions.¹² Similar defects of ristocetin induced aggregation occur in rural Nigerians where it is postulated their increased IgM and other macroglobulin production caused by parasitaemia may be important.¹⁶ In addition, macromolecules such as dextran are known to inhibit ristocetin induced platelet aggregation.¹⁷ The role of hyperviscosity in this patient's bleeding disorder is difficult to assess. Although the serum viscosity at times rose to very high levels (6.06 N mPa s), bleeding did not occur. Instead, this seemed to be related to the activity of her illness, and her pyroglobulin levels. We therefore suggest that her circulating IgA κ pyroglobulin blocked the platelet vessel wall interactions in a manner similar to lack of von Willebrand factor, perhaps by coating one or both surfaces and thereby producing defective ristocetin induced platelet aggregation.

We wish to thank Dr Brian Wisdom and Messrs Michael Rocks, Fred Lloyd and John Orchin for technical assistance and Miss Diane Barker for typing the manuscript.

MICHAEL MADDEN

T CARSON M MORRIS

DOROTHY HAYES

CAROLINE A HUMPHREY

JEFFREY H ROBERTSON

*Departments of Haematology and
Histopathology,
Belfast City Hospital, Belfast,
Northern Ireland*

References

- Zinneman HH. Cryoglobulins and pyroglobulins. *Pathobiol Annu* 1980;**10**:83-104.
- Martin WJ, Mathieson DR. Pyroglobulinaemia (heat coagulable globulin in the blood). *Proc Staff Meet Mayo Clinic* 1953;**34**:95-101.
- Fisher B, Schaer LR, Messinger S. The occurrence of pyroglobulins in unsuspected myeloma. *Am J Clin Pathol* 1963;**40**:291-4.
- Stefanini M, McDonnell EE, Andracki EG,

et al. Macropolyglobulinaemia: immunochemical studies in 3 cases. *Am J Clin Pathol* 1980;**54**:94-101.

⁵ Krauss S, Sokal JE. Paraproteinaemia in the Lymphoma. *Am J Med* 1966;**40**:400-13.

⁶ Born GVR. Aggregations of blood platelets by adenosine diphosphate and its reversal. *Nature* 1962;**194**:927-9.

⁷ Invernizzi F, Cattaneo R, Rossi DI, San Secondo V, *et al.* Pyroglobulinaemia. *Acta Haematol* 1973;**50**:65-74.

⁸ Sugai S. IgA Pyroglobulin, hyperviscosity syndrome and coagulation abnormality in a patient with multiple myeloma. *Blood* 1972;**39**:224-37.

⁹ Watanabe T, Oshima T, Minamizawa S, *et al.* Pyroglobulin developing in a case of IgA lambda type multiple myeloma presenting as plasmacytoma of the mandible. *Rinsho Ketsueki* 1980;**7**:984-90.

¹⁰ ten Cate JW, Jenkins CSP. Blood coagulation and haemostasis. In: Thompson J, ed. London: Churchill Livingstone, 1980:33.

¹¹ Castaldi PA, Penny R. A macroglobulin with inhibitory activity against coagulation factor VIII. *Blood* 1970;**35**:370-6.

¹² Hardisty RM, Caen JP. Haemostasis and thrombosis. In: Bloom AL, Thomas DP, eds. London: Churchill Livingstone, 1981: 301-20.

¹³ Perkins HA, McKenzie MR, Fudenberg HH. Hemostatic defects in dysproteinaemias. *Blood* 1970;**35**:695-707.

¹⁴ Vigliano EM, Horowitz HI. Bleeding syndrome in a patient with IgA myeloma: interactions of protein and connective tissue. *Blood* 1967;**29**:823-36.

¹⁵ Cohen I, Amir J, Ben-Shaul Y, *et al.* Plasma cell myeloma associated with an unusual myeloma protein causing impairment of film aggregation and platelet function in a patient with multiple myeloma. *Am J Med* 1970;**48**:766-76.

¹⁶ Dupuy E, Fleming AF, Caen JP. Platelet functions, factor VIII, fibrinogen and fibrinolysis in Nigerians and Europeans in relation to atheroma and thrombosis. *J Clin Pathol* 1978;**31**:1094-101.

¹⁷ Aberg M, Hedner U, Holmberg L, *et al.* Dextran induced changes of the factor VIII molecule (Abstract). *Thrombosis et Diathesis Haemorrhagica* 1975;**34**:903.

Notices

The British Digestive Foundation (Scottish Appeal)

The British Digestive Foundation (Scottish Appeal) exists to promote research into the alimentary tract and its diseases. The Awards Advisory Group of the Scottish Appeal invites applications from workers in Scottish Institutions who wish support for research work related to any aspects of normal or disordered structure and function of the alimentary tract. A wide variety

of forms of support will be considered ranging from that required for apparatus or reagents to Fellowships. There is no requirement that applicants be medically qualified.

The Awards Advisory Group meets annually to consider applications and these should be submitted before 15th September, 1983.

An application form can be obtained from: The Secretary, The British Digestive Foundation (Scottish Appeal), 9 Queen Street, Edinburgh, EH2 1JQ.

Plasma proteins in clinical diagnosis: IV European meeting

The Fourth European meeting on Plasma Proteins in Clinical Diagnosis will be held on 5-7 October, 1983 at the Centro Congressi Milanofiori, Milan, Italy.

For information, please write to: The Scientific Secretary, Dott Santica Marcovina, Laboratori di Ricerca-Istituto Scientifico S Raffaele, Via Olgettina, 60-20132 Milan, Italy.