



## Case report

# An uncommon presentation of a rare disease: A case of anti-glomerular basement membrane disease without renal involvement

Jeremy Polman<sup>\*</sup>, Rory Panzarello, Pratik Patel, Vasudev Tati

Baton Rouge General Internal Medicine Residency Program, USA



## ARTICLE INFO

## Keywords:

Goodpasture's disease  
Diffuse alveolar hemorrhage  
Rare presentation

## ABSTRACT

Anti-glomerular basement membrane disease (anti-GBM) is a well-documented, small vessel vasculitis that is classically associated with glomerulonephritis and alveolitis [1]. However, regardless of clinical process, not every patient will present with a constellation of classically associated symptoms. Literature review demonstrates that early anti-GBM disease can present as glomerulonephritis without alveolitis [2,3]. In this case report, we describe the unique clinical course of a 26-year-old male who originally presented with hemoptysis and his subsequent clinical workup revealing anti-glomerular basement membrane disease without renal involvement.

## 1. Introduction

Anti-glomerular basement membrane (*Anti-GBM*) disease is a rare autoimmune disease affecting the lungs and kidneys, with an estimated incidence of 0.5–1.64 cases per million people per year [4,5]. It is caused by antibodies that target the alpha-3 chain of type IV collagen. The alpha-3 chain is expressed highest in glomerular and alveolar basement membranes, compared to the more widely expressed alpha-1 and alpha-2 chains of type IV collagen. It is thought that there is an unknown stimulus triggering the production of the autoantibodies that precedes clinical symptoms, although one study showed that even normal individuals can have natural anti-GBM autoantibodies without a pathologic disease process [6]. Suggested triggers of the disease include a pulmonary (pulmonary infection, smoking, hydrocarbon solvents) or kidney (lithotripsy, urinary obstruction) injury.

The presentation of *Anti-GBM* disease consists of renal and pulmonary symptoms, and sometimes includes systemic features. Approximately 90% of patients present with rapidly progressive glomerulonephritis with non-nephrotic proteinuria, hematuria, and elevated creatinine. Pulmonary involvement is seen in 25–60% of patients, and usually consists of diffuse alveolar hemorrhage (DAH). Pulmonary symptoms can include cough, hemoptysis, shortness of breath, chest pain, and hypoxia. While pulmonary disease can predominate in up to 46% of cases [7], isolated pulmonary disease is seen in less than 10% of patients [8]. In this case report, we describe the unique clinical course of a 26-year-old male who originally presented with hemoptysis and his subsequent clinical workup, revealing anti-glomerular basement

membrane disease without renal involvement.

## 2. Case report

This is a 26 year old male with no significant past medical history who presented as a direct admission for hemoptysis. The patient originally noticed early morning hemoptysis for the preceding 3 months which would occasionally be associated with mild dyspnea and a sensation of chest tightness. He denied any associated nosebleeds, fever, chills, wheezing, night sweats, hematuria, weight loss, or skin rashes. He states that he has seasonal rhinitis after pollen exposure, however this is well controlled with fluticasone and cetirizine. He denied allergies to animal dander, of which he lives with a dog and ferret. He lives in a 60 year old home, however this was recently renovated within the last few years. The patient also mentions that he works as a machinist who cuts carbon steel on a daily basis, however he endorsed wearing appropriate goggles and respirator at all times. He admitted to a history of cigarette smoking however stated that he quit when he began to develop hemoptysis. He was a current smoker up until the onset of symptoms and had smoked 1 PPD/day for the last 4 years. He used vaping devices 2 years ago.

He was initially seen by his primary care provider for these complaints and was empirically treated with antihistamines. A CT chest performed the following week revealed patchy, ground glass opacities in bilateral lung fields, right greater than left and more prominent in the right middle lobe [Fig. 1]. He was subsequently treated with a course of doxycycline with no improvement or change in his symptoms. Given no

<sup>\*</sup> Corresponding author.

E-mail address: [jeremy.polman@brgeneral.org](mailto:jeremy.polman@brgeneral.org) (J. Polman).

<https://doi.org/10.1016/j.rmcr.2020.101282>

Received 7 September 2020; Received in revised form 11 October 2020; Accepted 2 November 2020

Available online 7 November 2020

2213-0071/© 2020 The Authors.

Published by Elsevier Ltd.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

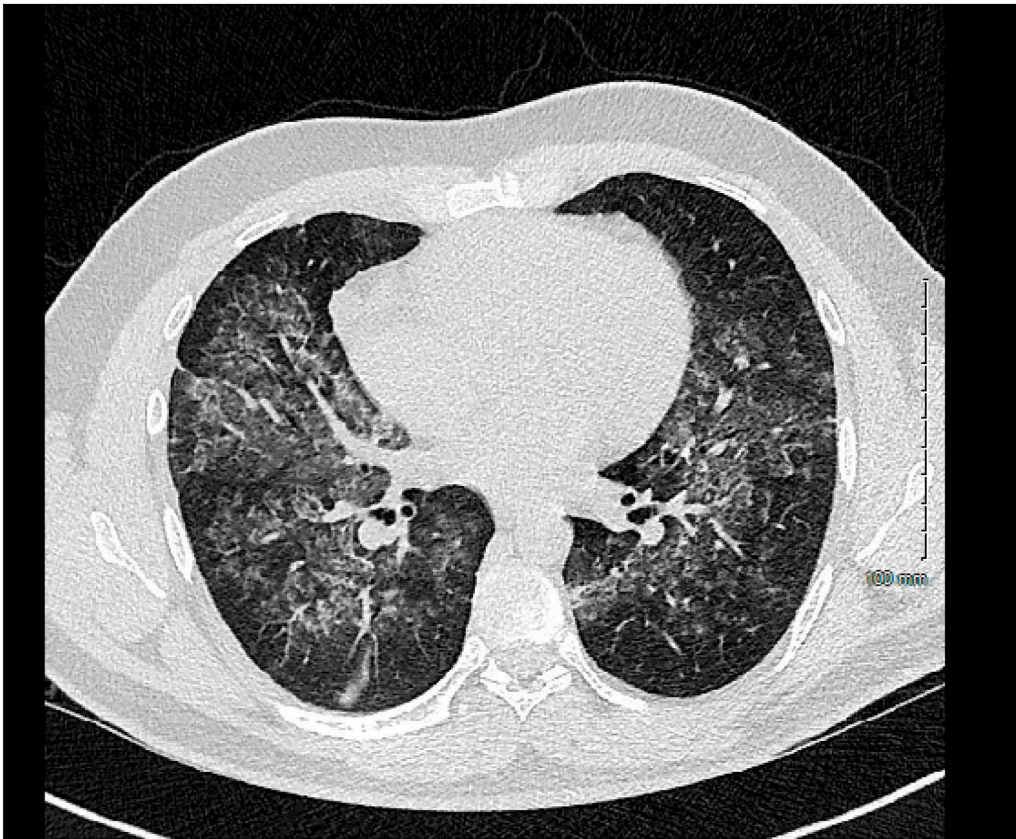


Fig. 1. CT chest demonstrating revealed patchy, ground glass opacities in bilateral lung fields, right greater than left and more prominent in the right middle lobe.

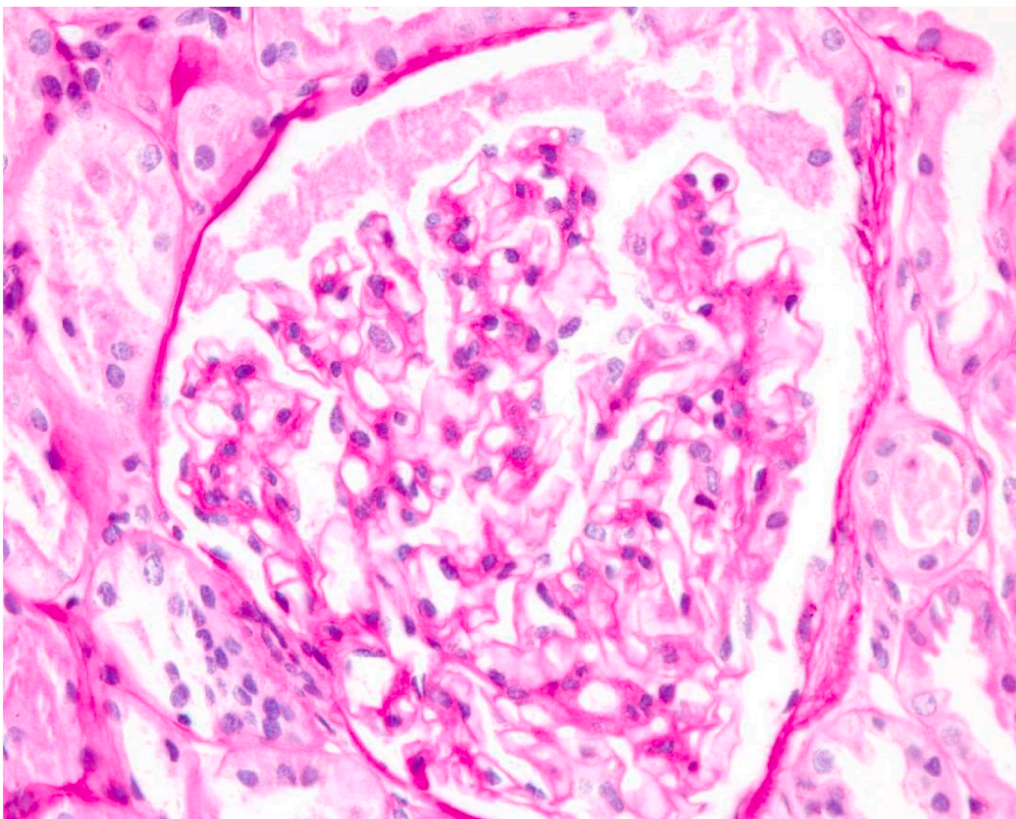
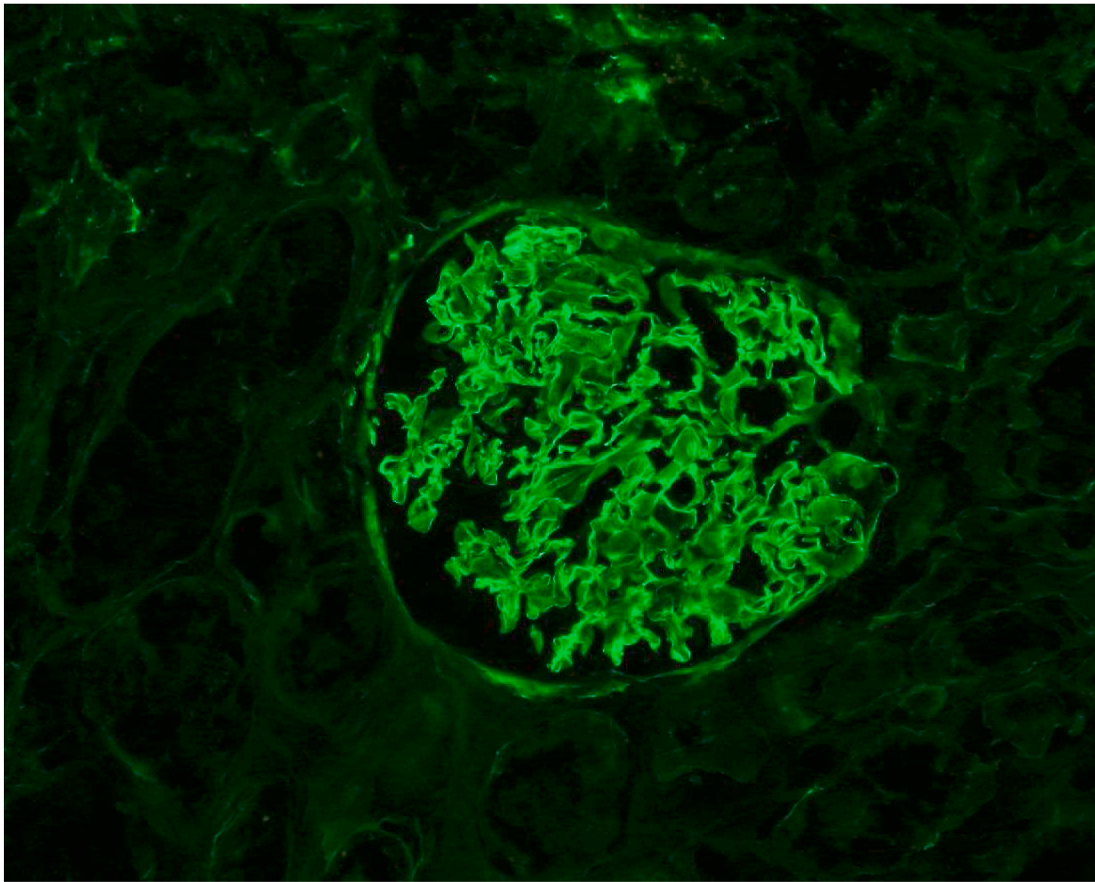


Fig. 2. Renal biopsy demonstrating a normal appearing glomerulus without inflammatory changes, sclerosis, or cellular debris.





**Fig. 3.** Renal biopsy with immunofluorescence staining for IgG demonstrating linear stranding along the basement membrane of the glomerulus.

improvement in symptoms, he was initiated on prednisone 40mg daily for one week and was referred to a pulmonologist upon completion. Upon pulmonology evaluation, suspicion for vasculitis was risen. Laboratory workup at that time included CBC, CMP, ESR, and urinalysis, all within normal limits. A subsequent ANA was positive in a 1:320 titer with a homogenous pattern. Reflex antibodies drawn demonstrated no detectable anti-DNA, anti-SSA, anti-SSB, anti-smith, anti-SCL, and anticentromere antibodies and negative ANCA screen. He had positive anti-glomerular basement membrane antibodies with a level of 4.6. Given laboratory findings and the unavailability of elective outpatient bronchoscopy secondary to the coronavirus pandemic, the patient was admitted to the hospital for further evaluation of his hemoptysis.

In the hospital, the patient underwent a repeat urine analysis that showed 10–20 red blood cells with no evidence of proteinuria and no casts. His renal function was normal with a BUN of 11 and a creatinine of 1.1 indicating an eGFR of 107. Bronchoscopy performed in the hospital demonstrated the entire tracheobronchial tree to be normal. Following lavage, frothy fluid was returned, each aliquot subsequently more bloody, consistent with diffuse alveolar hemorrhage. With the scope in the wedge position and using fluoroscopy, transbronchial biopsy forceps were used to take 5 biopsy specimens of the right middle lobe. The patient was treated with pulse methylprednisolone at a dose of 250 mg every 6 hours for 3 days, for a total of 3 g of methylprednisolone. Unfortunately the biopsies were not placed in the correct formula to be immunohistochemically stained. The patient had no episodes of hemoptysis during hospitalization and had resolution of his shortness of breath and chest tightness. He was discharged home on hospital day 5 and post op day 2 with 1 mg/kg prednisone (80 mg as this patient weighed 84 kg) with pulmonology and rheumatology follow up.

Within 12 hours of discharge, the patient presented to the emergency department with worsening hemoptysis and dyspnea. Patient was found

to be hypertensive, tachycardic, and hypoxic, requiring high flow nasal cannula to maintain oxygen saturations above 90%. Given overall clinical deterioration and failure of conservative immunosuppression, the patient was admitted to the ICU, where he received plasmapheresis. The following day, the patient reported significant improvement in hemoptysis and dyspnea following plasmapheresis and was able to be transitioned to supplemental oxygen via nasal cannula at 2 L. The patient was scheduled to receive daily plasmapheresis treatments until renal biopsy could be obtained to further direct therapy. On day 3 of his ICU stay, a renal biopsy was obtained, which revealed a normal appearing glomerulus without inflammatory changes, sclerosis, or cellular debris on light microscopy [Fig. 2]. However, immunofluorescence staining for IgG demonstrated linear stranding along the basement membrane of the glomerulus, confirming anti-glomerular basement membrane disease [Fig. 3]. Once clinically stable, the patient was stepped down from the ICU to the hospital floor, where he began treatment with cyclophosphamide and continued weight based steroid therapy.

### 3. Discussion

As demonstrated in the case above, not every patient will have the same clinical symptoms when presenting with anti-GBM disease. Not only was this patient unique in that there were only pulmonary symptoms on presentation, but the symptoms were present for approximately 3 months prior to diagnosis. Previous reports of patients with pulmonary manifestations of anti-GBM disease indicate that if pulmonary symptoms are the presenting symptom, it is quickly followed by renal symptoms [9]. As previously mentioned, diffuse alveolar hemorrhage can increase mortality in patients with anti-GBM disease, indicating that early diagnosis is of utmost importance.

A second interesting detail from the presented case is that the patient developed worsening of pulmonary symptoms after initiation of treatment with steroids. This is somewhat confusing, as one would anticipate the patient's symptoms to improve after initiation of treatment. While the exact reason for this acute worsening is unknown, literature search reveals that a similar presentation occurred in another patient with pulmonary involvement of anti-GBM disease, where the patient developed acute worsening after initiation of treatment. In both cases, the patient underwent diagnostic bronchoscopy, followed by acute worsening of diffuse alveolar hemorrhage soon after [10]. This clinical outcome should be considered when evaluating the risks and benefits of performing bronchoscopy on a patient with diffuse alveolar hemorrhage.

A third finding is that the patient presented is a cigarette smoker. Although cigarette smoking does not appear to be directly involved in the production of anti-GBM antibodies, previous studies have indicated that some environmental factors may be considered as causative agents to developing diffuse alveolar hemorrhage in patients with the disease [11,12]. Along with appropriate treatment therapy with steroids and immunosuppressive medications, it is important to encourage the patient to cease smoking to prevent further pulmonary injury.

The diagnosis is made by testing for anti-GBM antibodies in the serum, as well as obtaining a kidney biopsy. However, negative serum anti-GBM antibodies have been reported in some patients with the disease [13,14]. Renal biopsy should be obtained unless there is a contraindication. Immunofluorescence microscopy shows linear deposition of IgG along the glomerular capillaries and light microscopy shows crescentic glomerulonephritis. Plain chest x-ray may show patchy opacities and a high-resolution chest CT may show diffuse ground glass opacities. If pulmonary disease is present, a bronchoscopy may show diffuse alveolar hemorrhage. Although the patient in the case above did not have renal involvement, a renal biopsy was still obtained to confirm diagnosis.

Prognosis of anti-GBM disease without treatment is poor, with 90% of cases resulting in either death or life long dialysis. Prognosis with treatment is relatively good and is better with less renal impairment at presentation. The mainstay of treatment is a combination of plasmapheresis and immunosuppressive therapy. Immunosuppression consists of glucocorticoids and cyclophosphamide. Patients should receive pulse methylprednisolone (15–30mg/kg with a maximum of 1000 mg) daily for 3 days, followed by oral prednisone at 1mg/kg (max of 80mg/day) daily. Cyclophosphamide should be continued for 3 months, and prednisone continued for at least 6–9 months. Our patient was initiated on glucocorticoids and cyclophosphamide therapy, of which he tolerated well. Further clinical follow up will be needed to assess patient symptoms after receiving treatment.

In conclusion, anti-glomerular basement membrane disease remains a very rare condition. Even less common is to have isolated pulmonary involvement. A renal biopsy should always be obtained to establish the diagnosis, as it was in our case, although renal involvement was not present. Quick action and high clinical suspicion must be taken to treat the disease and halt disease progression.

## Support/funding

This case report did not receive any funding or additional support.

## Declaration of competing interest

There are no conflicts of interest to note.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmcr.2020.101282>.

## References

- [1] T. Hellmark, M. Segelmark, Diagnosis and classification of Goodpasture's disease (anti-GBM), *J. Autoimmun.* 48–49 (2014 Feb-Mar) 108–112, <https://doi.org/10.1016/j.jaut.2014.01.024>.
- [2] F. Dammacco, S. Battaglia, L. Gesualdo, V. Racanelli, Goodpasture's disease: a report of ten cases and a review of the literature, *Autoimmun. Rev.* 12 (11) (2013) 1101–1108, <https://doi.org/10.1016/j.autrev.2013.06.014>.
- [3] P. Giri, J.E. Taylor, Recurrent Goodpasture's disease with severe renal involvement after initial successful treatment, *Nephrol. Dial. Transplant.* 16 (9) (2001) 1952, <https://doi.org/10.1093/ndt/16.9.1952>.
- [4] R. Silvarino, O. Noboa, R. Cervera, Anti-glomerular basement membrane antibodies, *Isr. Med. Assoc. J.* 16 (11) (2014) 727–732.
- [5] M. Canny, P.V. O'Hara, et al., Spatial and temporal clustering of anti-glomerular basement membrane disease, *Clin. J. Am. Soc. Nephrol.* 11 (8) (2016), <https://doi.org/10.2215/CJN.13591215>, 1392–1939.
- [6] Z. Cui, H.Y. Wang, M.H. Zhao, Natural autoantibodies against glomerular basement membrane exist in normal human sera, *Kidney Int.* 69 (5) (2006), 894–869.
- [7] R. Lazor, L. Bigay-Game, V. Cottin, et al., Alveolar hemorrhage in anti-basement membrane antibody disease: a series of 28 cases, *Medicine (Baltim.)* 86 (3) (2007) 181.
- [8] B. Shiferaw, V. Miro, C. Smith, J. Akella, W. Chua, Z. Kim, Goodpasture's disease: an uncommon disease with an atypical clinical course, *J. Clin. Med. Res.* 8 (1) (2016) 52–55, <https://doi.org/10.14740/jocmr2379w>.
- [9] M. Hellmann, T. Gerhards, C. Rabe, Goodpasture's syndrome with massive pulmonary haemorrhage in the absence of circulating anti-AGM antibodies? *Nephrol. Dial. Transpl.* 21 (2) (2006) 526–529, <https://doi.org/10.1093/ndt/gfi279>.
- [10] T. Sismanlar-Eyuboglu, A. Aslan, D. Gezgin-Yildirim, What triggered massive hemoptysis in Goodpasture Syndrome with isolated pulmonary involvement in a 14-year-old boy? *Turk. J. Pediat.* 61 (2019) 611–614, <https://doi.org/10.24953/turkped.2019.04.022>.
- [11] J. Fort, E. Espinel, J. Rogriquez, Partial recovery of renal function in an oliganuric patient affected with Goodpasture's syndrome after treatment with steroids, immunosuppressives and plasmapheresis, *Clin. Nephrol.* 22 (1984) 211–212.
- [12] J.D. Escolar Castellon, P.A. Roche, A. Escolar Castellon, The modifications produced in allergic alveolitis and in Goodpasture's syndrome due to exposure to cigarette smoke, *Histol. Histopathol.* 6 (4) (1991) 535–547.
- [13] S. Ohlsson, H. Herlitz, S. Lundberg, D. Selga, J. Mölne, J. Wieslander, M. Segelmark, Circulating anti-glomerular basement membrane antibodies with predominance of subclass IgG4 and false-negative immunoassay test results in anti-glomerular basement membrane disease, *Am. J. Kidney Dis.* 63 (2) (2014) 289–293, <https://doi.org/10.1053/j.ajkd.2013.08.032>.
- [14] T.B. Vries, S. Boerma, J. Doornebal, B. Dikkeschei, C. Stegeman, T.F. Veneman, Goodpasture's syndrome with negative anti-glomerular basement membrane antibodies, *Eur. J. Case Rep. Intern. Med.* 4 (8) (2017), 000687, [https://doi.org/10.12890/2017\\_000687](https://doi.org/10.12890/2017_000687).