letter to the editor
Haematologica 1994; 79:569

THROMBOTIC THROMBOCYTOPENIC PURPURA AFTER DEFIBROTIDE THERAPY

Cesare Perotti, Lorella Torretta, Laura Costamagna, Laura Salvaneschi

Servizio di Immunoematologia e Trasfusione, I.R.C.C.S. Policlinico San Matteo, Pavia, Italy

Sir,

thrombotic thrombocytopenic purpura (TTP) is a rare clinical syndrome characterized by microangiophatic hemolytic anemia, thrombocytopenia, and fluctuating neurologic abnormalities. Etiology and pathogenesis are not fully understood. In some cases drugs have been described as related agents (oral contraceptives, chemotherapy agents, penicillina, ticlopidine).[1] An exalted platelet adhesion and aggregration and a deficiently prostacyclin synthesis by endothelium are considered of primary importance in the pathogenesis of TTP. These observations support the use of antiplatelet and antithrombotic agents in the therapy of the syndrome.[2] On the other hand, some authors reported cases of TTP developed during antithrombotic regimen in vascular disease.[3] We report a case of TTP in a female patient on therapy with defribotide, an antithrombotic drug.

A 39-year-old woman was admitted to our institute with aphasia, headache, sluggyness, severe anemia, thrombocytopenia. She had been on defibrotide 200 mg/day for 20 days as sole therapy for peripheral vascular disease. Laboratory findings were: hemoglobin 3.9 g/dL, white cell count 9.6×10^9/L, platelet count 16×10^9/L, reticulocytes 12%, total serum bilirubin 1.8 mg/dL, serum lactic dehydrogenase (LDH) 3200 U/L, serum creatinine level 0.8 mg/dL, severely fragmented red cells in peripheral blood film, negative Coombs' test. No laboratory signs related to disseminated intravascular disease were present; coagulation parameters were: prothrombin time 14.4 seconds, prothrombin 73%, partial thromboplastin time 12.7 seconds, fibrinogen 245 mg/dL, fibrin/fibrinogen degradation products less than 10 mg/mL. Immediatly defibrotide therapy was withdrawn and patient underwent intensive plasma exchange with fresh frozen plasma and cryosupernatant as replacement fluid, associated with corticosteroid therapy. There was a prompt clinical and laboratory improvement after three daily plasma exchanges and complete disease resolution was obtained after 20 procedures (platelet count 315×10^9/L, LDH 312 U/L, total bilirubin 0.24 mg/dL, Hb 11.3 g/dL). Patient is disease-free at 8 months.

In this patient the absence of any causes related to TTP and temporal association between defibrotide assumption and development of TTP was suggestive in considering defibrotide as potential prime mover of the disease. It's an antithrombotic drug that produces a release of the tissue plasminogen activator from the endothelial cells and that amounts prostacyclin level.

At our knowledge among antiplatelet drugs, cases of drug-related TTP have been described only for ticlopidine that acts on the platelet membrane and alters its reactivity by blocking ADP induced platelet interactions with fibrinogen and vWF. It's interesting that two antithrombotic drugs employed in TTP treatment could become inducer of the disease.

Considering in our country the wide employment of defibrotide in peripheral vascular illness, we suggest a carefully hematological surveillance of these patients during treatment.

References

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