

## Exceptional Case

# Cytomegalovirus-induced collapsing focal segmental glomerulosclerosis

Vanya Grover<sup>1</sup>, Meghana R. Gaiki<sup>2</sup>, Maria V. DeVita<sup>2</sup> and Joshua A. Schwimmer<sup>2</sup>

<sup>1</sup>Department of Medicine, North Shore-LIJ Health Care System-Lenox Hill Hospital, New York, NY, USA and <sup>2</sup>Department of Nephrology, North Shore-LIJ Health Care System-Lenox Hill Hospital, New York, NY, USA

Correspondence and offprint requests to: Vanya Grover; E-mail: grover.vanya@gmail.com

### Abstract

Collapsing glomerulopathy is an aggressive morphologic variant of focal segmental glomerulosclerosis which typically presents with nephrotic syndrome and rapidly progressive renal failure. Most cases of collapsing glomerulopathy are associated with human immunodeficiency virus infection. We present a rare case of collapsing glomerulopathy associated with acute cytomegalovirus (CMV) infection in an immunocompetent host with improvement in renal function after the treatment of CMV with ganciclovir. CMV may be an under-recognized cause of collapsing glomerulopathy which may respond to antiviral treatment.

**Keywords:** collapsing glomerulopathy; cytomegalovirus infection; focal segmental glomerulosclerosis

### Background

Collapsing glomerulopathy is a morphologic variant of focal segmental glomerulosclerosis (FSGS) which typically presents with nephrotic syndrome and renal failure requiring renal replacement therapy in 50% of the patients within 1 year [1]. Most cases are associated with human immunodeficiency virus (HIV) infection. Cases occurring after renal transplantation and rare cases associated with autoimmune diseases, malignancies, interferon- $\alpha$ , pamidronate and genetic disorders have also been reported [1–3]. In addition, two cases suggesting an association between acute cytomegalovirus (CMV) infection and collapsing glomerulopathy have been reported previously [4, 5]. We present a case of collapsing glomerulopathy associated with acute CMV infection in an immunocompetent host requiring hemodialysis. The patient's renal function subsequently improved with antiviral therapy for CMV.

### Case report

A 34-year-old Hispanic male was admitted with a 10-day history of malaise, headaches, poor appetite, nausea, vomiting and loose stools. Though medical records were unobtainable, the patient reports that his past medical history was significant for 'protein in the urine' at age 10, for which a kidney biopsy was performed. At the time, he was treated with steroids for several months with remission of proteinuria and his renal function remained normal. He denied recurrent renal disease. He reported a monogamous relationship with his wife for the past 8 years and denied any alcohol, intravenous drug or

tobacco use. There were no sick contacts and he denied any travel history.

On physical exam, the patient was found to have a blood pressure of 139/92 mmHg and pitting lower extremity edema up to the mid-calf. Initial laboratory tests revealed a serum creatinine (SCr) of 7.37 mg/dL. The urinalysis was positive for protein (3+) and hemoglobin (3+). Urine microscopy demonstrated 3–5 red blood cells (RBCs)/hpf, no RBC casts and no dysmorphic RBCs. A renal ultrasound revealed enlarged kidneys with an echogenic cortex (right: 13.7 cm, left: 13.5 cm). A 24-h urine collection revealed 21.7 g/day of proteinuria.

Hemodialysis was initiated on hospital day 4 for progressive renal failure with uremic symptoms. Anti-neutrophilic cytoplasmic antibodies, anti-nuclear antibody, HIV antibodies, polymerase chain reaction (PCR) for HIV RNA, hepatitis C antibodies, complement levels, anti-streptolysin O titers, hepatitis B antigen and antibodies were all negative or normal. Immunofixation (serum and urine) revealed an IgG-lambda monoclonal protein. A bone marrow biopsy was negative for plasma cell dyscrasias.

A renal biopsy was performed which demonstrated collapsing FSGS characterized by wrinkling and retraction of the glomerular basement membrane in four of eight glomeruli with swelling and proliferation of the overlying visceral epithelial cells. Three of the remaining glomeruli were globally sclerotic. Immunofluorescence on kidney biopsy was negative for light chain and immunoglobulin deposition. Electron microscopy revealed complete epithelial cell foot process effacement (Figures 1 and 2).

A serum PCR for parvovirus B19 was negative. Acute CMV infection was subsequently diagnosed based on the elevation of serum CMV DNA antibodies of both IgG (4.28 AU/mL; range: 0.00–0.90 AU/mL) and IgM (6.46 AU/

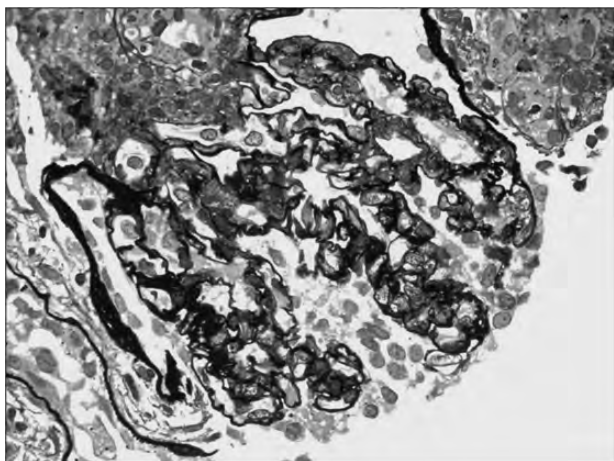


Fig. 1. Renal biopsy. Jones methenamine silver stain (JMS).

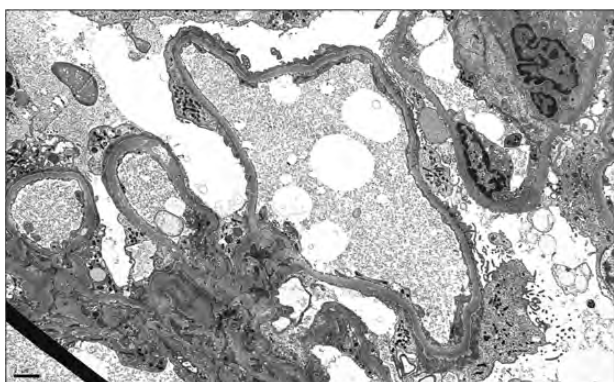


Fig. 2. Electron microscopy. The glomerular basement membrane is of normal thickness. No electron-dense deposits are present. Visceral epithelial cells show complete foot process effacement and microvillous transformation of the plasma membrane.

mL; range: 0.00–0.89 AU/mL), and a serum CMV DNA viral load of 1553 copies/mL. CMV DNA was not detected in the kidney biopsy. There were no CMV inclusions identified by light microscopy. Staining for CMV proteins was negative using standardized immunohistochemical staining methods with positive and negative controls. The test was run using the refine polymer detection and a low pH solution for ~20 min with 20-min antibody incubation. The patient was started on prednisone 120 mg every other day and antiviral treatment was initiated with intravenous ganciclovir 125 mg post-hemodialysis for one week. The patient then continued oral ganciclovir 250 mg twice a week for 3 weeks. On discharge, the patient's SCr was 9.21 mg/dL. Prednisone was tapered by 20 mg every 2 weeks, and then tapered by 5–10 mg every 2 weeks for a total duration of therapy of 6 months. After 6 months of treatment, the patient's SCr stabilized at 2.0 mg/dL and he no longer required hemodialysis.

## Discussion

This report demonstrates the third case of collapsing glomerulopathy associated with acute CMV infection in an immunocompetent host. In the first case report of CMV-

associated collapsing glomerulopathy, reported in 2000, the patient's renal function improved on glucocorticoid and ganciclovir therapy and his SCr stabilized at 250  $\mu$ mol/L for 2 years at the time of publication. There was no mention of the patient requiring hemodialysis [4]. In the second case, reported in 2003, CMV DNA was detected in the renal biopsy at a level of 280 copies per 20 mg of paraffin-embedded tissue. The patient did not receive antiviral therapy for CMV though the infection was cleared. His renal function did not improve; thus, the patient remained dialysis dependent [5].

Our case was unique, in that the treatment of acute CMV infection with ganciclovir was associated with improvement in renal function sufficient to allow the patient to discontinue dialysis. As spontaneous remission is extremely rare in patients with collapsing glomerulopathy [3], this suggests that acute CMV infection was causally related to this patient's renal disease and that antiviral treatment for the CMV infection led to improvement in this patient's renal function.

CMV is a known cause of infection in immunocompromised patients, but CMV infection in immunocompetent hosts causing organ damage is rare [6]. The mechanism by which acute CMV infection may lead to collapsing glomerulopathy is uncertain. The lesion of collapsing glomerulopathy is related to podocyte injury and detachment of podocytes from the glomerular basement membrane. Acute CMV infection may cause this podocyte injury through several possible mechanisms. These may include acute podocyte infection by CMV or injury to podocytes by CMV-related immune activation, possibly involving T-helper type 1 responses [1].

The first-line treatment of collapsing glomerulopathy consists of oral corticosteroids. Cyclosporine has been used as a first- or second-line agent, but prospective trials on which to base therapeutic strategies are lacking [3]. CMV infection is routinely treated with ganciclovir therapy, and early therapy appears to improve prognosis [6]. Our patient was treated with steroids and ganciclovir with subsequent improvement in renal function. This case report demonstrates an association between acute CMV infection and collapsing glomerulopathy in an immunocompetent host and suggests that the treatment of CMV may improve renal function. As CMV is not routinely tested for immunocompetent patients, CMV as a cause of collapsing glomerulopathy may be under-recognized. Cases of idiopathic collapsing glomerulopathy should be screened for acute CMV infection and antiviral treatment considered as these cases may respond to antiviral therapy.

*Conflict of interest statement.* None declared.

(See Editorial Comment by Chandra and Kopp. Viruses and collapsing glomerulopathy: a brief critical review. *Clin Kidney J* 2013; 6: 1–5)

## References

- Albaqumi M, Soos T, Barisoni L et al. Collapsing glomerulopathy. *J Am Soc Nephrol* 2006; 17: 2854–2863
- Laurinavicius A, Hurwitz S, Rennke HG. Collapsing glomerulopathy in HIV and non-HIV patients: a clinicopathological and follow-up study. *Kidney International* 1999; 56: 2203–2213
- Schwimmer JA, Markowitz GS, Valeri A et al. Collapsing glomerulopathy. *Semin Nephrol* 2003; 23: 209–218
- Prese C, Cordonnier C, Makdassi R et al. Collapsing glomerulopathy and cytomegalovirus, what are the links? *Presse Med* 2000; 29: 1815–1817

5. Tomlinson L, Boriskin Y, McPhee I *et al.* Acute cytomegalovirus infection complicated by collapsing glomerulopathy. *Nephrol Dial Transplant* 2003; 18: 187–189
6. Kanno M, Chandrasekar PH, Bentley G *et al.* Disseminated cytomegalovirus disease in hosts without acquired immunodeficiency syndrome and without an organ transplant. *Clin Infect Dis* 2001; 32: 313–316

Received for publication: 6.4.12; Accepted in revised form: 13.7.12