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Bronchiolitis obliterans organizing pneumonia in a BMT patient receiving FK506

Sir,

Thirman *et al.*[1] have reported a patient who twice underwent allogeneic BMT and developed bronchiolitis obliterans organizing pneumonia (BOOP) each time, once clearly in association with chronic GVHD. Based on their review of the literature, they concluded that BOOP may be a manifestation of chronic GVHD, albeit infrequently. Our recent experience with a patient who developed BOOP in the absence of chronic GVHD suggests otherwise.

A 23-year-old female received high dose thiotepa, CY, total body irradiation and a one-antigen mismatched marrow from her mother as treatment for ALL in second relapse. The marrow was partially depleted for $CD3^+$ cells. CYA, methylprednisolone (MP) and anti-CD5 ricin A chain immunoconjugate (XZ-CD5) were given post-transplant as GVHD prophylaxis.[2] The granulocytes exceeded $0.5 \times 10^9/l$ on day 10 after transplantation. XZ-CD5 and MP were discontinued on day 20 when capillary leak syndrome occurred, and the symptoms resolved with conservative management.

Grade II acute GVHD involving the skin occurred on day 34 and responded rapidly to treatment with high dose MP. She presented with hemolytic-uremic syndrome (HUS) manifested as microangiopathic hemolytic anemia and renal insufficiency on day 44. CYA was discontinued, and treatment consisted of high dose MP and plasma exchange. By day 86, the HUS had largely resolved, and a marrow biopsy showed no leukemia. Evaluation showed no evidence of acute or chronic GVHD, but she had developed moderately severe muscle weakness, hypertension, edema and hyperglycemia as a result of prolonged use of high dose MP. On day 88 she was started on FK506 for GVHD prophylaxis using a regimen reported previously,[3] and MP was tapered rapidly to 20 mg daily with resolution of the steroid-related problems and no HVS.

She did well until day 140 when she presented with a 2-day history of a non-productive cough without fever. Physical examination showed no evidence of chronic GVHD, and the liver enzymes were normal. A chest X-ray showed patchy infiltrates. Because of the suspicion of infection or EBV-lymphoproliferative disease, FK506 was discontinued. Culture of an oral lesion grew HSV, but cultures of bronchoalveolar lavage fluid were negative for bacteria, fungus, virus and opportunistic agents. The infiltrates progressed, and the patient required intubation despite administration of standard broad-spectrum antibiotics. Subsequent treatment consisted of vancomycin, aztreonam, amphotericin, trimethoprim/sulfamethoxazole, erythromycin, ganciclovir, iv immunoglobulin, isoniazid, rifampin, doxycycline, and high dose MP. An open lung biopsy on day 145 showed BOOP. The biopsy culture grew *Veillonella*, but this was considered to be a contaminant, as a bacterial process was not seen on the biopsy. Despite aggressive management, the patient died from respiratory insufficiency on day 160. An autopsy revealed BOOP in the lungs as was found in the biopsy. Chronic GVHD was not found in any organ at autopsy.

This patient is the second well-documented case of BOOP after allogeneic BMT. Our patient differs from that reported by Thirman *et al.* in that she had no evidence of chronic GVHD on clinical evaluation or at autopsy. It is possible that BOOP is a manifestation of chronic GVHD but other clinical disease in our patient was prevented by the use of FK506. Indeed, in a series of patients receiving FK506 for treatment of chronic GVHD, pulmonary involvement was least responsive to therapy.[3] Further experience will be required to characterize BOOP in the allogeneic BMT population completely, but our case suggests that BOOP should be included in the differential diagnosis of pulmonary infiltrates even in the absence of other manifestations of chronic GVHD.

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