American Journal of Transplantation Images in Transplantation – Continuing Medical Education (CME)

Each month, the *American Journal of Transplantation* will feature Images in Transplantation, a journal-based CME activity, chosen to educate participants on current developments in the science and imaging of transplantation. Participants can earn 1 *AMA PRA Category 1 Credit*™ per article at their own pace.

This month's feature article is titled: "Renal Failure in a Kidney Transplant Recipient—BK Virus Nephropathy or Rejection?"

Accreditation and Designation Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Blackwell Futura Media Services, the American Society of Transplant Surgeons and the American Society of Transplantation. Blackwell Futura Media Services is accredited by the ACCME to provide continuing medical education for physicians.

Blackwell Futura Media Services designates this journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Statement of Need

BK virus nephropathy (BKVN) is a significant cause of allograft dysfunction post–kidney transplant. Due to the similarities with acute rejection, BKVN may be misinterpreted as acute rejection. It is important to distinguish between the two since treatment for presumed rejection with increased immunosuppression may result in allograft loss.

Purpose of Activity

The activity is designed to improve the physician's knowledge about challenges in diagnosis of BKVN.

Identification of Practice Gap

Many transplant providers may lack experience in diagnosing, treating and distinguishing BKVN from acute rejection. Correct diagnosis of BKVN enhances kidney allograft survival.

Learning Objectives

Upon completion of this educational activity, participants will be able to:

- Recognize pitfalls in the diagnosis of BKVN.
- Differentiate BKVN from acute rejection.
- Understand appropriate treatment strategy for BKVN.

Target Audience

This activity has been designed to meet the educational needs of physicians and surgeons in the field of transplantation.

Disclosures

No commercial support has been accepted related to the development or publication of this activity. Blackwell Futura Media Services has reviewed all disclosures and resolved or managed all identified conflicts of interest, as applicable.

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Instructions on Receiving CME Credit

This activity is designed to be completed within an hour. Physicians should claim only those credits that reflect the time actually spent in the activity. This activity will be available for CME credit for twelve months following its publication date. At that time, it will be reviewed and potentially updated and extended for an additional twelve months.

Follow these steps to participate, answer the questions and claim your CME credit:

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- Read the article in print or online format.
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Images in Transplantation

Look and Learn

Renal Failure in a Kidney Transplant Recipient—BK Virus Nephropathy or Rejection?

A 53-year-old Hispanic female received a deceased-donor kidney transplant. Posttransplant, she achieved a baseline serum creatinine of 1.2–1.4 mg/dL. Her maintenance immunosuppression consisted of mycophenolate mofetil 720 mg twice daily, tacrolimus 6 mg twice daily and prednisone 5 mg daily. One-and-a-half years posttransplantation, patient was diagnosed with biopsy-proven BK virus nephropathy (BKVN) with a serum BK virus polymerase chain reaction (PCR) of 135,000 copies/mL. The immunosuppression was reduced (tacrolimus 3 mg twice daily and mycophenolate 360 mg twice daily). Subsequently serum creatinine improved to a baseline of 1.5–1.7 mg/dL and serum BK viremia became undetectable over the next year. She was continued on the lower immunosuppression, and 3 years posttransplantation, patient was admitted with serum creatinine of 2.5 mg/dL. Serum John Cunningham (JC) virus PCR was negative and BK virus PCR was undetectable at <5000 copies/mL. Donor-specific HLA antibodies were negative. The transplant kidney biopsy showed moderate interstitial fibrosis/tubular atrophy with inflammation (Figure 1), focal tubulitis (star, Figure 2) with tubular cells showing slightly enlarged and hyperchromatic nuclei (arrow, Figure 2). No viral cytopathic effects were identified. The stain for polyomavirus showed weak (1+) nuclear staining (Figure 3). The C4d stain was negative. Acute cellular rejection Banff 1B was diagnosed and patient was treated with high-dose intravenous steroids with improvement in serum creatinine to nadir of 1.8 mg/dL a week later. Subsequently, serum creatinine increased to 3.0 mg/dL a month later. A second transplant biopsy showed persistent inflammation with stronger polyomavirus staining compared to previous biopsy. Serum BK virus PCR was now detectable at 6800 copies/mL.

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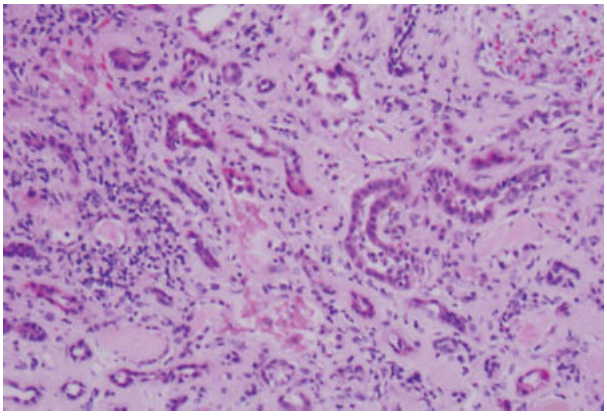

Figure 1: The hematoxylin and eosin stain of transplant kidney biopsy done 3 years posttransplantation reveals moderate interstitial fibrosis and tubular atrophy with inflammatory infiltration. Serum creatinine was 2.5mg/dL and serum BK virus PCR was undetectable at <5000 copies/mL on the day of biopsy.

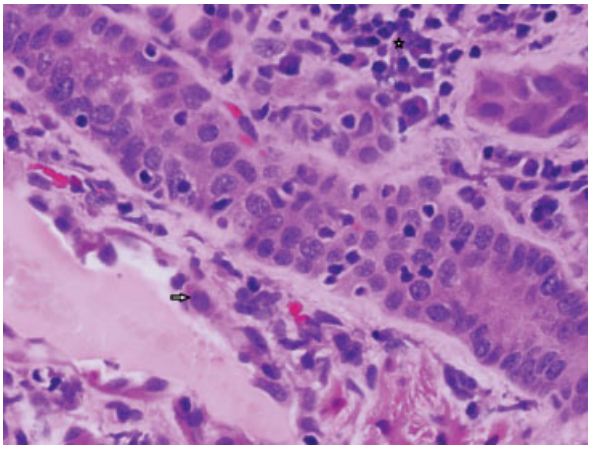

Figure 2: The hematoxylin and eosin stain of transplant kidney biopsy done 3 years posttransplantation shows area of tubulitis (star) and a tubular epithelial cell with an enlarged and hyperchromatic nuclei (arrow). No viral cytopathic effects were seen.

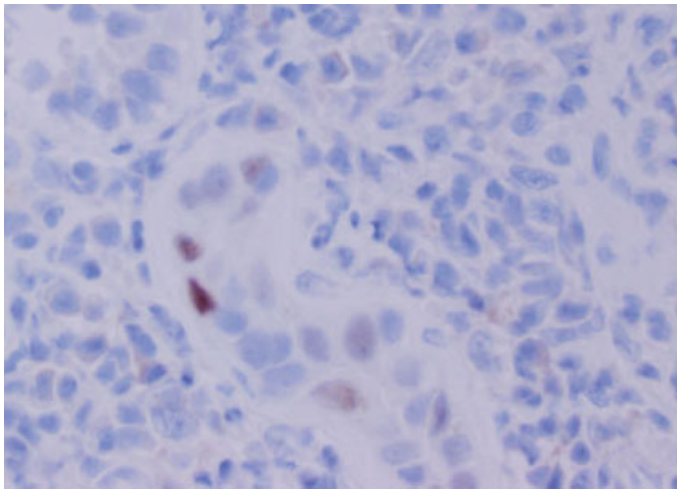

Figure 3: The immunohistochemistry of transplant kidney biopsy done 3 years posttransplantation shows a few tubular cells with weak (1+) stain for polyomavirus.

Questions

1. Which of the following statements is true about diagnosis of BKVN?

a. The absence of viral cytopathic effects in the transplant kidney biopsy (Figure 2) rules out a diagnosis of BKVN.
b. The BK virus inclusion bodies are characteristically present in the cell cytoplasm.
c. The onset of serum BK viremia usually coincides with the diagnosis of BKVN.
d. The positive and negative predictive value of BK virus PCR for diagnosis of BKVN is reported to be 60% and 100% respectively.
e. The detection of immunoglobulin-M (IgM) and the degree of rise of IgM levels may help in diagnosis of BKVN.

2. The biopsy confirmed polyomavirus nephropathy (PyVAN) may be seen in the absence of detectable serum BK viremia in all of the following conditions except:

a. JC virus nephropathy
b. Absence of BK virus–specific T cells
c. Residual BKVN posttreatment
d. Inter-laboratory variation in BK virus quantification
e. BK virus genotype variance

3. Which of the following tests may best help distinguish BKVN from acute cellular rejection?

a. Urinary mRNA for BKV-VP1
b. Urinary mRNA for granzyme B
c. Urinary interferon-gamma (IFN-γ)-inducible protein-10
d. Urine decoy cells
e. Plasma cell rich inflammation and increased HLA-DR expression on kidney biopsy

4. The most commonly accepted strategy for treatment of PyVAN is:

a. Reduction in immunosuppression
b. Leflunomide
c. Cidofovir
d. Ciprofloxacin
e. Intravenous immunoglobulin

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