Expecting the Unexpected: A Case Report of Anti-GBM Disease on Top of Diabetic Kidney Disease

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ABSTRACT

Diabetic kidney disease (DKD) is one of the most common causes of chronic kidney disease. Progression of DKD in elderly is a common cause of deterioration of renal function especially with uncontrolled diabetes mellitus. Other causes can be easily missed in elderly and many glomerular diseases can pass without being noticed if proper investigations were not requested on time. Therefore, we should expand our expectation and think out of the box to provide the appropriate management for our patients, as in our case which was found to have anti-GBM disease on top of DKD, while initially was suspected to have a progression of his DKD versus obstructive uropathy given the past history of recurrent renal stones.

Keywords: Chronic kidney disease (CKD), diabetes mellitus (DM), Anti- glomerular basement membrane disease (Anti-GBM disease), diabetic kidney disease (DKD).

BACKGROUND

Anti GBM disease is an autoimmune disease attacking small vessels specifically the α3 chain of collagen type 4 present in the glomerular basement membrane causing glomerulonephritis, and/ or the alveolar basement membrane causing pulmonary hemorrhage (Goodpasture Syndrome) which is a type of pulmonary renal syndromes. The median age of presentation is the 3rd decade of life, but it has been reported in extremes of age like 11 months and 90 years. Presenting symptoms maybe not be typical or can be labeled as a progression of an existing renal disease, as in our case, which could have possibly been misleading if proper investigations were not done[1].

CASE PRESENTATION

An 84-year-old male with past medical history of hypertension, long standing type 2 diabetes mellitus, benign prostatic hyperplasia (BPH), renal stone disease who underwent extracorporeal shock wave lithotripsy (ESWL), CKD secondary to DKD since 2015 with a baseline creatinine around 150 µmol/L. He had a renal ultrasonography done as a part of his workup in OPD clinic follow up which showed a non-obstructing right renal stone. His albumin creatinine ratio was 1.0 mg/mmol, serum albumin 37 g/L and urine routine microscopy did not show hematuria or proteinuria.

He presented to emergency room complaining of diffuse abdominal pain, lower limb edema and reduced urine output. Urgent ultrasound was performed which was significant only for the non-obstructing right renal stone. His serum creatinine increased to 330 µmol/L, urine routine was positive for albumin +3, RBC 2-5 cells/hpf, serum Albumin 27g/L, CBC and electrolytes were within normal range and vasculitis screen was collected. On examination, the patient had normal vital signs with blood pressure 130/85 mmHg and SPO2 96% on room air. His chest examinations showed bilateral fine basal crepitations. His abdomen was soft, lax with mild epigastric tenderness with no guarding or rigidity. Lower limbs showed bilateral grade 1 pitting edema. Other systemic examinations were unremarkable.

Patient was reviewed by urology and surgical for the abdominal pain suggested non-contrast CT scan which was not significant except for the non-obstructing renal stone.

The patient was admitted with the impression of acute kidney injury on top of CKD for further investigations and fluid overload. He was started on Furosemide IV. During his admission his urine output was around 1.7 L/24hr, however his urine output decreased gradually and started to complain of shortness of breath. His chest X-ray showed pulmonary edema with possible chest infection. So, hemodialysis was initiated along with antibiotics.

His labs showed further increase in creatinine and repeated urine showed +4 protein, RBCs more than 100 cells/hpf, and albumin creatinine ratio 97.1 mg/mmol creatinine.

After 3 sessions of hemodialysis the patient's dyspnea and CXR showed no improvement for that HRCT was performed and initially reported as fluid overload with chest infection.

After few days' vasculitis screen came out for low C3 26.4 mg/dL and strong positive of anti-GBM antibody by IF with titer of 1:64. So the patient was immediately started on plasmapheresis.

Septic work up including respiratory profile turned to be negative, however there was no improvement in his dyspnea and CXR and he became oliguric. The pulmonology team were involved and advised for bronchoscopy with bronchial wash but the patient refused the procedure.

His hemoglobin dropped to 8.5 g/dL from 12.7 g/dL so the chest images were reviewed again by the radiologist and noted the high suspicion of pulmonary hemorrhage. So, pulse steroid and IV cyclophosphamide were initiated after consenting the patient.

After 10 sessions of plasmapheresis, his urine output improved and creatinine dropped to 163 µmol/L hence hemodialysis was stopped.

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Intervention	Dosing	Duration of treatment
Plasma exchange	• 40–50 ml/kg ideal body weight exchange daily against 5% albumin • Add fresh frozen plasma at the end of plasma exchange in patients with alveolar hemorrhage and/or after kidney biopsy	Until circulating anti-GBM antibodies can no longer be detected; usually 14 days
Cyclophosphamide	• 2–3 mg/kg orally (reduce to 2 mg/kg in patients >55 years); experience with pulse intravenous cyclophosphamide is limited and efficacy is uncertain • Cyclophosphamide dosing should be reduced (or treatment interrupted) in cases of leukopenia • In patients not tolerating (or not responding to) cyclophosphamide, rituximab or mycophenolate mofetil may be tried but experience is limited and efficacy uncertain	3 months
Glucocorticoids	• Pulse methylprednisolone may be given initially up to 1000 mg/d on 3 consecutive days • Prednisone 1 mg/kg orally • Reduce to 20 mg/d by 6 weeks	6 months

Figure 99 | Treatment of anti-GBM disease. Adapted from *Journal of the American Society of Nephrology*, volume 10, issue 11, Kluth DC, Rees AJ. Anti-glomerular basement membrane disease, pages 2446–2453, Copyright © 1999, with permission from the American Society of Nephrology.[946] Adapted from *Clinical Journal of the American Society of Nephrology*, volume 12, issue 7, McAdoo SP, Pusey CD. Anti-glomerular basement membrane disease, pages 1162–1172, Copyright © 2017, with permission from the American Society of Nephrology.[931] Adapted from Kaplan AA, Appel GB, Pusey CE, et al. Anti-GBM (Goodpasture) disease: treatment and prognosis. UpToDate: Evidence-based Clinical Decision Support. Available at: www.uptodate.com. Accessed September 7, 2021.[945]

The patient received total of 12 plasmapheresis sessions after which his anti-GBM antibody titer became negative and his creatinine returned to his baseline and his urine output was around 2 liters/day.

Patient planned to continue cyclophosphamide every 2 weeks for total of 3 months and tapering steroids over 6 months.

Unfortunately, since admission we planned for renal biopsy but it was delayed initially due to the patient's condition as he was dyspneic and unable to lay down and later on due to shortage of intervention radiology staff.

DISCUSSION

Diabetic kidney disease DKD as a common complication of diabetes mellitus, and nowadays it is considered the main cause of chronic kidney disease leading to end stage renal disease. It manifests initially as microscopic albuminuria (Albumin creatinine ratio >30mg/g) and progresses gradually or sometimes rapidly with the progression of the chronic kidney disease[2].

In addition, hematuria can present with diabetic kidney disease and is associated with an increased risk of end-stage renal disease even in patients with early diabetic CKD[3].

In our patient who presented with microscopic hematuria and increase in proteinuria can be passed as progression of his diabetic kidney disease. In addition, the reduced in urine output and increase in his creatinine along with microscopic hematuria can raise the possibility of obstructive uropathy secondary to his renal stone disease. However, after ruling out the later we were kept between 2 diagnosis; the progression of his DKD or an rapidly progressive glomerulonephritis (RPGN). Therefore, requesting the vasculitis screen was mandatory and it revealed the diagnosis on anti-GBM disease.

Anti-GBM disease is considered as a rare disease with an incidence of less than 2 cases per million population across all racial groups although more in European Caucasians mainly in the third decade[4].

It is an autoimmune vasculitis affecting the small vessels caused by autoantibodies against Type 4 collagen specifically α3 chain in the glomerular basement membrane which leads to rapidly progressive glomerulonephritis (RPGN) and in alveolar basement membrane causing pulmonary hemorrhage[4].

PROGNOSIS

Although Anti-GBM disease is considered as a rare disease it has a combative course. With the introduction of plasmapheresis and immunosuppression, the mortality improved and renal survival improved to around 60-85% with respect to the degree of severity on presentation.

If on presentation serum creatinine was > 500 µmol/L, required dialysis the survival varies between 8% and 65%. Patients which creatinine was > 500 µmol/L and didn't require renal replacement therapy, the survival rates between 82-83%. On the other hand, presenting with creatinine <500 µmol/L the survival rates found to be of 95-100%.

Other factors reflecting unfavorable prognosis are:

- Oliguria or anuria
- Serum creatinine >530 µmol/L
- Biopsy proven crescents (> 50%) with significant tubular atrophy.
- Presence of HLA-DR W2 and HLA-B7[5].

MANAGEMENT

The main core of managing Anti-GBM disease is to start the management as soon as possible with plasmapheresis to remove antibodies and immunosuppression to prevent the production of these antibodies[6].

CONCLUSION

Anti-GBM disease is a rare disease with a median age of the 3rd decade but reported that it affects all ages with unusual presentation, it should be screened specially in elderly patients as other comorbidities may mislead and delay the diagnosis and treatment and is lifesaving in most of the cases.

In acute kidney injury and picture of rapidly progressive glomerulonephritis, regardless of age and other comorbidities, one should consider the wide range of differential diagnosis and think out of the box in order to start the proper management in a timely manner.

In oliguric or anuric patients with high positive titer of anti-GBM antibody, renal biopsy is not always needed to determine diagnosis or the prognosis of Goodpasture's Syndrome as oligo-anuria is a countable marker of critical outcome when histopathology is not available[8].

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