CASE REPORT

Atypical presentation of anti-GBM nephritis in a 90-year-old patient

Julie Omolola Okiro,¹ Chaudhry Adeel Ebad,² Amjad Zaman Khan¹¹Department of Medicine, Sligo University Hospital, Sligo, Co. Sligo, Ireland²Department of Nephrology, Sligo University Hospital, Sligo, Co. Sligo, Ireland

Correspondence to

Dr Julie Omolola Okiro, Julieokiro@gmail.com

Accepted 11 November 2016

SUMMARY

A 90-year-old woman who had bloody diarrhoea, nausea, weakness and reduced urine output was found to have acute kidney injury. Her inflammatory markers were raised and her chest X-ray suggested an inflammatory process. She was initially suspected to have acute kidney injury secondary to dehydration and sepsis but when her autoimmune screen returned positive for antiglomerular basement membrane antibodies our diagnosis and management strategy was reconsidered. This is a case report of Goodpasture disease presenting in an elderly patient.

BACKGROUND

Anti-glomerular basement membrane (anti-GBM) nephritis is an autoimmune disease where circulating autoantibodies attack the α -3 chain of type IV collagen located in the GBM and the alveolar basement membrane. Anti-GBM nephritis has been reported in all age groups but it is more noted in young men in their 30s and in both genders in patients in their sixth and seventh decades.^{1 2} The youngest reported case was of a 11-month-old girl¹ and the oldest an 81-year-old man.³ Elderly patients are more likely to present with isolated renal disease but younger patients may present with Goodpasture syndrome where pulmonary haemorrhage is associated with nephritis.² Presentation is usually dramatic in all age groups with signs and symptoms suggestive of acute kidney impairment and pulmonary haemorrhage. Patients may present with symptoms not usual for anti-GBM disease or in age groups not typically affected, as in our case. This may be misleading and lead to delayed diagnosis by general physicians.

CASE PRESENTATION

A 90-year-old woman, a non-smoker, was referred by her general practitioner with a 1-week history of bloody diarrhoea, nausea, vomiting and weakness. She had no urine output for 4 days and was very lethargic. She had presented to the emergency general practitioner service on a bank holiday. She was considered dehydrated and given intravenous rehydration but she showed no improvement. She was subsequently transferred by ambulance to the regional hospital where she was seen and assessed by the general medical team on call.

She had a medical history of asthma and her regular medications were durosic patch 12 µg/hour every 3 days for lower back pain. She denied any recent use of non-steroidal anti-inflammatory drugs, respiratory symptoms, haemoptysis,

haematuria or rashes. On clinical examination she appeared comfortable in bed and was alert. She was dehydrated and cachectic. Her blood pressure was 115/50 mm Hg and her pulse was 103/min. She was saturating at 98% on room air and was afebrile. There were bi-basal crepitations on chest auscultation. The rest of her systemic examination was non-contributory. She had no palpable bladder. After initial assessment a urine catheter was inserted to monitor urine output.

INVESTIGATIONS

For ease of reading please see [table 1](#) for blood investigations.

She was anaemic with a haemoglobin of 8.4 g/dL (13–18 g/dL) and mean corpuscular volume of 67 fL (78–98). Her white cell count was $11 \times 10^9/L$ (4–11) with normal differentials and her platelet count was elevated at $692 \times 10^9/L$ (140–450). Peripheral blood film reported schistocytes. Reticulocyte count was 0.5% (0.4–2.0), absolute reticulocyte count was 14×10^9 (30–100) and serum haptoglobin was 2.58 g/L (0.45–2.05). Coagulation screen showed prolonged prothrombin time of 13.5 s (10.2–11.8) and activated prothrombin time of 38.9 s (22.1–29.1) but her international normalised ratio was normal at 1.2.

Her C reactive protein was 240 mg/L (<5). Alkaline phosphatase was 232 U/L (40–130) but the rest of her liver profile was normal including bilirubin. Her renal profile and electrolytes were impaired with creatinine 946 µmol/L (62–80), urea 40 mmol/L (2.8–7.2), estimated glomerular filtration rate 4 mL/min/1.73 m² (>90), sodium 122 mmol/L (133–145), potassium 6.5 mmol/L (3.3–5.1) and calcium of 1.86 mmol/L (2.20–2.55). Urine osmolality and electrolyte tests were not performed as she was anuric.

Arterial blood gas on room air showed metabolic acidosis with pH of 7.3 (7.35–7.45), partial pressure of carbon dioxide 3.62 kPa (4.6–6), pO₂ 14.2 kPa (10.6–13.3) and bicarbonate 13.1 mmol/L (23–27).

ECG was normal. Chest X-ray ([figure 1](#)) revealed increased reticular markings within the lung bases bilaterally suggestive of an interstitial process. There was also patchy opacification within the right lower zone and biapical fibrotic changes. Renal ultrasound scan showed both kidneys of normal shape and size with diffusely increased echogenicity. There were no signs of obstruction and her bladder was empty.

Stool culture did not grow any pathogens and was negative for *Escherichia coli* 0157:H7.

CrossMark

To cite: Okiro JO, Ebad CA, Khan AZ. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-217990

Table 1 Laboratory investigations

	Patient's values	Laboratory normal range
Haematology		
Haemoglobin (g/dL)	8.4	13–18
Mean corpuscular volume (fL)	67	78–98
White cell count	11×10 ⁹ /L	4–11×10 ⁹ /L
Platelet	692×10 ⁹ /L (140–450)	140–450×10 ⁹ /L
Peripheral blood film	Schistocytes	
Reticulocyte count (%)	0.5	0.4–2.0
Absolute reticulocyte count	14×10 ⁹	30–100×10 ⁹
Serum haptoglobin (g/L)	2.58	0.45–2.05
Prothrombin time (s)	13.5	10.2–11.8
Activated prothrombin time (s)	38.9	22.1–29.1
International normalised ratio	1.2	<1.1
Biochemistry		
Alkaline phosphatase×the rest of her liver profile was normal including bilirubin (U/L)	232	40–130
Creatinine (μmol/L)	946	62–80
Urea (mmol/L)	40	(2.8–7.2)
eGFR	4 mL/min/ 1.73 m ²	>90 mL/min/ 1.73 m ²
Sodium×urine osmolality and electrolyte tests not performed as she was anuric (mmol/L)	122	133–145
Potassium (mmol/L)	6.5	3.3–5.1
Calcium (mmol/L)	1.86	2.20–2.55
C reactive protein	240	<5
Arterial blood gas on room air		
pH	7.3	7.35–7.45
pCO ₂ (kPa)	3.62	4.6–6
pO ₂ (kPa)	14.2	10.6–13.3
Bicarbonate (mmol/L)	13.1	23–27

eGFR, estimated glomerular filtration rate; pCO₂, partial pressure of carbon dioxide; pO₂, partial pressure of oxygen.

Urine dipstick was not performed as our patient was anuric. An urgent nephritic screen was conducted including antinuclear antibodies, antineutrophil cytoplasmic antibodies, complements C3 and C4, anti-GBM antibodies, serum electrophoresis, serum immunoglobulins, hepatitis viral screen, antistreptolysin-O titre, extractable nuclear antigens and antidouble-stranded DNA antibodies.

DIFFERENTIAL DIAGNOSIS

1. Acute tubular necrosis secondary to sepsis.
2. Legionella pneumonia (diarrhoea, chest X-ray changes and low serum sodium). Urinary legionella antigen test was not performed as our patient was anuric.
3. Dehydration (pre-renal failure).
4. Haemolytic uraemic syndrome (bloody diarrhoea and schistocytes on her blood film).
5. Rapidly progressive glomerulonephritis.

TREATMENT

After initial assessment, intravenous access was gained and she received 3 L of normal saline in the first 24 hours. A urine catheter was inserted for input/output monitoring but she was completely anuric. She received hyperkalaemic regimen including 10 mL of 10% calcium gluconate, 50 mL of 50% dextrose in

Figure 1 First chest X-ray.

Figure 2 Follow-up chest X-ray.

10 units of actrapid insulin and regular salbutamol nebulisers. She was started empirically on intravenous ceftriaxone 1 g twice daily. There was a known penicillin allergy. A four-hourly blood gas was planned and this showed worsening metabolic acidosis with pH of 7.24 and bicarbonate of 14 on day 1 of admission.

On day 2 of admission her fluid input was 2 L per 24 hours. She remained anuric and acidotic despite fluid rehydration and antibiotics for probably sepsis and thus a decision was made to start dialysis. She had a right internal jugular vascath inserted and a repeat chest X-ray was performed to confirm the position of vascath (figure 2). This showed worsening appearances with bilateral airspace opacification and increased reticular markings bilaterally. With her consent haemodialysis was started. On her first dialysis day predialysis creatinine was 904 μmol/L and urea was 40.3 mmol/L. Postdialysis creatinine was 654 μmol/L and urea 28.3 mmol/L. She received a unit of packed red cells (PRC) postdialysis. On day 3 of admission and her second day on dialysis she was transfused one unit of PRC. She remained anuric. Her third dialysis session was on day 4 during which she received another unit of PRC.

OUTCOME AND FOLLOW-UP

On day 4 she reported further episodes of diarrhoea and vomiting and stool cultures were repeated. On this day, the result of

her nephritic screen returned a strongly positive anti-GBM antibody titre at 932 U/L (<7). The rest of her nephritic screen was negative. The diagnosis of Goodpasture disease was concluded. Her case was discussed with the regional renal unit for consideration of further management but after discussing with the patient she opted to go the palliative route and to withdraw from dialysis and further treatment because of her age.

On day 6 she developed unwitnessed haematemesis and was given intravenous esomeprazole 40 mg twice daily. She was unwell with a normal blood pressure but a heart rate of 104/min and an oxygen saturation of 68% on room air. She now required 4 L of oxygen to maintain a saturation of >94%. She had scattered crepitations on chest auscultation. At this stage the palliative care team were involved for comfort measures and she was subsequently transferred to the hospice. She passed away 8 days after initial presentation.

DISCUSSION

In 1918, during the influenza pandemic, a young doctor named Ernest Goodpasture was the first to describe a clinical entity involving pulmonary haemorrhage and renal failure. Much later in the 1960s Lerner, Glasscock and Dixon discovered the antibodies involved in this pathology.⁴ These autoantibodies attack the so-called Goodpasture's epitope, a region in the α -3 chain of type IV collagen in the glomerular and alveolar basement membranes. This is the mechanism underlying the pulmonary and renal disease that is Goodpasture syndrome.

Though typically described as a pulmonary-renal syndrome, the disease could present with either pathologies in isolation.⁵

With an incidence of 1 in 2 000 000 per year, anti-GBM disease is rare.² It is a cause of up to 5% of all glomerulonephritis. It affects people in all racial groups but is more prevalent in people of European Caucasian descent.^{1 2}

The diagnosis of anti-GBM disease is based on the presence of anti-GBM antibodies in serum using ELISA or in the kidneys with immunofluorescent staining. Anti-GBM antibody is pathognomonic to this syndrome though false-positive results could occur in up to 1% of people. This could indicate that the assay has picked up antibodies against other chains of type IV collagen.¹ A high titre of serum anti-GBM antibodies predicts a poor renal outcome. Other factors that suggest an unfavourable renal disease progression include a high percentage of glomerular crescents, absence of normal glomeruli, high serum creatinine (>600 μ mol/L) and oligoanuria at presentation. Oligoanuria is the strongest prognostic factor for renal disease and patient survival.^{6 7} As reported by Alchi *et al*,⁷ in predicting renal outcome, kidney biopsy is not obligatory in oligoanuric patients. In their 2015 study they found that in patients who had renal biopsies, the presence of a high percentage of crescents (>75%) added no additional prognostic information when compared with the presence of oligoanuria. Our patient had a serum creatinine of >900 μ mol/L, was anuric and had a significantly high anti-GBM titre (932 U/L). In diagnostic uncertainty and where the likelihood of Goodpasture is high despite negative serum anti-GBM, renal biopsy is strongly recommended as there are reports of anti-GBM disease in which conventional methods of analysis (ELISA and western blot) failed to detect anti-GBM antibodies in serum.⁸

Initial treatment is general and involves blood pressure control, fluid status monitoring, electrolyte and acid-base correction and dialysis where necessary. This would be the primary approach pending diagnosis. Our patient was afforded these treatments on presentation. Treatment options available for Goodpasture syndrome include pulsed corticosteroids, plasmapheresis, immunosuppressants and renal transplant. The current

recommendation is early plasmapheresis combined with immunosuppressants. Pulmonary haemorrhage and 80% of patients with creatinine <600 μ mol/L respond to this. Unfortunately, response is unfavourable in those who present with serum creatinine levels of >600 μ mol/L or who require haemodialysis at the onset. In the poor prognostic groups especially in those without pulmonary haemorrhage, the risks of treatment far outweigh the benefits.^{1 2} Patients with mild disease, that is, mild renal failure and no pulmonary haemorrhage, may be treated with steroids alone. Renal transplant is an option in those with irreversible renal failure.¹ Unfortunately, prognosis is poor if anti-GBM disease is left untreated.

As in our case, patients should be a part of the decision-making process and palliative care options should be considered when the risks of treatment outweigh the benefits. The importance of palliative care is increasingly recognised in medical practice. It is not only about end-of-life comfort measures, but it is also a support system for the patient as well as their loved ones, leading to a dignified end of life.^{9 10}

In 2011, Se Jin Pak and colleagues wrote an article in which they proposed why presentation of anti-GBM nephritis and Goodpasture syndrome is milder in the elderly population compared with younger patients. In their article they appreciated that Toll-like receptors have a role in innate immunity and contribute to nephritis in anti-GBM disease. In summary, Toll-like receptors are proteins present on leucocytes. Their activation sees to the production of cytokines which are valuable in the pathogenesis of Goodpasture syndrome. They explained the role of proinflammatory cytokines like tumour necrosis factor- α , interleukin-1 (IL-1) and IL-6 in kidney and lung injury caused by anti-GBM antibodies. They proposed that the mechanism underlying milder disease in elderly patients is the reduction in Toll-like receptor function with age and as a result, a decrease in these proinflammatory cytokines in the elderly.¹¹

Our patient presented with dehydration, diarrhoea and gastrointestinal haemorrhage, signs suggestive of an atypical pneumonia, a chest X-ray that proposed an inflammatory pulmonary process, anaemia and an acute kidney injury. She had no strong evidence of haemoptysis. Whether her 'haematemesis' was actually haemoptysis is highly debatable. Though dehydration remains a very common cause of acute renal impairment in the elderly, we considered Goodpasture disease regardless of her age. Dehydration in our patient was likely secondary to her diarrhoea.

Learning points

- ▶ Anti-glomerular basement membrane (GBM) antibody is pathognomonic for Goodpasture syndrome and a high anti-GBM antibody titre detected by ELISA should be adequate for diagnosis of Goodpasture syndrome.
- ▶ In patients with anti-GBM nephritis who are oligoanuric, renal biopsy is not needed to ascertain prognosis as oligoanuria is a better marker of an unfavourable outcome than histopathology.
- ▶ Though dehydration is a well-recognised cause of acute kidney injury in the elderly, rapidly progressive glomerulonephritis should always be considered in all patients presenting with acute kidney injury regardless of age.
- ▶ Palliative care option should be included in the management plan if risks outweigh benefits of treatment

and vomiting, but undoubtedly uraemia contributed by causing nausea and lethargy and consequently, poor oral intake of fluids.

To the best of our knowledge, at 90 years of age, our patient is the oldest reported case of anti-GBM disease. Prior to our patient the oldest reported in the literature was an 81-year-old man.³ Following discussions with our patient and the regional centre for renal diseases, benefits of treatment were outweighed by the risks. In view of her age, she opted out of dialysis and further treatment.

Contributors JOO was involved in case presentation, background, differential diagnosis, treatment and discussion. CAE contributed to investigations, outcome, learning points and discussion. AZK was the admitting consultant, and contributed to background and discussion.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Agnieszka Swiatecka-Urban, Prasad Devarajan. Anti-GBM Antibody Disease. Pittsburgh: Medscape J M, Undated (updated 28 May 2014). <http://emedicine.medscape.com/article/981258-overview#a6>
- 2 Kluth DC, Rees AJ. Anti-glomerular basement membrane disease. *J Am Soc Nephrol* 1999;10:2446–53. <http://jasn.asnjournals.org/content/10/11/2446.full>
- 3 Volpi A, Battini G, Conte F, et al. Acute renal failure in elderly due to Goodpasture's syndrome. *Nephron* 1991;57:381–2.
- 4 Kathuria P, Sharma S, Stevenson FT, et al. Goodpasture Syndrome. Manitoba: Medscape J M, Undated (updated 25 August 2016). <http://emedicine.medscape.com/article/240556-overview#a3>
- 5 Turner AN, Rees AJ. Antiglomerular basement membrane disease. In: Davison AM, Cameron JS, Grunfeld JP, Kerr DNS, Ritz E, Winearls CG, eds. *Oxford textbook of nephrology*. 2nd edn. Oxford University Press, 1998:645–66.
- 6 Herody M, Bobrie G, Gouarin C, et al. Anti-GBM disease: predictive value of clinical, histological and serological data. *Clin Nephrol Sinico* 1993;40:249–55 <http://www.ncbi.nlm.nih.gov/pubmed/8281713>
- 7 Alchi B, Griffiths M, Sivalingam M, et al. Predictors of renal and patient outcomes in anti-GBM disease: clinicopathologic analysis of a two-centre cohort. *Nephrol Dial Transplant* 2015;30:814–21.
- 8 Salama AD, Dougan T, Levy JB, et al. Goodpasture's disease in the absence of circulating anti-glomerular basement membrane antibodies as detected by standard techniques. *Am J Kidney Dis* 2002;39:1162–7.
- 9 Brown EA, Chambers EJ, Eggeling C. Palliative care in nephrology. *Nephrol Dial Transplant* 2008;23:789–91.
- 10 Holley JL. Palliative care in end-stage renal disease: focus on advance care planning, hospice referral, and bereavement. *Semin Dial* 2005;18:154–6.
- 11 Park SJ, Kim JH, Shin JI. The influence of age on the clinical features and outcomes of anti-glomerular basement membrane disease. *Am J Kidney Dis* 2011;58:678; author reply 678.

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow