A 53-Year-Old Woman with Worsening Rash and Diarrhea

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A 53-year-old white female was admitted to the Bone Marrow Transplant Unit with a worsening pruritic rash.

The patient had a history of IgG lambda multiple myeloma status post autologous stem cell transplant one year prior and more recently, matched sibling allogenic transplant. Since transplantation, she had a history of rash, which was diagnosed as graft-versus-host disease (GVHD) by skin biopsy. During that same hospitalization, she had a transjugular liver biopsy to rule out GVHD which was complicated by a large intrahepatic and subcapsular hematoma. A catheter to drain the hematoma was placed by interventional radiology, which was still in place. The patient was discharged following her allogenic transplant with successful engraftment of donor stem cells on bone marrow biopsy, without evidence of residual multiple myeloma. She was on GVHD therapy with tacrolimus, prednisone, and Cellcept. Recently, her rash had returned and was becoming increasingly pruritic over several weeks prior to admission.

The patient did not report headache, sore throat, chest or abdominal pain, dyspnea, diarrhea, or dysuria. She had no other significant past medical or surgical history. She reported occasional alcohol consumption and a remote, but limited smoking history. Her activities had been limited recently by her illness and she denied any travel. She had no knowledge of starting any new medication, lotions, detergents, or soaps in the recent past.

On this admission, the vital signs were normal and she appeared chronically ill. The head, neck, lungs, and heart were unremarkable. Her abdominal exam was significant for a mildly tender right upper quadrant without rebound or guarding. She had normoactive bowel sounds. She had a right upper quadrant drainage catheter with serosanguinous drainage. Her dermatologic exam was notable for a maculopapular rash on her back, abdomen and thighs noted, which was non-blanching. There were no vesicles or bullae.

Upon admission, skin biopsy revealed interface dermatitis consistent with GVHD and the patient was placed on intravenous steroids. In addition, patient had an Adenovirus PCR of 4,600 copies. On hospital day 7, the patient developed acute diarrhea. Stool sample was positive for white blood cells; stool culture and C. difficile were negative. Adenovirus was isolated from the stool. Due to concern for GVHD of the colon, patient had a colonoscopy performed, revealing multiple ulcerations, colitis in the sigmoid colon, and diverticulosis (Figures 1 and 2). Biopsies were obtained from the ulcer and the sigmoid colon. Culture of the ulcer was positive for adenovirus and negative for CMV, HSV, and Enterovirus. Pathology of ulcer biopsy revealed glandular epithelial cells with acute inflammation and intranuclear inclusions, morphologically consistent with adenovirus. Immunohistochemical staining of the colon biopsy was negative for HSV and CMV and was eventually was positive for adenovirus.

Initially on steroids, her GVHD dermatitis resolved and she was treated with Cidofovir and IVIG for her adenovirus infection. Her diarrhea and adenovirus PCR titer both responded appropriately to treatment.

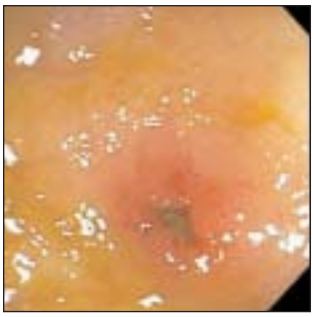

Figure 1. Area of ulceration in sigmoid colon.

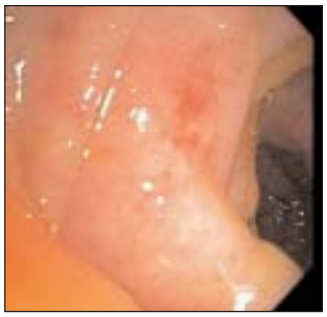

Figure 2. Punctate erythema of sigmoid colon.

Discussion

Adenovirus is a common infectant causing mild and self-limited infections in immunocompetent individuals. In an immunocompromised population, such as bone marrow transplant recipients, it can have severe consequences. Patients who have undergone allogenic stem cell transplant are at highest risk for adenovirus disease. Other risk factors are age (children more often than adults), T-cell depleted grafts, presence of GVHD, and the use of mismatched and unrelated donors. It can manifest as pneumonia, hepatitis, hemorrhagic cystitis, interstitial nephritis, gastroenteritis/colitis, and encephalitis. In one-half of the patients with invasive adenoviral disease, the outcome is death. Adenovirus can be acquired via a primary infection (person to person), or via reactivation of latent infection/donor organ infection. Adenovirus colitis is not well studied, as most studies rely on detection of virus in stool in symptomatic patients without tissue confirmation. Often adenoviral infections of the bowel coexist with GVHD.

Adenovirus can be diagnosed by a number of means. Viral culture it the most sensitive and specific. Cultures from stool or urine may be positive for months after an acute infection in an immunocompromised patient. Viral antigens detected by enzyme-linked immunosorbent assay (ELISA) are not as sensitive as culture, but can give rapid diagnosis. PCR can be used to detect adenovirus in body fluids and tissues and is highly sensitive and specific. Histopathology can also be used to identify the characteristic intranuclear inclusions seen in adenovirus infection. These can be similar to CMV; however, adenovirus does not cause intracytoplasmic inclusions or multinucleated cells like CMV. Immunohistochemical stains can be used to identify to identify HSV, CMV, or adenovirus. Electron microscopy can identify the characteristic icosahedral virus seen in adenoviral infections present in the nuclei of infected cells.

Since this infection is associated with significant mortality in the post-transplant population, it is often treated. Antiviral agents are the mainstay of treatment, although limited evidence is available for efficacy. ganciclovir, ribavirin, and vidarabine have shown some activity in vitro, and there are a number of case reports associating Ribavirin with a successful outcome. Cidofovir, a nucleotide analog effective against a number of viruses, has been shown to be active against adenovirus. No prospective, controlled studies have been performed to date. Intravenous Immunoglobulin (IVIG) theoretically contains neutralizing antibodies against adenovirus; it has been used in conjunction with antiviral therapy in a number of reports. Another strategy used is reduction in immune suppression as this allows clearance of virus in some patients. ■

References

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