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Case report

Adenovirus, herpes simplex virus and cytomegalovirus infection in a lung transplant recipient

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A B S T R A C T

Allograft infections post lung transplantation have a significant impact on morbidity and mortality. We report a rare case of triple viral infection with adenovirus, Herpes Simplex virus (HSV) and Cytomegalovirus (CMV) in a lung transplant recipient.

Case report

A 24 year old female was admitted with shortness of breath of 2 weeks duration. The patient's past medical history was significant for end stage bronchiectasis and common variable immunodeficiency for which she underwent double lung transplant (CMV donor negative/ recipient positive) 3 months prior to the current admission. She denied any fever, chills, cough or diarrhea. There was no history of any sick contacts or recent travel. The patient was maintained on tacrolimus, prednisone, voriconazole, and valganciclovir post-transplant.

On admission, the patient was febrile to 101 °F, tachypneic with a respiratory rate of 36/min, blood pressure 90/55 mm Hg, and pulse rate 130 beats/min. On examination, she was noted to have blistering lesions with crusts over lips, coarse breath sounds bilaterally. The remainder of the examination was normal. Laboratory studies revealed W3200 BCE/cmm with 77% neutrophils, hemoglobin 7.5 g/dL, platelets 152 × 10^3/μL, blood urea nitrogen 37 mg/dL, creatinine 1.41 mg/dL with normal liver enzymes. Blood cultures remained sterile for 5 days. CT of the chest revealed bilateral patchy and confluent infiltrates with areas of consolidations with involvement of the lung apices and small bilateral pleural effusions. (Fig. 1) The patient was intubated and placed on mechanical ventilation.

Respiratory cultures grew vancomycin resistant *Enterococcus faecalis* and the patient was started on linezolid. She continued to require high oxygen. Bronchoscopy with bronchoalvelolar lavage (BAL) and a biopsy were performed. Immunohistochemical stains were positive for both adenovirus and HSV, but negative for CMV (Fig. 2). A BAL HSV1 PCR viral load was 1.3 × 10^7 copies/mL and BAL adenovirus PCR was positive but not quantified. Serum HSV PCR was 58,800 copies/mL, and serum adenovirus PCR was 1,56,460 copies/mL, serum CMV PCR was 646 copies/mL.

The patient was started on intravenous cidofovir at 1 mg/kg three times a week with pretreatment with probenecid and normal saline. Oral prophylactic valganciclovir was changed to intravenous ganciclovir. Antiviral treatment was given for 4 weeks with complete resolution of her respiratory distress with clearance of HSV, CMV and adenovirus viral loads, but without significant changes on CT scan of the chest. She was eventually extubated and was discharged to a rehabilitation facility on oral valganciclovir. Few weeks after discharge, she was readmitted with respiratory distress, again requiring mechanical ventilator. She had negative serum viral PCR for all 3 viruses but had progressive respiratory failure and expired. A limited lung autopsy was consistent with acute pneumonia associated with extensive necrosis and abscess formation and immunohistochemical stain was positive for adenovirus predominantly in the lower left lobe (the area of infarction). HSV and CMV stains were negative on immunohistochemical stain (Fig. 3).

Discussion

HSV is a double stranded DNA virus, belongs to the family Herpesviridae. The overall incidence of HSV infections in lung transplant recipients is about 18%. Most of the cases of HSV occur in the immediate post-transplant period. HSV pneumonia tends to be florid with extensive necrosis and the presence of infected cells with intranuclear ground glass inclusions and occasional Cowdry type A inclusions. Rapid treatment with high dose acyclovir (10 mg/kg) is critical as the disease may be fatal if untreated. The use of HSV PCR both in BAL and serum greatly improves the diagnostic accuracy.

Adenovirus is a non-enveloped double stranded DNA virus, belongs to the family *Adenoviridae.* The incidence of adenovirus infection in solid organ transplant recipients is unknown [1]. Higher incidence is

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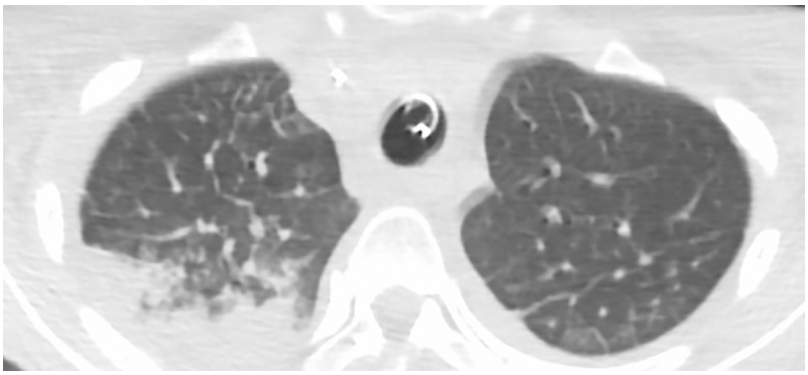

Fig. 1. CT Chest showing bilateral confluent infiltrates with consolidations and small bilateral pleural effusions.

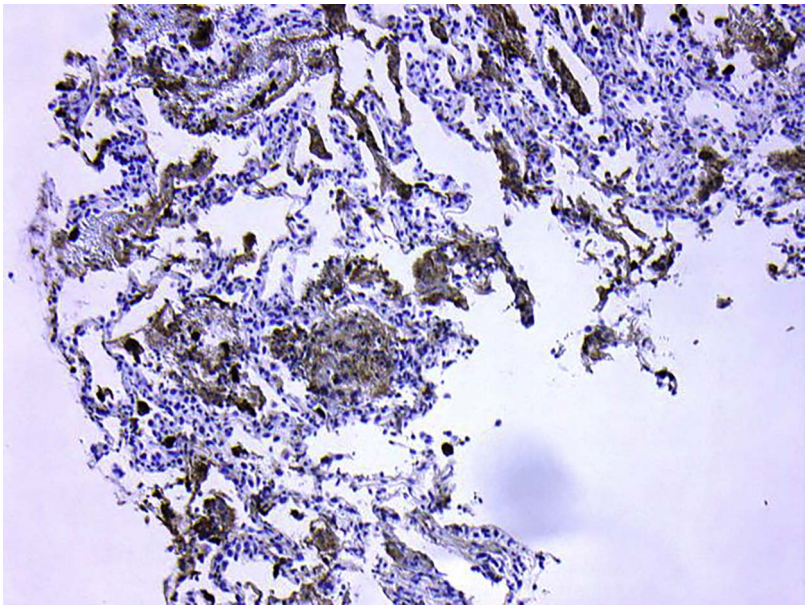

Fig. 2. Immunohistochemical staining showing adenovirus (Low power).

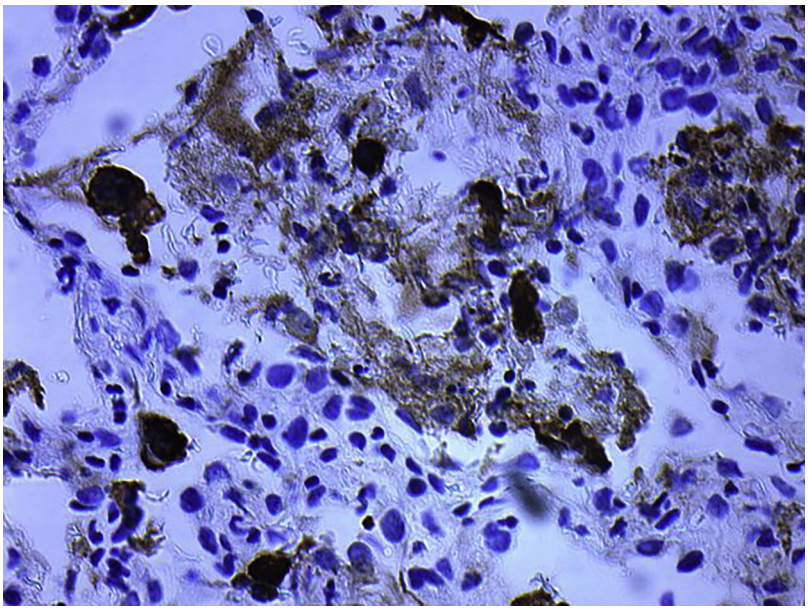

Fig. 3. Immunohistochemical stain showing adenovirus (high power).

seen in patients with donor positive/recipient negative adenovirus status. BAL offers a good diagnostic and prognostic tool. Histopathology with immune-staining remains the gold standard. Early diagnosis is critical in the management of adenoviral infections as the delay of antiviral treatment increases the likelihood of treatment failure [2]. Serum PCR testing offers the possibility for earlier diagnosis of adenovirus infection. A positive qualitative serum adenovirus PCR may predict subsequent disseminated infection in 75% [2]. The use of cidofovir in adenovirus infections is based on bone marrow transplant recipients' data, with an efficacy of about 50% in patients with disseminated disease [3].

The incidence of CMV infection in solid organ transplant recipients varies according to the transplanted organ and is particularly high in lung transplantation, reaching 40–50% [4]. The incidence of CMV viremia without end organ damage is approximately 30% with high risk of infections seen in CMV donor positive and recipient negative. Prophylactic use of ganciclovir has significantly decreased the incidence. CMV viral loads > 1000 copies/ml are more likely to be associated with high risk of CMV disease [5].

Our patient had a low CMV viral load with no evidence of end organ damage. The low level CMV viremia could have possibly potentiated the pathogenicity of the other two viruses and thought that pneumonia was caused by adenovirus and HSV in our patient with CMV Viremia as reactivation of the virus. The concept of viral interaction in transplant recipients was hypothesized to enhance pathogenicity by either virus–virus interaction or virus – host interaction resulting from modulation of the host cell immune function or production of suppressive cytokines [6].

To our knowledge, there are no reported cases of co-Infection with HSV and adenovirus in a lung transplant recipient.

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