

What Can We Do When All Collapses? Fatal Outcome of Collapsing Glomerulopathy and Systemic Lupus Erythematosus With Diffuse Alveolar Hemorrhage: Case Report

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ABSTRACT

Introduction. Collapsing glomerulopathy (CG) is a rare form of glomerular injury. Although commonly associated with human immunodeficiency virus (HIV) infection, it can occur in association with systemic lupus erythematosus (SLE).

Case Report. We present the case of a 50-year-old man, with chronic kidney disease secondary to focal and segmental glomerulosclerosis, who received a cadaveric kidney transplant in 2007.

There were no relevant interurrences until May 2015, when he presented with nephrotic range proteinuria (± 4 g/d). A graft biopsy was performed and it did not show any significant pathological changes. In September, he developed a full nephrotic syndrome (proteinuria 19 g/d) and a graft biopsy was repeated. CG features were evident with a rich immunofluorescence. Antinuclear antibodies (ANA) and anti-double-stranded DNA (anti-dsDNA) antibodies were positive; the remaining immunologic study was normal. Viral markers for HIV, hepatitis C virus (HCV), and hepatitis B virus (HBV) were negative. The patient was treated with corticosteroid pulses and plasmapheresis (seven treatments). A rapid deterioration of kidney function was seen and he became dialysis dependent. He was discharged with a low-dose immunosuppressive treatment. In October, he was hospitalized with diffuse alveolar hemorrhage (DAH). The auto-immune study was repeated, revealing complement consumption and positive titers of ANA and Anti-dsDNA antibodies. Anti-neutrophil cytoplasmic antibodies (ANCA) and antiglomerular basement membrane antibody (anti-GBM) were negative. Treatment with intravenous corticosteroids, plasmapheresis, and human immunoglobulin was ineffective and the outcome was fatal.

Conclusion. This case report highlights the possible association of CG and SLE. To our knowledge, it is the first case of SLE presenting with CG and DAH, with the singularity of occurring in a kidney transplant recipient receiving immunosuppression.

FOCAL segmental glomerulosclerosis (FSGS) is a histological pattern that may have different etiologies and that can occur in the kidney graft, both as recurrent or de novo disease [1]. Five histological patterns were established by the Columbia classification (tip lesion, cellular variant, collapsing variant, perihilar variant, and FSGS not otherwise specified), being associated with different etiologies,

clinical manifestations, and prognosis [2]. Collapsing glomerulopathy (CG) is a rare form of glomerular injury,

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generally associated with human immunodeficiency virus (HIV) infection but that can occur with other viral infections, autoimmune diseases, and drugs [3]. The association with systemic lupus erythematosus (SLE) is very unusual [4].

Diffuse alveolar hemorrhage (DAH) is a rare but potentially life-threatening manifestation of SLE. Despite treatment, it remains associated with high mortality [5,6].

We present a case of a CG in a kidney transplant recipient followed by DAH, both probably triggered by SLE, with a fatal outcome.

CASE REPORT

We present the case of a white 50-year-old man, with chronic kidney disease secondary to focal and segmental glomerulosclerosis, who received a cadaveric kidney transplant in 2007. The induction immunosuppression was basiliximab combined with methylprednisolone pulses, mycophenolate mofetil, and tacrolimus. He was kept under maintenance immunosuppression with tacrolimus, mycophenolate mofetil, and prednisolone. There were no relevant interurrences until May 2015, when he presented with nephrotic range proteinuria (4 g/d) and normal graft function. He was admitted in our department and a kidney graft biopsy was performed. It revealed no major pathological alterations, although it was a nonrepresentative sample (only 3 glomeruli). The patient was started on an angiotensin-converting enzyme inhibitor with reasonable proteinuria control. Two months later the patient developed full nephrotic syndrome with peripheral edema, hypoalbuminemia, and massive proteinuria (19 g/d) and was once again admitted in our department. The graft function was also deteriorated with a serum creatinine level of 1.7 mg/dL. From the immunologic study, antinuclear antibodies (ANA) and anti-double-stranded DNA (anti-dsDNA) were positive, with titers 1:160 and 302 IU/mL, respectively. The remaining immunologic study (anti-neutrophil cytoplasmic antibodies [ANCA], antiphospholipid antibodies, total complement level) was normal. Viral markers for HIV, hepatitis B virus (HBV), hepatitis C virus (HCV), parvovirus B19, human cytomegalovirus (CMV), Epstein-Barr virus (EBV), and polyomavirus (BK) were negative. The patient had a thoracoabdominopelvic computed tomography scan that was unremarkable. The graft biopsy was repeated, this time with features of CG (Fig 1). The immunofluorescence was positive, with a “full house” pattern. The graft function began to rapidly deteriorate and he was treated with corticosteroid pulses and started

plasmapheresis every other day. Graft function continued to deteriorate and the patient became dialysis dependent. After seven treatments of plasmapheresis there were no signs of remission and the proteinuria increased to 34 g/d. He was discharged on a regular hemodialysis program with low-dose immunosuppressive treatment. In October 2016, he was hospitalized with DAH that rapidly evolved with severe respiratory failure and he was admitted in the intensive care unit. The autoimmune study was repeated, revealing complement consumption, with positive ANA and anti-dsDNA antibodies. The ANCA and antglomerular basement membrane antibody (anti-GBM) were negative. Tracheobronchial aspiration was positive for blood and negative for malignancy, bacteria, mycobacteria, fungi, and *Pneumocystis jirovecii*. The patient was treated with corticosteroid pulses, plasmapheresis, and human immunoglobulin. There was no clinical response to treatment and the patient was kept under mechanical ventilation and eventually developed a ventilator-associated pneumonia with fatal outcome.

DISCUSSION

FSGS is characterized by a more aggressive course in recurrent disease, when compared with other glomerulonephritis, and it has an important impact on graft survival [7,8].

Treatment of recurrent post-transplantation FSGS has not reached a consensus but, in the majority of centers, the first therapeutic approach is the same as the one used in this patient, with corticosteroid pulses and plasmapheresis [1,9]. Other therapeutic strategies are also available, such as use of rituximab, but there is still no consensus on the timing, dose, or duration of therapy [10].

The collapsing variant of FSGS is associated with a poorer prognosis in allograft kidneys, compared with the other variants (similar to what happens in native kidneys) [11]. CG is generally associated with HIV infection but can occur with other viral infections such as parvovirus B19 [12]. The association with autoimmune diseases, such as SLE, and drugs is also known [3]. Some anecdotal cases have been published in the literature but in 2012 a large series of 19 cases of patients with CG and SLE or Lupus-Like Disease was published, adding support to this association [4,13].

DAH is a rare complication in patients with SLE, occurring in 2%–5% of cases, and is associated with a high mortality rate. The most commonly reported therapies

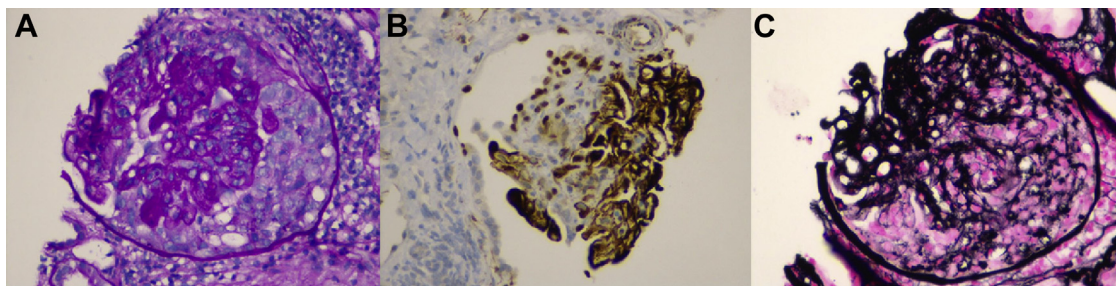


Fig 1. Light microscopy of the second graft biopsy showing features of CG. (A) Segmental and global collapse of the glomerular capillaries and marked hypertrophy and hyperplasia of podocytes using Periodic acid-Schiff stain (original magnification $\times 400$). (B) Segmental loss of WT-1 expression with WT-1 immunohistochemistry stain (original magnification $\times 400$). (C) Glomerular tuft collapse with Masson's trichrome stain (original magnification $\times 400$).

include corticosteroids, plasmapheresis, cyclophosphamide, and rituximab [5,6].

To our knowledge, this is the first case of SLE presenting with CG and DAH. It gains an increased importance because it occurred in a kidney transplant patient and had a fatal outcome.

In conclusion, CG is a rare diagnosis both in native and transplant kidneys. The majority of patients have a poor outcome. We describe a case of CG in a kidney transplant recipient, which presented with nephrotic syndrome and normal graft function that rapidly deteriorated. The presence of positive auto-immunity and “full house” immunofluorescence and the development of DAH favor the diagnosis of SLE, which could have been the trigger for the glomerular and pulmonary disease.

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