

## Case Report

# A Rare Case of C3 Glomerulonephritis Presenting as Pulmonary Renal Syndrome

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### Abstract

#### Description

C3 glomerulonephritis (C3GN) is a rare disease that falls under the umbrella of C3 glomerulopathy (C3G). Classic manifestations of C3G include acute renal failure, proteinuria, and hematuria. In some cases, extrarenal manifestations can include ocular drusen. Until recent reports, C3G manifesting with pulmonary symptoms has not been reported. In this report, we describe a patient that initially presented with hemoptysis and acute renal failure, eventually leading to a diagnosis of pulmonary renal syndrome. Renal biopsy showed C3GN. The patient's symptoms improved with pulse dose steroids, plasmapheresis and mycophenolate mofetil. C3G presenting with pulmonary symptoms is rare. Further research is needed to understand the mechanism of complement deposition in the lung parenchyma and to determine a standard therapy to treat these patients. Clinicians should be aware of the potential pulmonary manifestations that can be caused by C3GN.

#### Keywords

C3 glomerulonephritis; glomerulonephritis; glomerulonephritis/diagnosis; biopsy; diffuse alveolar hemorrhage; complement cascade; complement C3; acute kidney injury; pulmonary renal syndrome

### Introduction

C3 glomerulonephritis (C3GN) is a rare disease that falls under the umbrella of C3 glomerulopathy (C3G). Classic manifestations of C3G include acute renal failure, proteinuria, and hematuria. In some cases, extrarenal manifestations can include ocular drusen. Until recent reports, C3G manifesting with pulmonary symptoms has not been reported.<sup>1-3</sup>

### Case Presentation

The patient is a 21-year-old Caucasian male with no past medical history that presented with a chief complaint of acute hemoptysis. One week prior to admission, he visited an urgent care center with symptoms of cough, rhinorrhea and congestion. He was diagnosed with acute bronchitis and treated with steroids, bronchodilators and a 3-day course of cefdinir. The symptoms initially improved after completion of the antibiotic course, but the day prior to admission, he experienced fevers, chills,

night sweats and hemoptysis. On exam he was noted to have dried blood in the oral mucosa and rhonchi in the posterior bilateral lower lung fields.

Laboratory tests showed an elevated creatinine of 1.73 mg/dL (0.6–1.3 mg/dL) and hemoglobin of 11.9 g/dL (12–16 g/dL). Urinalysis revealed dipstick protein (>500 mg/dL) and hematuria (RBCs too numerous to count). Inflammatory markers ESR and CRP were elevated, 18 (0–15 mm/Hr) and 13.1 (<0.29 mm/L), respectively. A complete list of laboratory data are included in **Table 1**. He worked as a prison guard in the last year and, due to hemoptysis, tuberculosis was considered and induced sputum for an acid-fast bacillus test was sent for three days that was negative. The patient was started on broad spectrum antibiotics and methylprednisolone. Computed tomography showed extensive bilateral parenchymal infiltrates with associated pleural fluid suspicious for diffuse

**Table 1.** Laboratory Evaluation.

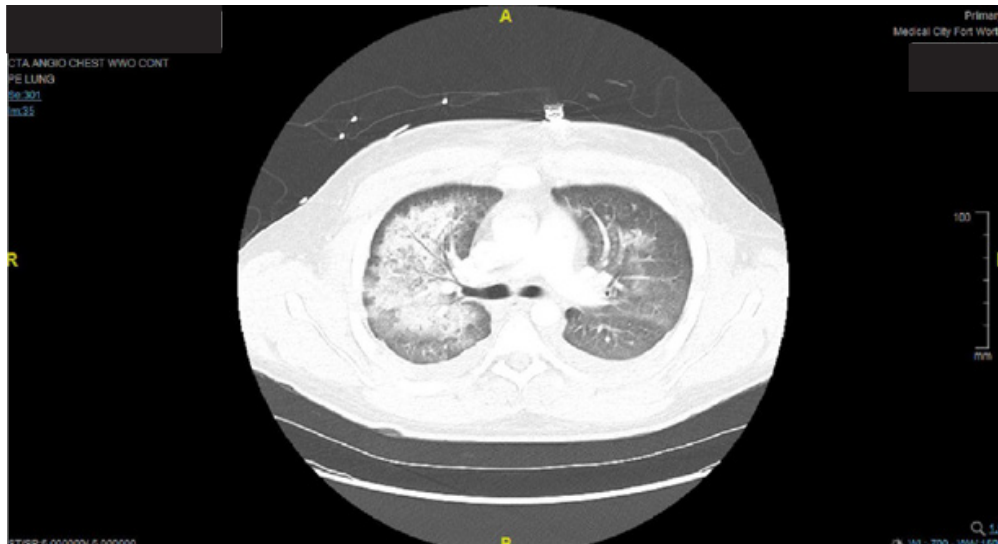
Name of assay	Values	Normal range
Hemoglobin	12.7 g/dl	14–18 g/dl
Platelet count	124 k/mm <sup>3</sup>	130–400 k/mm <sup>3</sup>
Creatinine	1.7 mg/dl	0.6–1.3 mg/dl
BUN	29 mg/dl	7–18 mg/dl
CRP	13.1 mg/dl	<0.29 mg/dl
ESR	18 mm/Hr	0–15 mm/Hr
T spot	negative	NA
Anti-streptolysin O	171.6 u/ml	0–200 u/ml
C-ANCA	<1:20	Neg <1:20
P-ANCA	<1:20	Neg <1:20
X-ANCA	<1:20	Neg <1:20
C3	51 mg/dL	82–167 mg/dl
C4	19 mg/dl	14–44 mg/dl
HIV	non-reactive	NA
ANA	negative	NA
Anti-GBM	4 units	0–20 units
Anti-Cardiolipin Igm Ab	28 U/ml	0–12 U/ml
IgG	995 mg/dl	700–1600 mg/dl
IgA	160 mg/dl	90–386 mg/dl
IgM	60 mg/dl	20–172 mg/dl

alveolar hemorrhage. (**Figure 1**) Infectious and autoimmune workup was negative, except for a low complement 3 level of 51 mg/dL. Autoimmune workup included antistreptolysin O, antineutrophil cytoplasmic antibodies and anti-glomerular basement membrane titers. Due to worsening hemoptysis, the patient underwent bronchoscopy and the results were consistent with diffuse alveolar hemorrhage. His respiratory status worsened despite high dose steroids and broad-spectrum antibiotic therapy. He was transferred to the intensive care unit and placed on a mechanical ventilator. As his acute kidney injury (AKI) worsened with no definite etiology and while awaiting results of the autoimmune panel, an ultrasound guided percutaneous renal biopsy was performed. Light microscopy showed mesangial and endocapillary hypercellularity with immunofluorescence showing granular stains along the mesangial regions with C3 complement depo-

sition consistent with C3 glomerulonephritis. (**Figure 2**) After confirmation of the diagnosis, the patient underwent eight sessions of plasmapheresis and was also started on mycophenolate mofetil (MMF) 1 g twice daily. His renal function returned to baseline normal range (0.9 mg/dL) and his pulmonary symptoms subsided. Patient was discharged on prednisone of 60 mg/day and MMF-1 g twice daily.

### Discussion

Pulmonary renal syndrome (PRS) is a rare condition that includes diffuse alveolar hemorrhage (DAH) and glomerulonephritis. Oftentimes, its rapid deterioration can lead to death. In recent years, studies have shown a mortality rate of up to 25%. For that reason, a rapid diagnosis of the underlying disease is crucial for improved survival. Commonly, PRS is associated with autoimmune etiologies such as systemic vasculitis, Goodpasture's disease

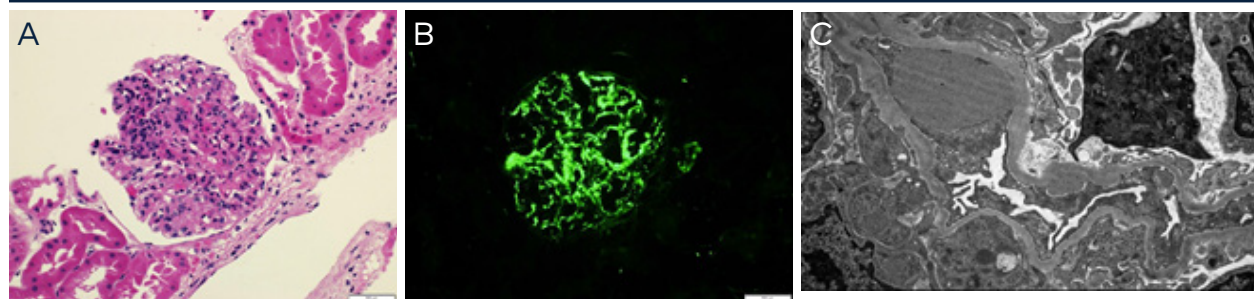


**Figure 1.** Computed tomography angiography showing bilateral ground glass opacities with smooth interlobular septal thickening.

and systemic lupus erythematosus.<sup>4,5</sup> To have a diagnosis of PRS caused by C3G is rare. C3 glomerulonephritis falls under the umbrella of C3 glomerulopathy and is a result of the abnormal activation of the alternative complement cascade. C3 glomerulopathy can be divided into Dense Deposit Disease and C3 Glomerulonephritis. These two diseases are differentiated by distribution of complement deposition in the glomeruli.<sup>1,2</sup>

Development of C3G can be divided into genetic and acquired disease. In the acquired form most patients develop renal disease after an infection. This seems to be the case in our patient. The patient was first diagnosed with bronchitis and then presented with hemoptysis

and renal failure. In most cases of C3G, patients seek medical attention for renal manifestations, such as hematuria.<sup>1</sup> In our case, the initial symptoms involved the respiratory system. It is important to note that in cases where PRS is caused by other autoimmune disorders, such as Goodpasture's disease, there is immune complex deposition that leads to lung injury.<sup>6</sup> In most cases of C3G, pathology findings on renal biopsy show complement deposition but in some cases immune complex deposits have also been described. In this particular case, immunofluorescence microscopy was only positive for C3+. The exact mechanism by which complement leads to lung injury in these patients is not well known.



**Figure 2.** Renal histopathology, representative light, immunofluorescence and electron microscopy in C3GN. A. Light microscopy showing segmental and global mesangial and endocapillary hypercellularity with scattered polymorphonuclear leukocytes. The glomerular capillary lumens are narrowed or obliterated by these cells and there are single contoured capillary walls. B. Immunofluorescence microscopy showing granular stains along the mesangial regions with C3 (3+). Immunoreactants to IgG, IgA, IgM, C1q, albumin, fibrinogen and kappa/lambda immunoglobulin light chains are negative. C. Electron microscopy showing scattered sub epithelial hump-like electron dense deposits are seen along with rare intramembranous, subendothelial and mesangial deposits. Partial foot process effacement was present (30–40%).

Management of PRS depends on treating the underlying cause as therapies may differ. In one reported case of Dense Deposit Disease and PRS, the patient was treated with plasma exchange and pulse dose steroids. Despite therapy, the patient developed end-stage renal disease and succumbed to his illness.<sup>7</sup> In contrast, in another case of C3G and PRS, the patient was treated with pulse dose steroids, plasmapheresis and mycophenolate mofetil with improvement in symptoms. After 2 years of prednisone and mycophenolate mofetil the patient's renal function started to decline requiring eculizumab. After 12 months of eculizumab therapy, the patient developed end-stage renal disease and was started on hemodialysis.<sup>8</sup> In our case, despite high dose steroids his respiratory status worsened necessitating intubation. The addition of concurrent plasmapheresis and mycophenolate mofetil 1g BID helped to improve the patient's acute presentation. The patient was discharged with prednisone 60 mg daily and mycophenolate mofetil 1 g BID. Given the low number of cases with C3G and PRS there is currently no consensus on optimal medical management. One aspect that is unique to this case is the initial presentation of respiratory symptoms, specifically, hemoptysis. In the 2 reported cases above, 1 patient initially presented with shortness of breath and anuria. During hospitalization the patient developed hemoptysis leading to a PRS diagnosis. In the second case, the patient presented with hematuria and developed hemoptysis after starting pulse dose steroids.

## Conclusion

C3 glomerulonephritis is a disease that presents mostly with renal manifestations. In rare cases, C3 complement can lead to lung injury and diffuse alveolar hemorrhage. Further research needs to be done in order to fully understand the mechanism behind lung injury and development of optimal medical management for this condition.

## Conflicts of Interest

The authors declare they have no conflicts of interest.

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