CASE REPORT

A unique way to treat Goodpasture's disease

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SUMMARY

A 21-year-old man with no medical history presented to the emergency department with fatigue, oliguria and lower extremity oedema. Initial laboratory tests showed that the patient was in acute renal failure with a creatinine of 12.8 mg/dL (normal 0.51–1.18 mg/dL). Further work up showed crescentic glomerulonephritis on renal biopsy, and serology was positive for antiglomerular basement antibody (titre 191 U/mL, normal 0–0.7 U/mL). Shortly after diagnosis he developed haemoptysis and chest imaging was consistent with pulmonary haemorrhage. The standard immunotherapy for Goodpasture's disease is cyclophosphamide, but due to known reproductive toxicities associated with cyclophosphamide and the patient's age, it was decided to use alternate but less studied therapies for treatment. At discharge, the patient had undergone five plasmapheresis treatments, had received two doses of Rituximab with a steroid taper, and his antiglomerular basement membrane level had decreased significantly.

BACKGROUND

Goodpasture's disease (GD) is rare, but knowledge about the disease and early diagnosis is key because the antiglomerular basement membrane (GBM) antibody can cause end stage renal failure if untreated. The gold standard for treating GD is plasmapheresis, corticosteroids and cyclophosphamide. Unfortunately, cyclophosphamide can cause several toxicities, so trialing less toxic agents is essential. Our case demonstrates the use of Rituximab along with plasmapheresis and steroids to treat GD with good outcomes for the patient.

CASE PRESENTATION

A healthy 21-year-old man presented to the emergency room with symptoms of fatigue, oliguria and lower extremity oedema. He was found to be in acute renal failure, with blood urea nitrogen 115, creatinine 12.8 mg/dL and potassium 6.8. Urinalysis showed large blood and >300 mg/dL of protein. Renal ultrasound showed diffusely echogenic kidneys. The patient began dialysis immediately. He had no family history of renal disease and he did not smoke, drink alcohol or use illicit drugs. A week after presentation, he developed mild haemoptysis. Further work up showed his serologies were negative for antinuclear antibody, antinuclear cytoplasmic antibody (ANCA), C3 and HIV, but positive for anti-GBM with a titre of 191 U/mL. A renal biopsy was performed, which showed 100% cellular crescentic glomerulonephritis (figure 1) and positive linear GBM staining for IgG (figure 2). A Chest CT showed ground glass opacity in the right upper lobe consistent with pulmonary haemorrhage (figure 3).

Figure 1 Crescentic glomerulonephritis.

The patient was diagnosed with GD and was treated aggressively with immunosuppressive therapy.

TREATMENT

Given 100% glomerular involvement, renal recovery was not expected, but the goal was to prevent further pulmonary involvement. The patient received five cycles of plasmapheresis alternating days with haemodialysis for his end-stage renal disease. He also received high-dose methylprednisone three times (1 g intravenous every day), which was then switched to 80 mg oral Prednisone. The patient received his first dose of Rituximab on the day he started oral Prednisone, at which point he had already had three plasmapheresis treatments. He subsequently underwent two more

Figure 2 Renal Goodpasture's disease using immunofluorescence.

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Figure 3 Pulmonary Haemorrhage.

plasmapheresis treatments, and received a total of two Rituximab treatments 2 weeks apart. His Prednisone was tapered down on subsequent follow-up visits.

OUTCOME AND FOLLOW-UP

The patient's anti-GBM level was 22.4 U/mL at time of discharge and 15.6 U/mL at the time of his second Rituximab dose. The patient was seen in the rheumatology clinic 4 months after discharge and found to be doing well. He continued to be dialysis dependent but denied any recurrent haemoptysis. His anti-GBM level had decreased to 3 U/mL. Thus, his prednisone dosage was tapered down to 5 mg per day with a plan to follow-up in 4 weeks. The patient is compliant with his peritoneal dialysis regimen and is currently being reviewed for kidney transplant candidacy.

DISCUSSION

GD is a life-threatening autoimmune condition associated with the formation of autoantibodies directed against the α -3 chain of the GBM type IV collagen causing glomerulonephritis in the kidney and alveolar haemorrhage in the lungs.^{1 2} GD is extremely rare, with an estimated incidence of less than 0.5—1 per million cases per year. Typically appearing in a bimodal age distribution, the first peak is at a young age (<30 years) and the second is in the sixth to eight decades of life.³ Without treatment the prognosis is poor, ultimately ending in death from pulmonary haemorrhage or renal failure.⁴ The largest report of outcomes in patients with GD showed that prognosis was worse if initial creatinine was above 5.7 mg/dL (503.8 μ mol/L) or if dialysis was required at presentation. In that study, patients who required dialysis at presentation and had 100% crescents on renal biopsy did not recover renal function.⁵

The current treatment for anti-GBM disease is plasmapheresis combined with immunosuppressants. Plasmapheresis removes anti-GBM antibodies and other inflammatory mediators, while immunosuppressive agents reduce antibody formation. The gold standard for GD treatment is plasmapheresis, corticosteroids and cyclophosphamide, an alkylating agent with potent immunosuppressive activity.⁶ Possible side effects of cyclophosphamide include haemorrhagic cystitis, gonadal suppression and sterility.⁷ Owing to the side effects of cyclophosphamide, using a less toxic immunosuppressant to treat the autoimmune diseases is ideal.

In GD the B lymphocyte plays a pivotal role in the destruction of the GBM by autoantibody production and production of inflammatory cytokines. Therefore, B cell depletion has been an attractive therapeutic target in the treatment of glomerulonephritis. Rituximab (Rituxan, IDEC Pharmaceuticals, California, USA) is a chimeric monoclonal antibody that binds CD20 to induce B cell apoptosis and depletion by activation of downstream tyrosine kinases.⁸ The multicentre Rituximab in ANCA-Associated Vasculitis (RAVE) trial compared Rituximab with standard cytotoxic therapy for inducing remission in patients with severe ANCA vasculitis and found that Rituximab therapy was not inferior to standard cyclophosphamide treatment for the induction of remission in ANCA-associated vasculitis.⁹ For GD a review of the literature demonstrated a handful of cases in which Rituximab has been used for treatment. In 2002, Arzoo *et al* reported using Rituximab to treat a patient with relapsing GD who had initially undergone conventional treatment with cyclophosphamide. The patient received six weekly doses of Rituximab with marked symptom improvement and undetectable anti-GBM antibodies. He was reported to be in remission 10 months after treatment.¹⁰ Wechsler *et al*¹¹ reported a case of using Rituximab to treat anti-GBM disease in an immunocompromised HIV+ patient who recovered renal function with the disappearance of anti-GBM antibodies after treatment with steroids, mycophenolate mofetil and Rituximab. Shah *et al* reported three cases in which Rituximab was used to treat anti-GBM disease.¹² In this case report series two of three patients had a favourable renal outcome, and all three patients were shown to have undetectable levels of anti-GBM after treatment. In one case, the patient initially presented with severe renal failure and required dialysis on presentation, and was initially treated with one dose of cyclophosphamide and then switched to Rituximab due to concerns of marrow suppression. Although his anti-GBM levels disappeared, he remained dialysis dependent, similar to our patient.¹² Another recent study reported a patient with anti-GBM disease who developed thrombocytopenic purpura (TTP) on the standard triple therapy regimen. When cyclophosphamide was switched to Rituximab, her clinical condition improved with undetectable anti-GBM antibody levels, although she did not recover renal function. She too required dialysis at the outset with a creatinine of 11.3 mg/dL (998.9 μ mol/L).¹³ Thus, a timely diagnosis is imperative in the prevention of end-stage renal disease. Adoption of triple therapy comprising plasmapheresis, corticosteroids and an immunosuppressive drug can significantly improve the prognosis of GD. This case adds to the limited body of literature suggesting that Rituximab is effective immunotherapy for the treatment of GD, and can be used in lieu of traditional cytotoxic agents to limit toxic side effects.

Learning points

- ▶ Goodpasture's disease is a triad of antiglomerular basement membrane (GBM) circulating antibodies, glomerulonephritis and pulmonary haemorrhage.
- ▶ Successful treatment for Goodpasture's disease rests on early diagnosis as creatinine above 5 mg/dL and requiring dialysis at presentation portends poor prognosis.
- ▶ Random control trials using Rituximab as part of triple therapy for Goodpasture's disease do not exist. We report a case of a young patient who was treated with Rituximab instead of cyclophosphamide with a subsequent drop of anti-GBM antibodies and no recurrent pulmonary symptoms.

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Competing interests None.

Patient consent Obtained.

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