

# CJASN

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### 546 Use of Causal Diagrams to Inform the Design and Interpretation of Observational Studies: An Example from the Study of Heart and Renal Protection (SHARP)

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#### On the Cover

A 77 year-old man status post renal transplant in 2014 presented with acute kidney injury (serum creatinine of 4.4 mg/dl, elevated from his baseline of 0.7 mg/dl). Prior to this presentation, the patient had a history of upper respiratory infection with bilateral pulmonary infiltrates, and was treated with antibiotics and steroids for one month without improvement of symptoms and with a progressive decline in renal function. A kidney biopsy was performed with clinical concern for rejection. By light microscopy, patchy necrotizing granulomatous inflammation was identified (left image). Special stains for fungal organisms and acid fast bacilli (AFB) were negative. Rare tubular epithelial cells demonstrated viral cytopathic effect with enlarged, smudgy-appearing nuclei (center, top). These same cells show strong nuclear immunoreactivity for adenovirus (center, bottom) and were negative for cytomegalovirus and polyoma virus. Subsequent testing by PCR revealed high titer adenovirus in the serum. Electron microscopy identified nuclei with viral inclusions composed of organized arrays of non-enveloped polyhedral viral particles characteristic of adenovirus (right image). These findings are consistent with Adenovirus nephropathy.

Polyoma viruses (*e.g.*, BK and JC virus) are the most common viral infections of the kidney allograft. Adenovirus, a non-encapsulated DNA virus can rarely cause renal dysfunction that can be serious in immunocompromised allograft recipients. Necrotizing granulomatous inflammation is often seen in adenoviral infections of the kidney allograft, and its presence should trigger appropriate workup to rule out other infectious etiologies that have similar histologic findings (*e.g.*, infections caused by fungal organisms and acid fast bacilli). Since it is rare, treatment methods reported in the literature vary from supportive care to reduction of immunosuppression with addition of IVIG and/or anti-viral agents such as cidofovir or gancyclovir. (*Images provided by Mirna Tokatly, Renal Pathology Fellow and Shreeram Akilesh, Assistant Professor, University of Washington, Seattle, Washington*)