short report
Haematologica 1994; 79:283-285

PRIMARY HYPERFIBRINOGENOLYSIS IN A PATIENT WITH ANAPHYLACTIC SHOCK

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ABSTRACT

Although systemic hyperfibrino(geno)lysis during hypotensive crisis is known, there do not seem to be recent reports of episodes of primary acute fibrinogenolysis during anaphylactic shock. We report the case of a 61-year-old male admitted to the hospital for anaphylactic shock due to an insect bite who presented a clinical and laboratory picture of severe acute generalized hyperfibrinogenolysis not secondary to disseminated intravascular coagulation (DIC). Without specific therapy, the clinical picture resolved itself spontaneously within 40 hours of onset.

Careful clinical examination and the execution of simple laboratory tests permitted a rapid diagnosis and therapeutic success.

Key words: primary hyperfibrino(geno)lysis, hyperfibrino(geno)lytic syndrome, anaphylactic shock

Primary systemic hyperfibrino(geno)lysis is characterized by spontaneous activation of plasminogen into plasmin, which causes: 1) generalized fibrinogenolysis with abnormal production of fibrinogen/fibrin degradation products (FDP); 2) degradation of coagulation factors V, VIII, IX, XI; 3) degradation of the fibrin present in any pre-existing localized thrombi and hemostatic clots.[1-2]

During systemic hyperfibrino(geno)lysis, lysis occurs in the macro circulation, probably as a consequence of the release of activators by endothelial cells[1] and of activation of the intrinsic pathway of the fibrinolytic system. Acute conditions such as a state of shock, surgical procedures,[3] liver transplantation,[4] acute leukemia[5] or administration of thrombolytic agents can cause this syndrome. It can also be caused by a few chronic conditions such as neoplasia[6] or chronic liver diseases.[7]

The degradation of fibrinogen and other coagulation factors induces a hemorrhagic condition without thrombocytopenia or thrombotic organ damage. Bleeding can also be due to lysis of recently formed hemostatic clots.

We describe a case of severe generalized hyperfibrinogenolysis in a patient with anaphylactic shock due to an insect bite.

Case report

A 61-year-old Italian male was admitted to our Hospital on 6 February, 1992 with a diagnosis of anaphylactic shock due to an insect bite.

On admission the patient presented shock with obnubilation, diffuse rash and trismus. Blood pressure was not measurable and peripheral pulses were absent.

The hemoglobin level was 14.3 g/dL, hematocrit 43, white blood cell count 10×10^9/L and platelet count 389×10^9/L; there were no schisto-

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Acknowledgments: the authors wish to thank Mrs. L. Geremia for her collaboration in typing the manuscript.
Received December 15, 1993; accepted April 12, 1994.

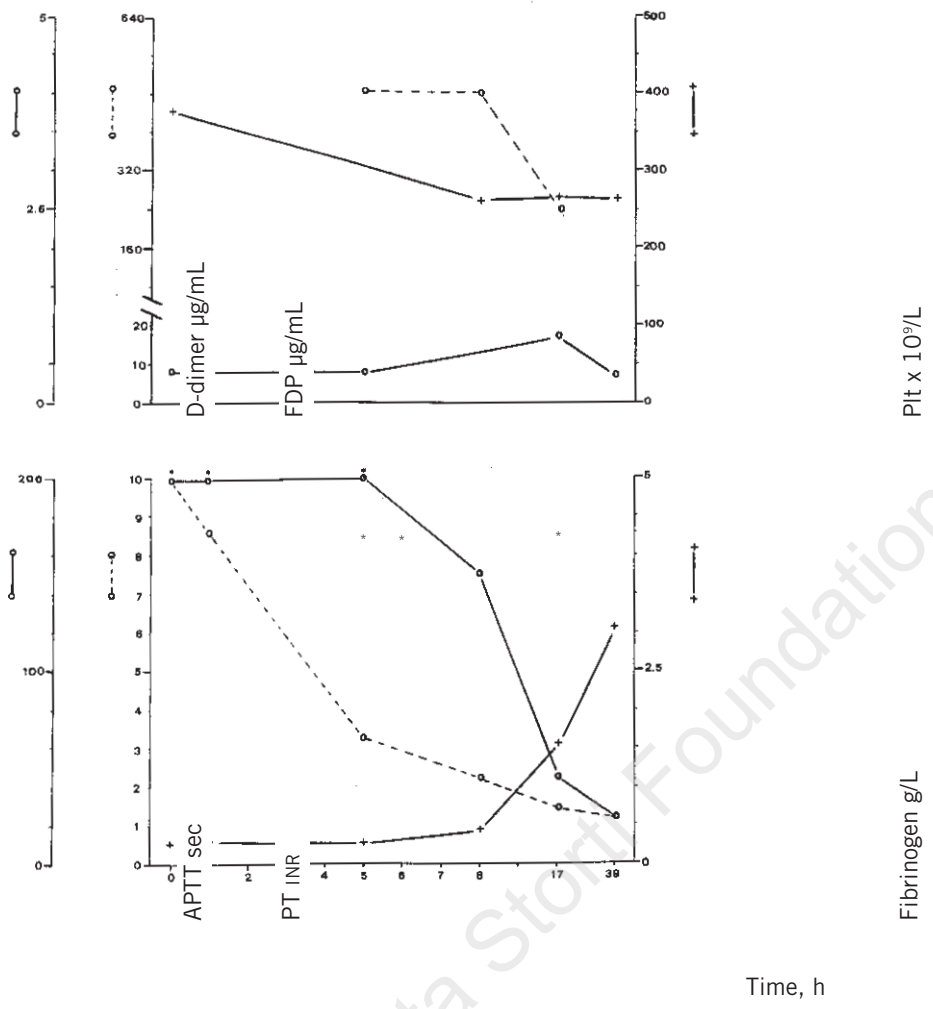

Figure 1. Changes in plasma PT, aPTT, fibrinogen, D-dimer, FDP and platelet count during the course of hyperfibrinogenolytic syndrome in a patient with anaphylactic shock. (*) no-clotting.

cytes in the peripheral blood smear. The prothrombin time (PT) was 88 sec. (INR >8.5), activated partial thromboplastin time (aPTT) >220 sec (control 22.7 sec), and the fibrinogen level was 0.25 g/L. Fibrin degradation products (D-dimer) were <0.5 μg/mL (normal range). Anti-thrombin III (ATIII) level was within normal limits.

After one hour, while PT, aPTT, fibrinogen level and D-dimers remained constant, the fibrinogen/fibrin degradation product levels were markedly elevated with values between 320 and 640 g/mL (normal limits: <10 μg/mL). Within 40 hours of admission all tests returned to almost normal values (Figure 1). Afterwards, the level of plasminogen activity was 59% and did not increase in subsequent blood tests.

Blood counts were performed by an autoanalyzer according to standard techniques. Activated partial thromboplastin time (THROMBOFAX, ellagic acid, ORTHO Systems, Raritan N.J., USA) and prothrombin time (THROMBOREL S, BEHRINGWERKE AG, Marburg, Germany) were measured using standard methods. Fibrinogen was measured by the method of Clauss (MULTIFIBREN, Ist. BEHRING SpA, L'Aquila, Italy). Plasma levels of AT III were determined by amydolytic assay using COATEST ANTITHROMBIN III Kit (KABI, Stockholm, Sweden). Plasminogen plasmatic activity was

measured by amydolytic assay using TEST PLASMINOGEN (Instrumentation Laboratory, Milan, Italy). Levels of D-dimer were established by latex-agglutination test (D-DIMER BOEHRINGER MANNHEIM GmbH, Mannheim, Germany), and levels of FDP by THROMBWELLCOTEST (WELLCOME Diagnostics, Dartford, England).

Discussion

It is very rare to encounter a state of primary acute hyperfibrino(geno)lysis.[1]

We refer to primary fibrino(geno)lysis when there is a primary activation of the fibrinolytic system, while secondary fibrinolysis is due to DIC. It is extremely important in all cases of hyperfibrino(geno)lytic syndrome, as in our patient, to distinguish between primary and secondary states since the treatment of the two forms differs notably.

The normal platelet count, the absence of schistocytes in the peripheral blood smear, the absence of D-dimers and non-involvement of the microcirculation were suggestive of a primary form, which often resolves spontaneously. In the absence of severe hemorrhage and with the possibility of subclinical DIC, we did not prescribe fibrinolysis inhibitors (i.e. ε-aminocaproic acid) but chose to follow the evolution of the syndrome while closely monitoring vital signs.

Primary generalized hyperfibrino(geno)lysis could be due to activation of the intrinsic pathway of the fibrinolytic system (Hageman factor, kinin system, urokinase-type plasminogen activator), and to the release of tissue-type plasminogen activator by endothelial cells injured by anaphylactic shock.[8-10]

The present case demonstrates that an accurate clinical observation and the execution of simple laboratory tests can make the diagnosis easier.

We found a quantitative defect of plasminogen activity in the propositus and in one of his sons, but its connection with the fibrinogenolytic syndrome is unknown. Family studies on physiological inhibitors of fibrinolysis are being carried out.

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