Case report of an unusual manifestation of anti-GBM disease

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ABSTRACT

Background: Anti-GBM disease is a small vessel vasculitis that occurs when circulating antibodies against the glomerular basement membrane develop. It is a relatively rare disease, occurring in less than two cases per million population. The usual presentation is with renal or lung manifestations or with a combination of both.

Case Presentation: Our case reports a patient who presented with end-stage renal disease secondary to anti-GBM disease, with no pulmonary manifestations, who later presented with a syndrome suggesting cerebral vasculitis, that responded to immunosuppressive treatment.

Conclusion: Cerebral involvement in anti-GBM disease is very rare and to our knowledge, only a few cases have been so far reported.

Keywords: Anti-GBM disease, cerebral vasculitis, immunosuppression, small vessel vasculitis.

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Background

Anti-GBM (Glomerular basement membrane) disease is well-understood vasculitis with typical renal and pulmonary involvement. Here we present a case with renal manifestations and a rare sequela of neurological involvement.

Case Presentation

A 60-year-old white male presented with nephrotic syndrome with serum creatinine level of 347 umol/l, potassium of 6.61 mmol/l, albumin of 21.5 g/l, and proteinuria of 2 g/24 hours. Clinically, patient had extensive bilateral lower limb edema and congested lungs on both physical examination and on chest X-ray. He underwent immediate hemodialysis and subsequent investigations showed a positive anti-GBM antibody with a titer of 93.4 U/ml. A renal biopsy showed severe crescentic glomerulonephritis with associated tubular interstitial inflammation, all consistent with a diagnosis of anti-GBM disease. A Computer tomography (CT)-thorax was performed for completeness confirmed no lung involvement. As the patient was dialysis dependent at this stage, with no other organ involvement, treatment with immunosuppressants was not started. He recovered clinically on hemodialysis and was discharged home.

Fifty days after starting the patient on hemodialysis, he presented to the emergency department with new onset generalized tonic-clonic seizures. The patient was treated with Levetiracetam and an inpatient neural Magnetic resonance imaging (MRI) and Magnetic resonance angiography (MRA) showed T2-FlAIR hyperintense changes in the cerebellar, occipital, and temporal lobes, together with multiple foci of stenosis in frontopolar, M2, bilateral Middle cerebral artery (MCA), and Anterior cerebral artery (ACA) (Figure 1). Such findings were in keeping with possible secondary Central nervous system (CNS) vasculitis. Due to the elevated anti-GBM antibodies (recorded at 37.5 U/ml) and MRI changes, the patient underwent four sessions of plasmapheresis and started on prednisolone and cyclophosphamide.

The patient recovered well, though remained dialysis dependent. He has had no further seizures. Repeat MRIs demonstrated resolution of T2 FLAIR and MRA changes (Figure 2) and patient's anti-GBM antibody has remained undetectable (Table 1). The rapid improvement of the MRI changes also shed light on posterior reversible encephalopathy syndrome (PRES) as a differential.

Discussion

Anti-GBM disease, formerly known as Goodpasture's Disease, is a small vessel vasculitis in which antibodies against the glomerular basement membrane and the

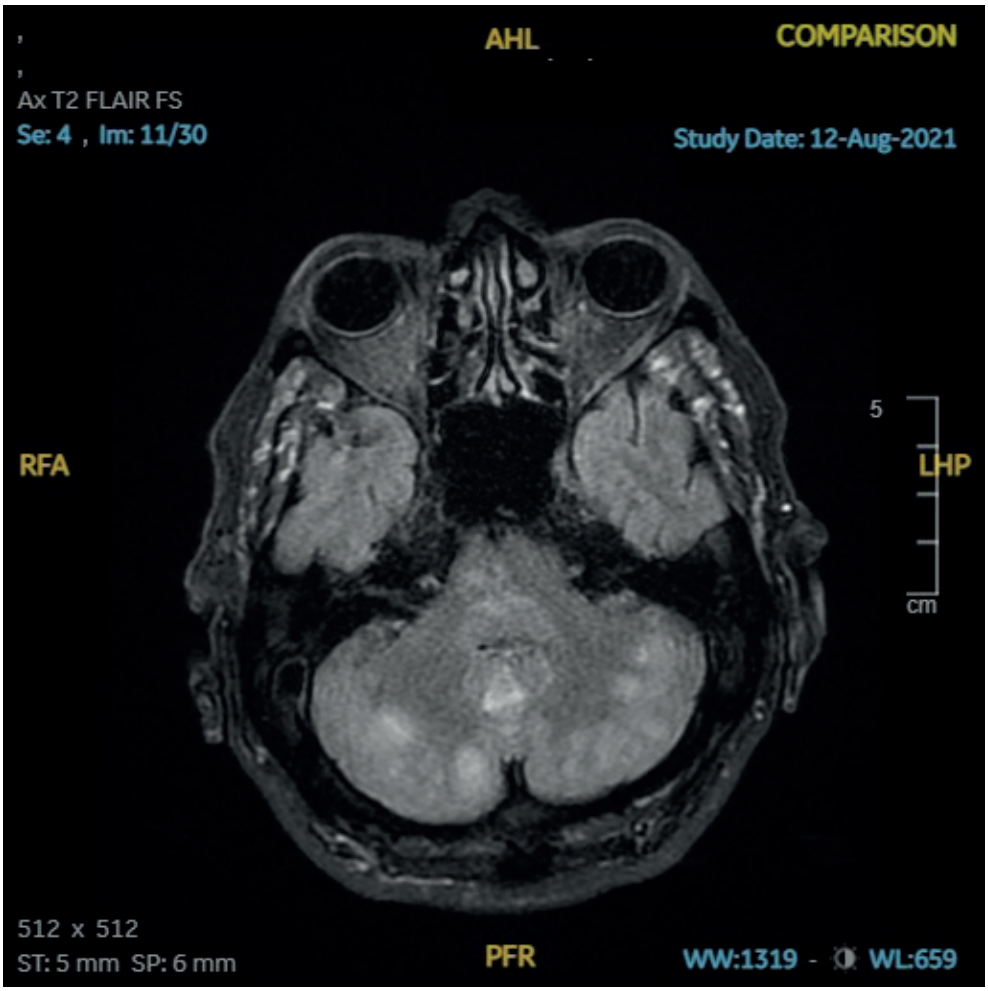

Figure 1. *MRI showing bilateral T2 hyperintensities on FLAIR sequences in the cerebellum, parietal, and occipital lobes.*

alveolar basement membrane develop. These antibodies are directed against an intrinsic antigen in the basement membrane. This results in a rapidly progressive glomerulonephritis with or without lung involvement that results in lung hemorrhage. Anti-GBM disease is rare, estimated to occur in fewer than two cases per million population [1]. Studies report both temporal and spatial clusters of cases suggesting the role of environmental triggers for the disease [2,3].

The principal target for the anti-GBM antibodies is the NC1 domain of the alpha-3 chain of type IV collagen (alpha-3(IV) chain) [4]. This reflects the distribution of damage that is limited to the basement membrane of the glomeruli and alveoli as expression of the alpha-3 chain is highest in these sites. Anti-GBM antibodies are usually IgG, with IgG1 and IgG3 subclasses predominant [5]. Clinical studies suggest that autoreactive T cells might also play a role in the development of anti-GBM disease [6,7].

Most (approximately 90%) patients with anti-GBM disease present with clinical features of rapidly progressive glomerulonephritis. Between 25% and 60% present with concomitant alveolar hemorrhage, and a small proportion of patients present with isolated pulmonary findings. Systemic complaints and signs, such as malaise, weight loss, fever, or arthralgia, are usually experienced only for a few weeks. The presence of such signs for a longer period suggests that the patient is double positive for anti-GBM and anti-myeloperoxidase [Myeloperoxidase-anti-neutrophil cytoplasmic antibodies (MPO-ANCA)] and has features of concurrent vasculitis. Other variants of atypical anti-GBM disease have been reported including double-positive anti-GBM and ANCA-associated disease, anti-GBM disease associated with membranous nephropathy (several cases of anti-GBM disease associated with membranous nephropathy have been described), anti-GBM disease without detectable circulating anti-GBM antibodies. A rare variant of anti-GBM disease, described as "atypical anti-GBM nephritis," has been reported in a series of 20 patients who presented with hematuria, proteinuria, and mild renal insufficiency, without pulmonary hemorrhage [8].

Renal manifestations

The presentation of anti-GBM disease is similar to that of other forms of rapidly progressive glomerulonephritis:

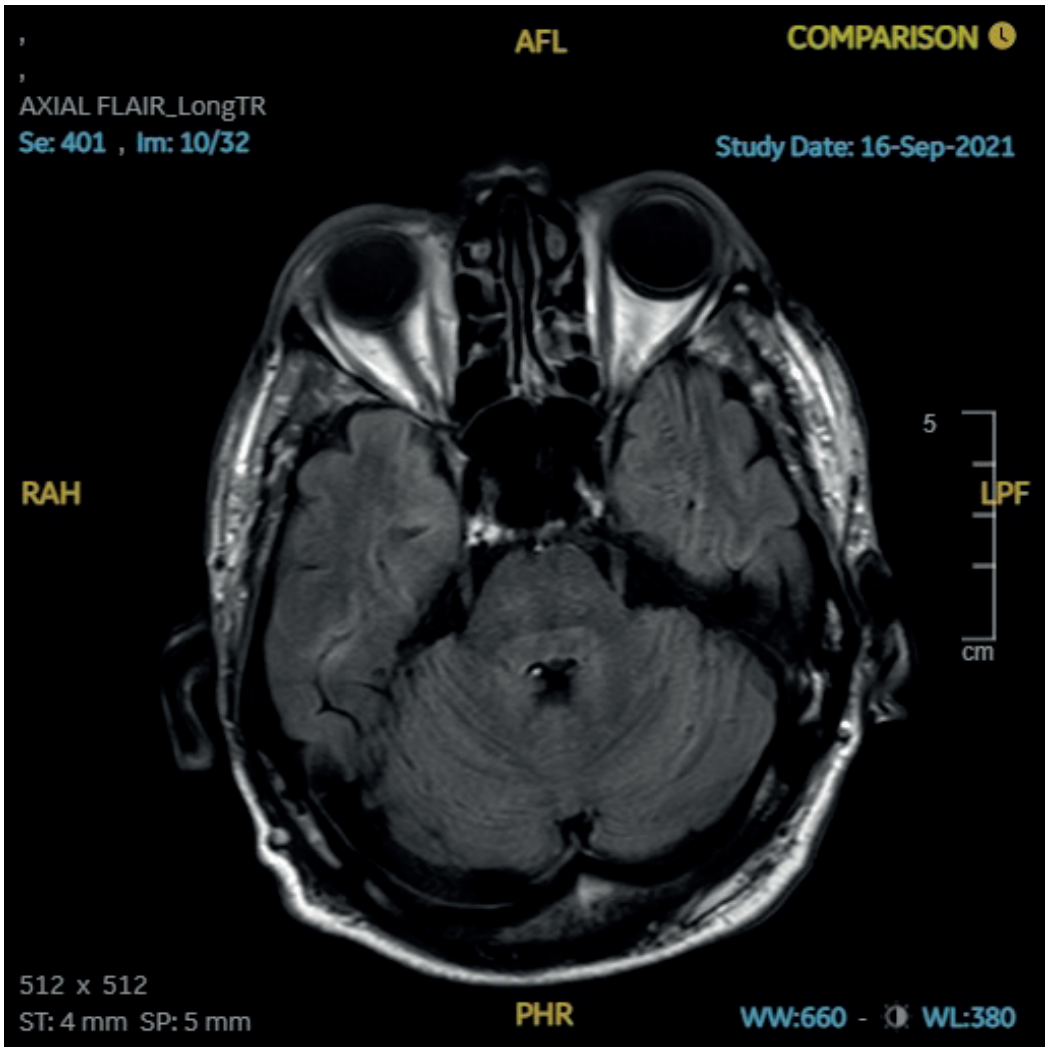

Figure 2. *MRI i0maging on repeat scanning showed rapid resolution of T2 hyperintensities.*

Table 1. *ANTI-GBM Regression Over Time.*

	ANTI-GBM SERUM (0.0-20.0 U/ML)
At presentation	93.4
Onset of neurological symptoms	32.3
1 week post plasmapheresis	6.9
1 month post plasmapheresis	5.0
2 month post plasmapheresis	3.2
3 month post plasmapheresis	<2.0

relatively acute kidney injury with a urinalysis showing proteinuria (which is usually not in the nephrotic range), and a nephritic sediment characterized by dysmorphic red cells (including acanthocytes), white cells, and red cell and granular casts. Macroscopic hematuria is more common in anti-GBM disease compared with other forms of rapidly progressive glomerulonephritis.

A relatively mild degree of renal involvement may be more common than previously appreciated in patients with anti-GBM disease. A retrospective review from one center in Australia found that 5 of 14 patients (36%) with this disorder had hematuria and/or proteinuria but a normal creatinine clearance or serum concentration of creatinine.

Pulmonary manifestations

Pulmonary involvement, generally consisting of alveolar hemorrhage, affects 25%-60% of patients. In rare cases, pulmonary disease predominates. Pulmonary manifestations include shortness of breath, cough, sometimes overt hemoptysis, pulmonary infiltrates on chest radiograph, and an Diffusing capacity of the lungs for carbon monoxide (DLCO) due to the presence of hemoglobin in the alveoli. Iron deficiency anemia, possibly due to prolonged pulmonary bleeding, may be seen.

Neurological manifestations

Few case reports have reported involvement of CNS vasculature in the setting of ant-GBM vasculitis. Brain MRI changes typically demonstrated beading of the large intra-cranial vessels, together with multi-focal cortical

ischemic infarcts posteriorly: mainly involving the occipital and parietal lobes [9]. The gold standard for diagnosis is a brain biopsy. However, CNS vasculitis should be considered depending on the clinical and radiological findings, together with response to immunosuppressive agents. PRES is another differential which might strongly mimic CNS vasculitis. Patients also typically present with ictal activity in the setting of uremia and MRI changes.

Conclusion

Anti-GBM disease usually presents with renal and pulmonary manifestations. Presentation can be fulminant and even life-threatening if not identified early and treated accordingly. Rare manifestations can occur, such as the involvement of the central nervous system. Therefore, we must be vigilant in these cases to these rare manifestations, which may require more aggressive treatment.

What is new?

Anti-GBM typically presents with renal and/or pulmonary involvement. Here the authors present a patient that presented with end-stage renal involvement with no pulmonary manifestations, who later with syndrome suggesting cerebral vasculitis.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

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Consent for publication

Written and informed consent was taken from the patient to publish this case report.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Male, 60 years old
2	**Final diagnosis**	Anti-GBM disease with primarily renal involvement but also cerebral
3	**Symptoms**	Acute kidney injury, encephalopathy
4	**Medications**	Steroids, cyclophosphamide, plasma exchange, and anti-epileptics
5	**Clinical procedure**	Hemodialysis and plasma exchange
6	**Specialty**	Nephrology and neurology