CLINICAL CASE:

LYMPHADENOPATHY IN THE HIV-POSITIVE PATIENT

Suki Subbiah, MD

A 37-year-old man presented with a complaint of slowly enlarging non-tender cervical lymphadenopathy for approximately one year with more rapid enlargement within the past two months. He also reported occasional subjective fevers and chills as well as intermittent night sweats. He denied decreased appetite, weight loss, fatigue, other lumps or bumps, dental pain or infections, sick contacts, dysphagia, odynophagia, cough, shortness of breath, chest pain, abdominal pain, nausea or vomiting, diarrhea or constipation, blood in stool, blurry vision, headache, weakness, gait instability, or bone pain.

He has a past medical history of HIV/AIDS (diagnosed in 2002) along with previous diagnoses of cryptococcal meningitis, pulmonary tuberculosis, disseminated histoplasmosis, and Pneumocystis jiroveci pneumonia. He has no active infections currently. He was initially compliant with combination antiretroviral therapy (cART) for the first several years, but then self-discontinued for a prolonged period of time (more than ten years). For the past two years, he has been fully compliant with his cART regimen. He denies history of surgical procedures. His current medication list includes emtricitabine/tenofovir alafenamide, dolutegravir, darunavir, ritonavir, sulfamethoxazole/trimethoprim, and fluconazole. He has never smoked cigarettes or used chewing tobacco. He does not drink alcohol or engage in recreational drug use. He is married and lives with his wife and daughter. He works at a plant nursery as a landscaper. He denies family history of malignancy. Upon examination, the patient was noted to have a temperature of 98.9 degrees Farenheit, pulse of 105 beats per minute, blood pressure of 110/76 mm Hg, respiratory rate of 22 breaths per minute, oxygen saturation of 100% on room air, weight of 236 pounds, and height recorded as 165.1 centimeters. Bulky bilateral cervical lymphadenopathy, right greater than left, was appreciated on palpation. There was no palpable supraclavicular, axillary, or inguinal lymphadenopathy. Cardiac examination demonstrated regular rhythm without murmurs, rubs, or gallops. Lungs were clear bilaterally on auscultation. Abdomen was non-tender and non-distended to palpation with normoactive bowel sounds present and no palpable hepatosplenomegaly. The skin demonstrated no evidence of rash or lesions. Neurological exam revealed no focal deficits, with normal strength and sensation in all extremities.

Complete blood count was normal with a white count of 6,700 cells/µL and normal differential, hemoglobin of 13.5 g/dL, and platelet count of 235,000 cells/µL. Alkaline phosphatase was elevated at 291 units/L (normal range 20-120 units/L), and total protein was also elevated at 10.3 g/dL (6.0-8.0 g/dL). Remainder of comprehensive metabolic panel was normal, including transaminases. Serum protein electrophoresis demonstrated elevated gamma globulin fraction of 4.0 g/dL (0.5-1.5 g/dL) but was found to be polyclonal gammopathy as no monoclonal spike was detected. HIV viral load was undetectable (<20 copies/mL), and CD4 count was decreased at 131 cells/µL (359-1519 cells/µL) with low CD4/CD8 ratio of 0.05 (0.92-3.72) and CD4% of 4.1% (31-59%). Hepatitis B and C testing were negative. Erythrocyte sedimentation rate (ESR) was markedly elevated at 95 mm/hr (0-15 mm/hr).

CT of neck with contrast noted extensive lymphadenopathy in soft tissues of neck, particularly on the right. He underwent core needle biopsies of right cervical lymph node with pathology confirming classical Hodgkin lymphoma (Epstein Barr virus-positive). PET/CT demonstrated several areas of abnormal hypermetabolic activity: multiple nodal masses in the right neck (largest measuring 6.0 cm), bilateral axillary and supraclavicular lymphadenopathy, multiple liver lesions with adjacent enlarged gastrohepatic lymph nodes, multiple bilateral lung lesions, and multiple areas within the pelvic bones. Imaging findings were consistent with Stage IVB disease (lung, liver, bone) with a calculated International Prognostic Score of 3 indicating 60% predicted 5-year rate of freedom from progression of disease and 78% estimated rate of overall survival. Echocardiogram and pulmonary function testing showed normal cardiac and lung function.

He initiated treatment with a combination chemotherapy regimen of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) with pegfilgrastim support. cART regimen was continued. Interim PET/CT restaging after 2 cycles noted complete metabolic response. Thus, regimen was de-escalated to AVD (discontinuation of bleomycin) for 4 further cycles. He tolerated chemotherapy well without any delays or dose adjustments required. Post-treatment ESR and total protein demonstrated normal values.
phenomenon is not yet clearly understood but suggests that there is another etiology for immunocompromise.

Although our patient had a preexisting diagnosis of AIDS due to CD4 count and opportunistic infections at the time of HIV diagnosis nearly two decades prior, Hodgkin lymphoma in itself is not an AIDS-defining malignancy, and remains one of the most common non-AIDS-defining malignancies in PLWH. Therefore, malignancy must be considered in the differential diagnosis of lymphadenopathy in the HIV-positive patient, even when the viral load is undetectable. Other causes of lymphadenopathy include reactive follicular hyperplasia, infection, and sarcoidosis.

In considering treatment of HIV-associated Hodgkin lymphoma, initial concerns arose over further immunosuppression and infection rate, the ability of patients to tolerate intensive chemotherapy regimens, and the potential for drug-drug interactions between cART and chemotherapy that may lead to unanticipated toxicity. Despite advanced stage disease, patients with HIV-associated Hodgkin lymphoma are able to tolerate combination chemotherapy and cART, and achieve similar outcomes to their non-HIV counterparts.

In addition, studies have demonstrated that combining cART and chemotherapy is both feasible and efficacious in improving immune function. Prognosis is favorable in patients who achieved a complete remission after completion of chemotherapy, such as our patient. Given that HIV-associated Hodgkin lymphoma is potentially curable in the majority of patients, aggressive therapy is warranted.

REFERENCES