Severe Unresponsive Thrombocytopenia in a Transplantated Patient with Chronic Werlhof 's Disease: Correction after Splenectomy

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Dear Sir,

Werlhof s disease is one of the commonest causes of platelet depletion [1, 2]; it can affect patients with a renal transplantation.

We describe the case of a woman in whom this disease manifested itself with a severe clinical picture only 13 years after transplantation.

This disease was being checked in its expression by the association of immuno-suppressive drugs (azathioprine and steroids) assisting the transplant, since they are also known to be effective as Werlhof s disease therapy. This treatment changed the expected clinical outcome in so far as it delayed the identification of the problem by limiting the degree of platelet destruction. Careful investigation of the case produced the clues to proper diagnosis and effective treatment.

Case Report

A 42-year-old woman with chronic renal failure secondary to glomerulonephritis underwent cadaver donor renal transplantation in January 1980. The graft functioned well, with 75 mg/day azathioprine and 5 mg/day prednisone. In December 1993, severe platelet depletion was detected (16,000 platelets/ mm³).

An accurate revision of previous records revealed 3 occasional drops in the platelet count in the posttransplantation follow-up to values as low as 50,000-100,000 platelets/ mm³, followed by spontaneous normalization. Episodes of metrorrhagia had persisted even after cavity overhaul for polypectomy

of the cervix uteri in June 1980. In April 1992, for the first time, platelets fell to 50,000/mm³, but the search for antiplatelet antibodies proved negative and the medullary biopsy showed normal maturing normal-cell marrow, with a megakaryocyte count in the normal range.

Creatininemia was 1.5 mg/dl.

On admission (December 1993) there was no clinical bleeding, but only a few petechiae on the trunk and abdomen and a sub-conjunctival hemorrhagic flush. Creatinine was 1.5 mg/dl, uric acid 8.4 mg/dl, RBCs 4,000,000/mm³, Hb 37%, 25,000 platelets/mm³, VES 3, low C4 (14 mg/dl), with negative cryoglobulins, anticardiolipin antibodies, FAN, and normal lymphocyte sub-population. Antiplatelet antibodies were present at a low titer (technique: direct and indirect immunofluorescence; method: flow cytometry) [3]. A bone marrow test confirmed the normal pattern.

Spleen and liver were of normal size at ultrasonography, and other potential causes of thrombocytopenia due to increased peripheral loss were excluded [4], especially that due to drugs. The diagnosis was therefore of chronic Werlhof's disease.

During her hospital stay, the platelet count fell further to 1,000 platelets/mm³, and some hemorrhages appeared (skin, petechiae, metrorrhagia). Treatment with methylprednisone (60 mg/day) and platelet infusion (8 U/day for 5 consecutive days) were tried without any benefit. The patient's clinical decline led us to recommend splenecto-

my. High-dose immunoglobulin was administered (30 g/day for 5 days), together with steroids (60 mg/day), which raised the platelet count to 100,000-150,000 platelets/mm³. Splenectomy normalized the clinical and laboratory picture in 4 weeks, which, 5 months later, continued to be excellent with a platelet count remaining in the range 120,000-280,000 platelets/mm³.

Discussion

Werlhof's disease is one of the commonest causes of platelet depletion in adults, and can be diagnosed once drug-induced platelet depletion has been ruled out [5].

In the case we examined, the possibility that azathioprine might be responsible for thrombocytopenia was excluded because no signs of myelodepression were found; moreover discontinuation of the drug did not improve the platelet count, but induced a further drop in the count (from 25,000 to 16,000 platelets/mm³), which supports the role it plays in limiting platelet loss.

It must be mentioned that the clinical course of this pathology is marked by the paucity of the symptoms. It is hard to detect unless laboratory tests coincide with the fleeting asymptomatic moment in which the low count can be detected.

Immunosuppressive therapy established a state of thrombocytolysis offset by increased marrow production which balances peripheral platelet loss. Should this precarious equilibrium be upset, the onset of platelet depletion becomes manifest. In this patient, the occasional finding of thrombocytopenia, despite constant ingestion of azathioprine and corticosteroids since 1980 as anti-rejection therapy, documents the episodes of momentary breakdown in the equilibrium whenever the drug combination happened to lose effect. A careful review of clinical records, as in this case, enables the phenomenon to be set in context so that a therapy strategy may be implemented which will enable one to cope with a clinical condition that may take a sudden and dramatic turn.

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