Plasma Fibronectin in Sick Cell Disease

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Key Words

Plasma fibronectin

Sickle cell disease

Abstract

Immunoturbidimetric assay technique was used to determine plasma fibronectin concentration in healthy Nigerian children (age 2–14 years), patients with sickle cell disease in steady state and patients with sickle cell disease in crises. Compared with controls, the plasma levels of fibronectin were greatly reduced in patients with sickle cell crises. Values within the normal reference range were seen in the group of patients with sickle cell disease in steady state. The data suggest that the significantly ($p < 0.001$) reduced plasma fibronectin in patients with sickle cell crisis may be due to the consumption of this plasma protein in the process of erythrocyte endothelial adhesion.

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Introduction

Fibronectin is a major glycoprotein found in vertebrate blood and organ or tissue [1,2]. The form which is found in plasma is called cold-insoluble globulin [2,3]. Its molecular weight is about 440,000 daltons and it is composed of two 200,000–220,000-dalton subunits held together by disulphide bonds [4, 5]. Fibronectin interacts with heparin [6, 7] and fibrin in the cold [8] and binds to collagen [9, 10]. It is also part of the normal blood clot [4, 11]. Serum concentration of fibronectin is less than the plasma concentration [12,13].

Plasma fibronectin concentration has been reported to be reduced in disseminated intravascular coagulation (DIC) [4], infection [14], sepsis, trauma, burns, following surgery and fulminant hepatic failure [15–17]. Results of plasma fibronectin measurement in patients with sickle cell disease have not been fully reported so far. This communication reports our preliminary findings in the assay of plasma fibronectin in sickle cell disease patients in steady state and in crises. age-matched, was also included in the investigation. Ten patients were relatively asymptomatic (i.e. in steady state), while 5 patients were in crisis at the time blood samples were taken for the assays. The diagnosis of sickle cell was based on clinical grounds and confirmed by the finding of a haemoglobin SS pattern on cellulose acetate strip electrophoresis in the laboratory, after preliminary investigation had revealed very low haemoglobin and haematocrit values. All the control subjects had haemoglobin AA and no evidence of anaemia, infection, inflammation or injury.

Blood samples were collected in EDTA and were spun immediately to obtain plasma samples which were stored at -20°C . They were thawed just before use.

The fibronectin concentration was determined by an immunoturbidimetric method using a commercially available kit, (Boehringer Mannheim GmbH). All measurements were performed in duplicate. Results are expressed as $\mu\text{g/ml}$.

Results

Table I summarizes the mean values for the plasma fibronectin in 10 normal controls, in patients with sickle cell disease in steady state and patients with sickle cell crisis. The mean plasma fibronectin concentration was significantly reduced ($p < 0.001$) in patients with sickle cell crisis.

Patients and Methods

A total of 15 homozygous (SS) sickle cell disease patients, age 2–14 years were studied. Patients were first seen in the emergency and outpatient departments of the Lagos University Teaching Hospital, Lagos, Nigeria. A reference control group ($n = 10$), sex and

Discussion

Our evaluation of fibronectin levels in patients with sickle cell crisis showed that plasma fibronectin

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Table I. Plasma fibronectin (mean $\pm$ SD) in normal controls, patients with sickle cell disease in steady state and patients with sickle cell crises

concentrations dropped below $367.2 \mu\text{g/ml}$, the lower level of normal. Previous studies have found reduced plasma fibronectin values in patients with disseminated intravascular coagulation [4], infection such as Rocky Mountain spotted fever [14], sepsis, trauma, burns and following surgery [15–17].

In sickle cell disease crisis, there is intracapillary aggregation of red blood cells which causes stasis with its intravascular complications and the consequences of tissue anoxia. Thrombosis occurs in the capillaries during erythrocyte sludging and stasis. In the process of thrombosis, there is consumption of platelets and some coagulation factors [18] so that these are reduced in circulation. Recent reports have shown that coagulation alterations recorded in sickle cell anaemia during vascular occlusive episodes could potentiate erythrocyte-endothelial cell interaction [19,20].

In conclusion, this study has shown that plasma fibronectin concentration is reduced during sickle cell disease crisis, which may be due to consumption of this protein in the process of erythrocyte-endothelial adhesion.

References

- Linde, A.; Johnson, R.: Immunofluorescent localization of fibronectin in human oral mucosa. *Archs. oral Biol.* 27: 1047–1052(1982).
- Ruoslahti, E.; Engvall, E.; Hayman, E.G.: Fibronectin: current concepts of its structure and functions. *Collagen Res.* 1: 95–128 (1981).
- Mosesson, M.W.; Umfleet, R.A.: The cold-insoluble globulin of human plasma. V. Purification, primary characterization, and relationship to fibrinogen and other cold-insoluble fraction components. *J. biol. Chem.* 245: 5728–5736 (1970).
- Mosher, D.F.; Williams, E.M.: Fibronectin concentration is decreased in plasma of severely ill patients with disseminated intravascular coagulation. *J. Lab. clin. Med.* 91: 729–735 (1978).

Mosesson, M.W.; Chen, A.B.; Huseby, R.M.: The cold-insoluble globulin of human plasma: studies of its essential structural features. *Biochim. biophys. Acta* 386: 509–524 (1975).

Stathakis, N.E.; Mosesson, M.W.: Interactions among heparin, cold-insoluble globulin and fibrinogen in formation of the heparin-precipitable fraction of plasma. *J. clin. Invest.* 60: 855–865 (1977).

Mosher, D.F.: Cross-linking of cold globulin by fibrin-stabilizing factor. *J. biol. Chem.* 250: 6614–6621 (1975).

Ruoslahti, E.; Vaheri, A.: Interaction of soluble fibroblast surface (SF) antigen with fibrinogen and fibrin. Identify with cold insoluble globulin of human plasma. *J. exp. Med.* 141: 497–501 (1975).

Engvall, E.; Ruoslahti, E.: Binding of soluble form of fibroblast surface protein, fibronectin to collagen. *Int. J. Cancer* 20: 1–5 (1977).

Ruoslahti, E.; Engvall, E.: Complexing of fibronectin, glyco-saminoglycans and collagen. *Biochim. biophys. Acta* 631: 350–358 (1980).

Mosher, D.F.: Action of fibrin-stabilizing factor on cold-insoluble globulin and α_2 macroglobulin in clotting plasma. *J. biol. Chem.* 251: 1639–1645 (1976).

Saba, T.M.; Albert, W.H.; Blumenstock, F.A.; Evanega, G.; Staehler F.; Cho, E.: Evaluation of a rapid immunoturbidimetric assay for opsonic fibronectin in surgical and trauma patients. *J. Lab. clin. Med.* 98: 482–491 (1981).

Eriksen, H.O.; Clemmensen, I.; Hansen, M.S.; Ibsen, K.K.: Plasma fibronectin concentration in normal subjects. *Scand. J. clin. Lab. Invest.* 42: 291–295 (1982).

Mosher, D.F.: Changes in plasma cold-insoluble globulin concentration during experimental Rocky Mountain spotted fever infection in rhesus monkeys. *Thromb. Res.* 9: 37–45 (1976).

Saba, T.M.; Blumenstock, F.A.; Scovill, W.A.; Bernard, H.: Cryoprecipitate reversal of opsonic α_2 surface binding glyco-protein deficiency in septic surgical and trauma patients. *Science* 201: 622–624 (1978).

Scovill, W.A.; Saba, T.M.; Kaplan, J.E.; Bernard, E.; Powrs, S., Jr.: Deficits in reticuloendothelial humoral control mechanisms in patients after trauma. *J. Trauma* 16: 898–904 (1976).

Gonzalez-Calvin, J.; Scully, M.F.; Sanger, Y.; Fok, J.; Kakkar, W.W.; Hughes, R.D.; Gimson, A.E.S.; Williams, B.: Fibronectin in fulminant hepatic failure. *Br. med. J.* 285: 1231–1232 (1982).

Edington, G.M.; Giles, M.: Pathology of sickle-cell anaemia and sickle-cell haemoglobin C disease; in Edington, Biles, *Pathology in the tropics*; 2nd ed., pp. 437–447 (Arnold, London 1981).

Wautier, J.L.; Wautier, M.P.; Pintigny, D.; Galacteros, F.; Cou-rillon, A.; Passa, P.; Caen, J.P.: Factors involved in cell adhesion to vascular endothelium. *Blood cells* 9: 221–234 (1983).

Wautier, J.L.; Pintigny, D.; Wautier, M.P.; Paton, R.C.; Galacteros, F.; Passa, P.; Caen, J.P.: Fibrinogen, a modulator of erythrocyte adhesion vascular endothelium. *J. Lab. clin. Med.* 101: 911–920 (1983).