Fellows' Corner

by Michael A. Papper and Bhavik M. Bhandari

An 18-year-old African American male without significant past medical history presents with a one-year history of non-bloody loose stools and 35 lb weight loss. The patient noted worsening of his diarrhea including symptoms of nausea, vomiting and loss of appetite prompting him to come to the Emergency Department for evaluation. His physical exam is significant for a thin male without cachexia and a soft, non-distended abdomen with hepatomegaly. His rectal exam is positive for occult blood and a healed perianal scar. His initial laboratory workup reveals a microcytic anemia (Hgb = 7.2, MCV = 79), BUN of 67 and Creatinine of 3.2. The remainder of his initial blood work was notable for AST = 62, ALT = 22, Amylase = 97, AP = 312 and an Albumin of 1.7. His initial stool studies showed WBC-negative, *Clostridium difficile*-negative and O&P negative but abundant Candida were seen on culture. In light of patient's sexual history, remarkable for multiple sexual partners, HIV testing was performed. Rapid HIV was positive and subsequently confirmed by Western Blot. His CD4 count was 29 and quantitative HIV was greater then 750,000 copies. Upper endoscopy (Figure 1) and colonoscopy (Figure 2) were performed to evaluate etiology of symptoms and anemia.

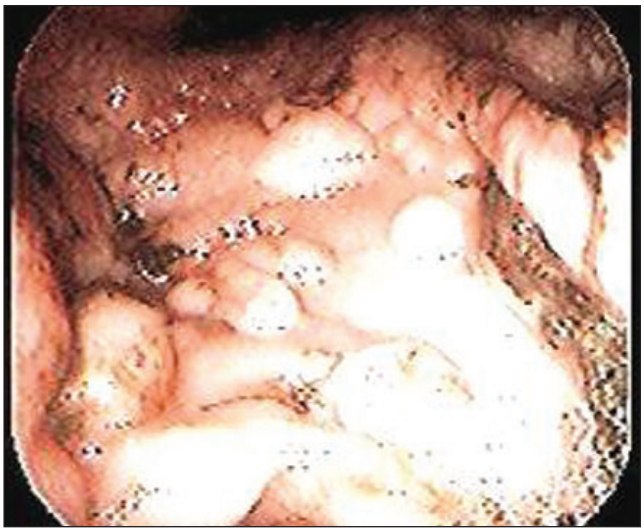

Figure 1. Upper endoscopic image.

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Questions

1. What are considerations in the differential diagnosis of patient with HIV and diarrhea?
2. What is the diagnosis based on endoscopic findings?
3. What is the pathogenesis of this disease and how is it treated?

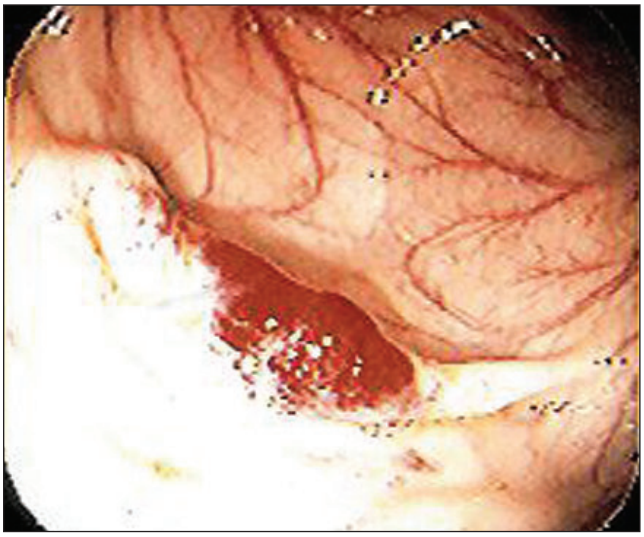

Figure 2. Colonoscopic image.

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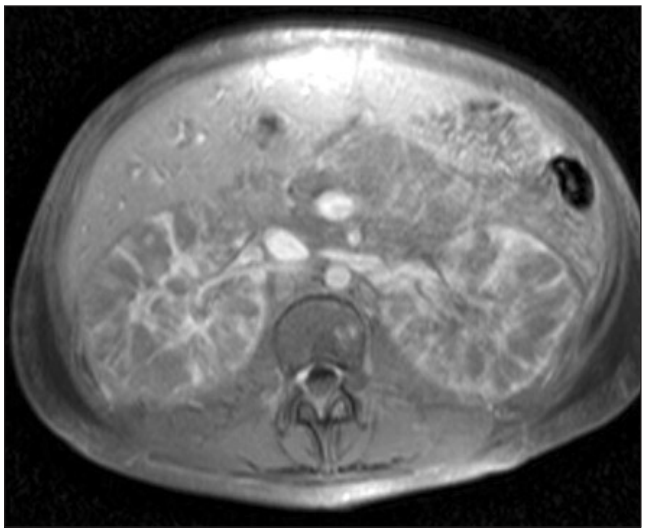

Figure 3. MRI of abdomen.

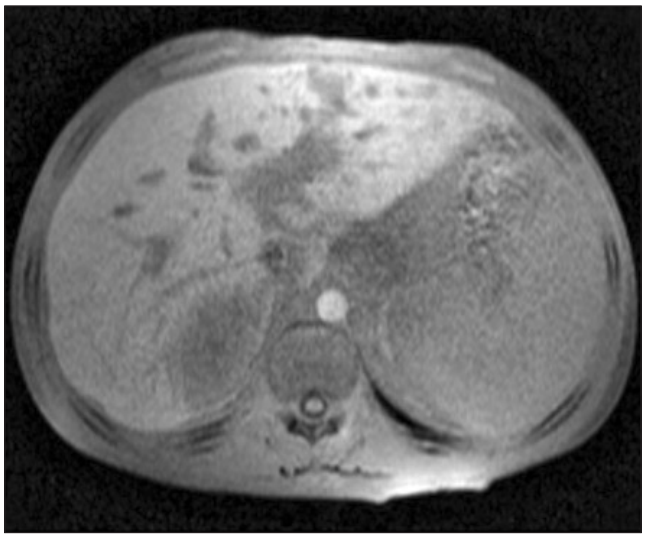

Figure 4. MRI of Liver.

CASE DISCUSSION

In the differential diagnosis of diarrhea and weight loss in someone with HIV it is helpful to separate into infectious and non-infectious etiologies. Infectious diarrhea can be secondary to Protozoa (*Microsporidium, Cryptosporidium, Isospora, Toxoplasma, Giardia, Entamoeba or Leishmania*); Bacteria (*C. difficile, Salmonella, Shigella, Campylobacter, Mycobacterium, Vibrio* or bacterial overgrowth); Viruses (*CMV, HSV, HIV, Rotavirus, Adenovirus* and *Norwalk virus*); or, Fungi (*Histoplasmosis, Coccidiomycosis, Cryptococcus, Candida* and *PCP*). It is important to remember that in a patient with HIV, opportunistic as well as non-opportunistic causes of diarrhea are plausible. Non-infectious diarrhea include neoplasms such as lymphoma and Kaposi's sarcoma, idiopathic causes such as AIDS enteropathy, drug induced such as those seen with protease inhibitors, or pancreatitis of any etiology.

In this patient, multiple biopsies from the stomach, duodenum and colon revealed a high grade B cell lymphoma (CD20+, CD10+, BCL-6+) consistent with Burkitt-like lymphoma. In patients with HIV associated lymphomas, the vast majority (70–90%) are large B cell or Burkitt-like lymphoma. A high percentage of patients

present with constitutional "B" type symptoms such as weight loss, fever and malaise, along with abdominal pain or loss of appetite (1). At the time of diagnosis, up to 80% of patients present with Stage IV disease. Given this fact, patients found to have gastrointestinal Burkitt's lymphoma should undergo lumbar puncture as asymptomatic leptomeningeal involvement is common early in the disease and responds well to chemotherapy. The patient in this case had an MRI which demonstrated lymphomatous involvement in the left lobe of the liver as well as the kidneys and a lumbar puncture which showed CNS involvement. With respect to distribution of Burkitt-like lymphoma in the gastrointestinal tract, the stomach is involved in 23%, the terminal ileum in 39% and the colon in 46% of cases (2).

There are several proposed mechanisms of pathogenesis in HIV associated lymphoma. HIV infection appears to impair dendritic cell function which in turn releases cytokines that drive lymphoid cell production thereby increasing the likelihood of cell dysregulation in cells with defects in tumor suppressor genes. HIV Tat protein absorbed by lymphocytes results in dysregulation of an oncosuppressor protein (pRb2/p130) and augments angiogenic properties of VEGF and fFGF thereby supporting cell proliferation (3). Due to T-cell defects resulting from HIV infection, there is increased susceptibility to EBV infection, accounting for the observed increased EBV viral loads seen in these patients. A possible theory is that immunosuppression coupled with EBV infection drives B cell proliferation including those cells that have undergone changes in oncogenes (4).

The prognosis for Burkitt's has improved dramatically since the advent of highly active antiretroviral therapy and concomitant multidrug chemotherapy regimens. This case patient was started on HAART therapy (zidovudine, lamivudine, and evafrirenz) and underwent chemotherapy with cyclophosphamide, vincristine and prednisone as well as intrathecal chemotherapy, with a rapid reduction in diarrheal symptoms after a single course of chemotherapy. ■

References

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