Case Reports and Technical Notes

Acute Fibrinolysis Following Craniotomy and Removal of Metastatic Tumor of the Cerebellum

Case Report

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The clinical syndrome of acute severe generalized bleeding represents an uncommon life-threatening catastrophe requiring prompt recognition and treatment. This paper reports such a case and reviews the differential diagnosis and treatment.

Case Report

A 49-year-old white woman had a radical mastectomy for carcinoma of the breast in 1962. She did satisfactorily until August, 1968, when she developed right sciatica and numbness in the left leg. A scalene node biopsy revealed carcinoma. Stilbesterol therapy was begun. In September, 1968, she developed diplopia and decreased visual acuity associated with bowel and bladder urgency. A trial of corticosteroids failed to improve her symptoms. There was no history of any bleeding disorder.

Examination. The patient had mild ataxia on the right, and bilateral hypesthesia below T-6. The right breast had been removed. The remainder of the physical and neurological examination was normal. Skull and chest x-ray films were also normal. Pertinent laboratory studies on admission were: hemoglobin 12 gm%; hematocrit 36.5%; white blood cells 7280; platelets 201,000; prothrombin time: patient 11.8 sec and control 11.6 sec; bilirubin content: total 0.3 mg% and direct 0.2 mg%; alkaline phosphatase 1.8 Bodansky units; serum glutamic oxaloacetic transaminase (SGOT) 13 units/cc; and total protein 6.3 mg%. A brain scan showed an area of increased uptake in the right posterior fossa, confirmed by a pneumoencephalogram.

Operation. A suboccipital craniectomy was done on October 24, 1968. A discrete metastatic adenocarcinoma compatible with breast origin was removed from the lateral surface of the right cerebellar hemisphere.

Postoperative Course. The patient awoke within 30 minutes after surgery. She was alert, talking, and without neurological deficit. Two hours after surgery a severe generalized bleeding diathesis suddenly developed over 10 minutes' time with diffuse ecchymoses, hematuria, bloody cerebrospinal fluid, and profuse bleeding at the ventriculostomy and craniectomy sites. The patient became semicomatose. Laboratory studies done immediately revealed the following: low fibrinogen screen (less than 100 mg%), normal platelet count, prolonged prothrombin time (patient time 21.3 sec and control 13.8 sec), prolonged clotting time (greater than 30 min), and clot observation showed a loose friable clot at 30 min with lysis at 45 min. These findings were compatible with an acute fibrinolytic syndrome. Treatment was begun with fibrinogen (8 gm) and epsilonaminocaproic acid (5 gm).

Three hours after surgery the patient was returned to the operating room in an attempt to decompress the brainstem. On reopening the posterior fossa wound there was a gush of blood under increased pressure. Her blood failed to clot for 1½ hours then began to clot slightly. The dura was left open and the wound packed open. Blood loss was estimated to be 7 units. This was replaced with 5 units of whole bank blood and 2 units of fresh blood. She received an additional 10 gm of fibrinogen and 7 gm of epsilon-aminocaproic acid. A fibrinogen screen was normal (greater than 200 mg%); however, it was felt that the coagulation defect was never completely corrected.
The patient died 4 hours after the onset of the bleeding diathesis, presumably of diffuse hemorrhage and brain stem failure. An autopsy could not be obtained.

Discussion

Normal blood clotting is a dynamic process in which forces leading to coagulation are antagonized by contrary forces, including natural anticoagulants and agents that remove the formed clot. A simplified schematic representation of the clotting process is shown in Fig. 1. Clot dissolution or fibrinolysis is equally important. Sherry's concept of the human fibrinolytic enzyme system in plasma is shown in Fig. 2. Central in this process is plasmin, an active fibrinolytic enzyme, and its precursor plasminogen. Clot lysis takes place primarily as the result of diffusion or incorporation of the activator into the thrombus. Thereby the fibrinolytic process remains essentially a localized one. Fibrinolysis is held in check by inhibitors. These are of two kinds: inhibitors of activators, such as antistreptokinase and antitrypsin, and antiplasmins. Factor XIII stabilizes fibrin, thus making it more resistant to fibrinolysis.

Fibrinolysis means the enzymatic liquefaction of a blood or fibrin clot. The clinical picture may develop with great suddenness and is characterized by the appearance of severe generalized bleeding, hypotension, and extensive ecchymoses. Acute fibrinolysis is life-threatening and requires immediate diagnosis and treatment. Primary fibrinolysis is rare, while secondary fibrinolysis is more common. Fearnley reported that testosterone and corticosteroids, used to treat metastatic breast cancer, both increase fibrinolytic activity in the blood. It has been shown that filling the cerebral ventricular system with air provides an excellent stimulus for endogenous activation of the human fibrinolytic system. Stress, anesthesia, and surgery may also produce a fibrinolytic reaction in certain patients. Some tumors, notably carcinoma of the lung, pancreas, and prostate, have been implicated in the release of procoagulants into the blood stream at a relatively slow rate over a relatively long period of time. Since the procoagulant activity in the autoinfused material is probably weak and mixed with plasminogen activator, the outstanding feature might not necessarily be that of disseminated intravascular coagulation but rather a fibrinolytic state.

A related syndrome is disseminated intravascular clotting, an acute transient coagulation occurring in the blood flowing through-

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**Fig. 1.** The blood coagulation mechanism.

**Fig. 2.** Human fibrinolytic enzyme system (in accordance with the views of Sherry; reproduced through the courtesy of the editors of Series Haematologica).