Case #1

Dr. Erika Bracamonte
Associate Professor of Pathology
University of Arizona, College of Medicine
Banner University Medical Center, Tucson

Case History

• 14 year old girl with ESRD due to obstructive uropathy underwent cadaveric renal transplant
• Post-transplant course
  – Multiple UTI's
  – Leukopenia, anemia, reticulocytopenia
• Serology positive: Parvovirus B19
  – Dx: Aplastic anemia secondary to Parvovirus

ACCME/Disclosure

Dr. Bracamonte has nothing to disclose

Case History

• 6 months post-transplant
  – Bilateral native nephrectomies due to UTI's
• 1 year post-transplant
  – Allograft dysfunction: SCr 1.2 mg/dL
Case History

- CBC:
  - WBC: Normal
  - RBC: 4.13 (borderline low), low Hgb and Hct

- Urinalysis:
  - Mild protein: 30 mg/dL
  - Minimal blood
  - No casts or dysmorphic RBC’s
  - Urine culture: Negative

Case History

- Serology:
  - Negative: CMV, EBV, BK, HIV, Hepatitis
  - Positive: Parvovirus B19 (IgG and IgM)

- HLA Antibody Testing
  - Positive: Class I and Class II
  - Donor Specific Antibodies detected
    - A2 (7,313 MFI)
    - DQA1*01:03 (1,839 MFI)
    - Cw7 (1,086 MFI)

Allograft Biopsy #1

1 year post-transplant
Diagnoses

- Acute antibody mediated rejection
- Immune-complex mediated glomerulonephritis
- Features suggestive of early transplant glomerulopathy?
• Immune complex GN
  – De novo
  – No features of autoimmune disease or other infections
  – Possibly associated with Parvovirus B19 infection?

• Kidney biopsy sent for Parvovirus B19 testing by PCR → Positive

Parvovirus B19

• Single stranded DNA virus
• Tropism for erythroid progenitor cells which express parvovirus receptor
• Receptor also found in synovial, heart, renal, endothelial tissue
• 85% adults have serologic evidence of prior infection

Parvovirus B19 Renal Disease

• Link reported 1978 Markenson et al:
  – Sickle disease, nephrotic syndrome and hypoplastic crisis
    • Renal lesion: focal segmental glomerulosclerosis

• 1997 Moudgil et al:
  – Transplant patient with PVB19 and collapsing glomerulopathy
Parvovirus B19 Renal Disease

• PB19-associated renal disease
  – Adult and pediatric patients
    • Female predominance (67%)
  – Renal dysfunction + evidence of PVB19 infection
    • Positive blood serology and/or tissue PCR
  – Reported cases
    • Native kidneys: 75%
    • Allograft kidneys: 25%

Parvovirus B19 Renal Biopsy Lesions

• Native Kidneys
  – Collapsing glomerulopathy
    • Moudgil et al, 2001: 23 pts with collapsing GN
      – Increased incidence PVB19 detected in blood (vs HIVAN, FSGS)
      – PVB19 DNA detected in 78% renal biopsies by PCR
        » 25% normal controls also positive
  – Proliferative GN
    • Endocapillary (55%) > mesangial (15%) > mesangial + endocapillary (12%)
    • Occasionally crescentic
    • Occasionally with associated FSGS
  – Thrombotic microangiopathy
    • With and without associated proliferative features

Parvovirus B19 Renal Biopsy Lesions

• Proliferative GN
  – Immunofluorescence
    • IgM (70%) > IgG (63%) > IgA (40%) 
      – Predominantly capillary loops
    • C3 (80%)
    • C1q (20%)
  – Electron Microscopy
    • Subendothelial immune deposits (92%)
    • Mesangial deposits (50%)
    • Subepithelial deposits (25%)

Human Parvovirus B19-Induced Acute Glomerulonephritis: A Case Report

Honmaru Shintohara, Takashi Itaguchi, Yujiro Ogawa, Shogo Fujita, Mito Nagai, Masahiro Itama, Hiroshi Maruyama, Kouichi Hiyayama and Masaki Kobayashi
Department of Nephrology, Tokyo Medical University Saiseikai Medical Center, Inzai, Japan

Renal Failure, 2013; 35(1): 159-162
Parvovirus B19 Renal Biopsy Lesions

- Transplant Kidneys
  - Other lesions:
    - Small and medium sized vessel vasculitis
    - Collapsing GN/FSGS

- PVB19 Detected:
  - Parietal and visceral epithelial cells
    - Collapsing glomerulopathy, FSGS
  - Endothelium
    - Thrombotic microangiopathy, vasculitis
  - Immune complex mediated proliferative GN
    - Precedent for viral etiologies (Hep C)
    - Association vs direct causality
      - PVB19 positive IHC/ISH only rarely demonstrated in glomerular tissue with proliferative GN
Our patient...

- De novo immune complex GN would be more consistent with native kidney
  - No other features of infection, autoimmune disease
  - Due to inadequate immunosuppression?
- AMR Treatment: Plasmapheresis, IVIG
- Repeat biopsy 4.5 months later
3rd Biopsy

3 years post transplant
Take Home Points

• PVB19-associated glomerular injury may occur or be exacerbated in transplant setting
• Morphologic distinction from lesions of rejection (acute glomerulitis, transplant glomerulopathy, vasculitis) can be challenging
• Clinical significance and contribution of PVB19 to graft dysfunction and overall clinical picture is unclear

References


Acknowledgement

Beth Braunhut, MD