Hemolytic-Uremic Syndrome after Cancer Chemotherapy without Mitomycin C

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Dear Sir,

Thrombotic microangiopathy with renal failure occurs due to treatment with mitomycin C [6, 7], which has been recognized as being nephrotoxic. Recently, similar findings have been reported after cancer chemotherapy without this drug [2, 4]. We wish to report the case of a tumor-free patient who also developed hemolytic-uremic syndrome (HUS) after a combination chemotherapy which did not include mitomycin C.

Case Report

A 43-year-old woman was admitted in September 1981 with a malignant melanoma of the leg (superficial spreading melanoma with Clark's level III and a thickness of 2.9 mm). After surgery, she received the following monthly combination chemotherapy:

Dactinomycin 0.25 mg/m² i.v. on day 1

Vincristine 0.6 mg/m² i.v. on day 1

CCNU 80 mg/m² per os on day 2

Vindesine 1.5 mg/m² i.v. on day 15

Bleomycin 10 mg/m² i.m. on day 15

Dacarbazine 500 mg/m² i.v. on day 1 and 15

On March 25, 1982, a mild pancytopenia was discovered: hemoglobin 88 g/l, WBC 3,000/mm³ with 69% PMNs, platelet count 110,000/mm³. The 5th course was therefore given without CCNU after a blood transfusion. However, 3 weeks later the anemia became more severe and the platelet count had fallen: hemoglobin 43 g/l, WBC 4,100/mm³ with 80% PMNs, platelet count 20,000/mm³. Three others units of packed erythrocytes were transfused.

On May 3, 1982 (day 1), our patient was admitted because of obvious HUS: hemoglobin was 37 g/l without signs of bleeding, reticulocyte counts varied from 100,000 to 140,000/mm³ with mild hyperbilirubinemia (54 µmol/l), a fall of haptoglobin (less than 0.2 g/l) and a considerable raise of LDH (from 960 to 1,100 IU/l, normal less than 195 IU/l). The Coombs' test was negative and peripheral blood smear showed numerous schistocytes. Platelet count was 16,000/mm³, and she had multiple bruises. Prothrombin, partial thromboplastin and thrombin times were normal.

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nogen was from 2 to 3.2 g/l, fibrin degradation products were above 10 but below 40 µg, and ethanol gelation test was negative. Bone marrow biopsy was moderately hypocellular but polymorph, with adequate megakaryocytes, a mild erythroid hyperplasia (40%) and no evidence of malignant cells.

Oliguric renal failure developed progressively so that on day 10 the patient had an anasarca and a blood pressure of 210/100 mm Hg. Serum creatinine concentrations rose from 190 (day 1) to 709 µmol/l (day 10), and urinalysis showed proteinuria (from 3.7 to 7 g per day) and microscopic hematuria (100 erythrocytes/mm³). CH₅₀ was normal and circulating immune complexes were not detected. Ultrasound, urography, cavography and renal arteriography were normal. Kidney biopsy was not done because of refractory thrombocytopenia. Congestive heart failure with pulmonary edema was noted after blood transfusions. Mild cholestasis was present, without modification of transaminases. Liver ultrasonography was normal and transjugular biopsy excluded suspected hepatic thrombosis and showed no major histological abnormalities. No neurological symptom was present.

Furosemide, clonidine and hemodialysis were associated with dipyridamole (450 mg per os) and aspirin (500 mg i.v. per day). Plasmapheresis with fresh frozen plasma (45–50 ml/kg) were performed on days 17–20, 22–24, 28 and 32. Hemolysis was rapidly but incompletely improved: LDH was still elevated to 400 IU/l and schistocytes were yet present on day 24; LDH was 310 IU/l and schistocytes were uncommon on day 36. The rise of hemoglobin was moderate (65 g/l after day 30, 80 g/l after day 45) probably because of the persistence of renal failure. Platelet count was above 30,000/mm³ on day 22 and above 50,000/mm³ on day 32. The renal function did not improve: serum creatinine concentration was between 700 and 900 µmol/l under hemodialysis.

Our patient is now on chronic hemodialysis. Hematological status is normal and the malignant melanoma has not yet recurred after a follow-up of 49 months totally.

Comments

Disseminated carcinoma can produce thrombotic microangiopathy [1], but our patient was tumor-free and therefore in the absence of other known cause, we postulate that this HUS was induced by the antineoplastic chemotherapy. Thrombotic microangiopathy with renal failure is well recognized after mitomycin C [6, 7] but

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recently, Jackson et al. [4] have reported on five patients who also developed this complication after cis-platinum, bleomycin and a vinca alkaloid.

In our opinion, the drug responsible for HUS would be either bleomycin as suggested by Jackson et al. [4] or dacarbazine which has also been incriminated with the cause of Budd-Chiari syndrome [3]. These drugs have been also used in another case of HUS; chemotherapy consisted of vinblastine, doxorubicin, dactinomycin, bleomycin, vincristine and dacarbazine [2].

The aggravating effect of the blood transfusions reported by several investigators [5–7] may also have occurred in our patient, since a decrease of platelet count was noted in April 1982 after the first blood transfusion, until hospitalisation. Finally, the discrepancy between the positive effect of plasmapheresis on the HUS and the persistence of renal failure, as was observed before [7], should be noted.

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