

CORRESPONDENCE

REMISSION OF A HIGH-GRADE GASTRIC MUCOSA ASSOCIATED LYMPHOID TISSUE (MALT) LYMPHOMA FOLLOWING *HELICOBACTER PYLORI* ERADICATION AND HIGHLY ACTIVE ANTIRETROVIRAL THERAPY IN A PATIENT WITH AIDS

To the Editor:

Patients with human immunodeficiency virus (HIV) infection have an increased incidence of B-cell non-Hodgkin's lymphomas that are usually of a high-grade histologic type and show an aggressive clinical behavior with low rates of response to chemotherapy (1). Immunological reconstitution following highly active antiretroviral therapy (HAART) may influence the prognosis of some of these HIV-associated lymphomas by analogy to cases of post-transplantation lymphomas that remit following diminished immunosuppression. Recent data have emphasized the possibility of treating B-cell lymphoproliferative disorders etiologically related to viruses with specific virostatic agents in the context of immunodeficiency states (2,3). We report on a case of a patient with AIDS in whom remission of a gastric high-grade

mucosa associated lymphoid tissue (MALT) lymphoma was achieved following *Helicobacter pylori* eradication therapy and HAART.

A 42-year-old man presented with a 4-month history of intermittent epigastric pain, low-grade fever, and a progressive weight loss of 20 kg. A diagnosis of HIV-1 infection was established with a severe CD4+ lymphocyte depletion (4 cells/mL) and a high HIV viral load (950,000 copies per mL). Upper gastrointestinal endoscopy showed a 15 mm ulcer in the gastric antrum with thickened periulcer mucosal folds. Multiple biopsy samples revealed lymphoepithelial lesions with diffuse mucosal infiltration by large lymphoid cells characteristic of a high-grade MALT lymphoma (Figure) and the presence of multiple *H. pylori* organisms in the gastric mucosa. Immunohistochemistry confirmed a monoclonal B-lymphocyte proliferation with positive CD20 and negative CD3, CD5, and CD10 staining. Staging procedures confirmed a stage-I high-grade MALT lymphoma. *H. pylori* eradication therapy with amoxicillin, tinidazole, and omeprazole was started together with antiretroviral therapy with stavudine (40 mg twice daily), lamivudine (150 mg twice daily), and indinavir (800 mg three times daily). The patient gained weight, and the epigastric pain disappeared. Viral load became undetectable (below 50 copies/mL) and CD4+ lymphocyte

count increased to 124 cells/mL at 1 month and to 548 cells/mL at 6 months. Follow-up endoscopy at 2, 3, and 6 months showed the healing of the gastric ulcer, and repeated biopsies documented the disappearance of the malignant lymphoid tissue, as well as the *H. pylori* infection.

Gastric MALT lymphoma is etiopathogenically related to chronic infection of the stomach by *H. pylori*, and the possibility of inducing remission with *H. pylori* eradication therapy is well recognized in cases of low-grade MALT lymphoma in immunocompetent hosts. Surprisingly, a full remission of a high-grade gastric MALT lymphoma was achieved in our patient following *H. pylori* eradication therapy associated to HAART. This previously unreported event indicates that antibacterial therapy together with antiretroviral therapy may be effective for the treatment of gastric high-grade MALT lymphomas in the context of HIV-immunodeficiency. Therefore, this approach should be attempted in similar cases before using the aggressive chemotherapy recommended for such lymphomas. An analogy can be drawn with the recent report of a remission of an advanced lymphoproliferation associated to Epstein-Barr virus in a HIV-infected patient that was achieved with foscarnet and HAART (2). In addition to the control of the abnormal antigenic stimulation by *H. pylori* eradication, it is plausible that HAART-induced T-cell lymphocyte functional recovery (4) may have contributed to the remission of the gastric high-grade MALT lymphoma in our patient, in view of the hypothesis that impaired T-cell regulation of B-cell proliferation is also involved in the pathogenesis of MALT lymphomas (5).

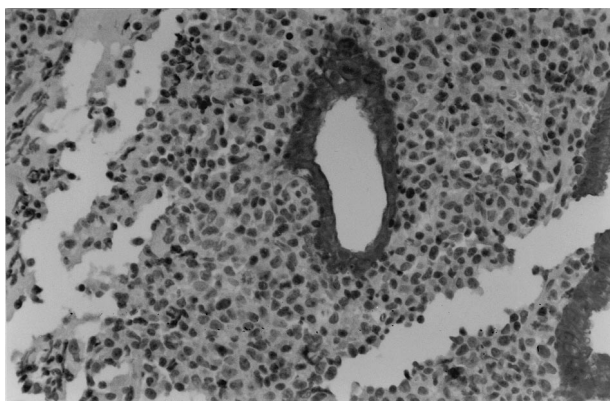


Figure. Section of gastric mucosa showing a high-grade MALT lymphoma with lymphoepithelial lesions and a diffuse infiltration of the mucosa with large lymphoid cells.

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ACUTE FEBRILE MYELODYSPLASIA AND PNEUMONITIS DUE TO HUMAN HERPESVIRUS 6 AFTER ACCELERATED CHEMOTHERAPY

To the Editor:

Nearly all primary human herpesvirus-6 (HHV-6) infections are acquired during early childhood, and most of these are asymptomatic. The seroprevalence among adults ranges from 60% to 90%, and reactivation is rare (1,2). Clinical disease associated with HHV-6 reactivation has been described in recipients of solid organ, blood, and marrow transplantation recipients and in patients with acquired immunodeficiency syndrome (AIDS) (3-6). We describe a patient with profound myelosuppression and pneumonitis due to HHV-6 infection after conventional chemotherapy.

A 48-year-old man with a 3-year history of malignant astrocytoma

presented with fever (39°C) and profound granulocytopenia 22 days after his last 2-week cycle of oral procarbazine (150 mg/m² daily). He had been on maintenance therapy consisting of oral dexamethasone (8 mg per day) for 2 months. He complained of non-productive cough, progressive dyspnea on exertion, and fever. Pertinent findings on physical examination included febrile diaphoresis, reduced breath sounds accompanying crackles at both lung bases, and minimal expiratory wheezing. Laboratory tests showed the following: white blood count 400 cells per mm³ and absolute neutrophil count 100 cells per mm³, hemoglobin 8.8 g/dL, and platelet count 38,000 cells per mm³. *Candida albicans* was the only microorganism isolated from bronchial and oropharyngeal specimens. Results of all other respiratory cultures including cytomegalovirus (early antigen detection by shell vial) and respiratory viruses (including rapid detection tests for adenovirus, respiratory syncytial virus, influenza A and B, and parainfluenza viruses) were negative. Multiple blood cultures remained sterile for bacteria, fungi, and viruses. A total body computed tomography scan revealed perihilar consolidation with bilateral pleural effusions. Magnetic resonance images of the head were consistent with tumor recurrence and expansile calvarial metastasis. There was no clinical improvement after 12 days of empiric therapy with broad-spectrum antibacterial (ceftazidime, 6 g daily; amikacin, 15 mg/kg daily; vancomycin, 2 g daily), antifungal (amphotericin B, 1 mg/kg daily) and antiviral (acyclovir, 30 mg/kg daily) agents. Bone marrow biopsy analysis revealed a hypocellular marrow involving all cell lines and large myelocytes with moderate toxic granulation; viral cytomegalovirus inclusions were not seen. After 23 days of persistent granulocytopenia and fever ($\geq 40^\circ\text{C}$), foscarnet (180 mg/kg daily) was started empirically for presumed HHV-6 infection. Ninety-six hours

later, the patient became afebrile, and the white blood count (6200 cells per mm³) improved significantly. The platelets (42,000 per mm³) and hemoglobin (9.0 g/dL) were slower to recover. This recovery of leukocytes was accompanied by resolution of the pulmonary process over the following week. Human herpesvirus-6 (variant B) DNA was detected (PCR Viomed Laboratories Inc., Minneapolis, Minnesota) from the patient's peripheral blood on the 22nd day of the granulocytopenia. That suggested acute viremia, probably as a result of reactivation of a remote childhood infection (7). All other antimicrobial agents were discontinued, and the patient was treated with foscarnet for a total of 4 weeks (14-day induction dose, 180 mg/kg daily). No relapses were observed when antiviral therapy was discontinued.

This dramatic presentation of severe myelosuppression, involving multiple lineages of bone marrow cell lines due to HHV-6 infection, has been described in allogeneic marrow transplantation recipients, and may present as an "empty marrow" (8). In most cases, however, the myelodysplasia due to HHV-6 manifests as modest, chronic pancytopenia and is often mistaken for secondary graft failure (9). The spectrum of diseases due to HHV-6 infection is evolving, and the relevance of asymptomatic HHV-6 viremia in the immunocompromised host remains uncertain (10). Human herpesvirus-6 infection may be considered a potential cause of myelosuppression in patients undergoing accelerated chemotherapy for refractory cancer. A high level of suspicion leading to prompt therapy with foscarnet may reverse this life-threatening complication.

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