International Journal of Research in Medical Sciences
Doshi RP et al. Int J Res Med Sci. 2016 Jan;4(1):322-325
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20160051

Case Report

Pulmonary renal syndrome: treatment of acute renal failure secondary to double positive goodpasture syndrome

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Received: 10 November 2015
Accepted: 15 December 2015

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ABSTRACT

This is a case of a 34 year old female who presented with lower epigastric pain, flank pain and hematuria. Her symptoms started two days after being treated on Trimethoprim+Sulfamethoxazole for urinary tract infection. Worsening of her symptoms despite switching to Cephalexin prompted her to come to the emergency department. On admission, her creatinine was 5.3 mg/dL with potassium of 5.2 mEq/L and albuminuria of 100 mg/dL. Chest computed tomography (CT) without contrast revealed findings consistent with goodpasture disease. Biopsy of the kidney confirmed diffuse necrotizing and crescentic glomerulonephritis consistent with anti-glomerular basement membrane antibody disease. She was treated with plasmapheresis and steroids with complete resolution of symptoms at follow up.

Keywords: Acute renal failure, Goodpasture syndrome, Plasmapheresis

INTRODUCTION

Goodpasture disease is a rare autoimmune disease associated with rapidly progressing glomerulonephritis and sometimes pulmonary hemorrhage with a presence of anti-glomerular basement membrane (anti-GBM) antibodies. It has a complex pathogenesis which is not clear. It can be triggered by various substances like virus, bacteria, cigarette which damage the intact membrane of lung or kidney. The immune system's faulty response to their own body leads to damage of the membrane and might lead to bleeding from kidney or lung. Most patients present with symptoms related to kidney but can be present with pulmonary symptoms also. Diagnosis can be done with the help of anti-GBM antibody and kidney biopsy. Treatment is mostly based on removing the antibodies from plasmapheresis and pulsed steroids to suppress the immunity. Prognosis is depending on anti-GBM antibodies and initial kidney damage before starting the treatment.

CASE REPORT

A 34 year old woman presented to the ED with intermittent non radiating upper abdominal pain and flank pain associated with nausea, unrelated to intake of food and blood in urine. Her symptoms were not associated with vomiting, dysuria, shortness of breath or chest pain. Her hematuria started two weeks prior to admission which prompted her to seek outpatient consult. She was diagnosed with a Urinary Tract Infection and was started on Trimethoprim+ Sulfamethoxazole. Subsequently, she developed episodes of heartburn, nausea and epigastric pain. Upon consult, she was switched to cephalexin. Worsening of her symptoms prompted admission. Her vital signs revealed a BP of 122/66, pulse of 86 RR of 18/min with a temperature of 98.2F.Physical exam was

unremarkable. Her past medical history is significant for Gastro esophageal reflux, hemoptysis (1 week), hypertension and Migraine. Her surgical history includes removal of the left ovary. She is a former smoker. Patient experienced intermittent episodes of hemoptysis subsequently after admission.

Investigations

Routine complete blood count revealed an elevated count of WBC at 13,100 cells/mm3, red blood cells of 3280 cells/mm3, anemia with hemoglobin of 9.9 g% and a hematocrit of 28.9%. Her blood chemistry panel was significant for blood urea nitrogen value of 58 mg/dL (elevated), serum creatinine of 7.34 mg/dL (elevated), hyperkalemia with serum potassium of 5.2mEq/L (elevated), serum albumin of 3.4 g/dL, blood chloride levels of 105mEq/L, CO2 of 20 mEq/L with an anion gap of 15 indicating metabolic acidosis.Haptoglobin level was 344 mg/dL which suggested extra vascular hemolysis. Albumin/globulin ratio was 1.0. Liver enzymes were within normal limits. Her serum anti-nuclear antibody (ANA) and anti-nuclear cytoplasmic antibody (ANCA) were positive. Her anti-glomerular basement membrane antibody (anti-GBM) level was >8 U.

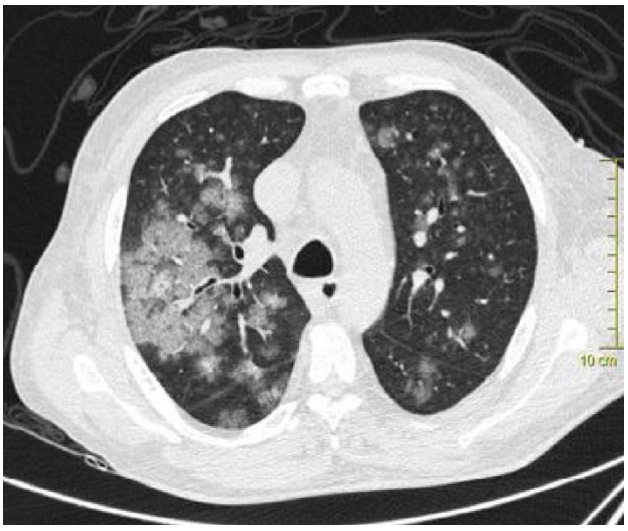

Figure 1: Axial HRCT scan shows areas of ground glass opacity with interlobular septal thickening in bilateral upper lobes.

Urine analysis revealed pink hazy urine with protein of 250 mg/dL (proteinuria), presence of 4+ blood (hematuria) and dysmorphic red blood cells in urine. Rest of the components were within normal limits. With a presumed diagnosis of pulmonary renal syndrome, computed tomography (CT) guided biopsy of her kidney with immunofluorescence revealed diffuse necrotizing and crescentic glomerulonephritis consistent with anti-glomerular basement membrane antibody disease/ goodpasture disease. Out of 13 glomeruli examined, 10 showed global sclerosis. All of the globally sclerotic glomeruli showed prominent disruption of bowmen's capsule associated with residual cellular crescent formation. Of the remaining glomeruli, all but two showed predominantly circumferential cellular crescent associated with prominent disruption of the glomerular basement membrane and fibrin deposit. Immunofluorescence studies revealed IgG (3+), kappa (3+), lambda (3+) light chains in a linear pattern along the glomerular capillary loops. One glomerulus showed strong segmental staining by fibrinogen (3+). Chest computed tomography without contrast revealed primary central pleuroparenchymal pattern with some tree in bud appearance suggesting an infectious process with a predominance in the left (Figure 1, 2). Pretreatment chest X ray (Figure 3) showed diffuse infiltrate in mid and lower lung fields which was resolved later after the treatment (Figure 4).

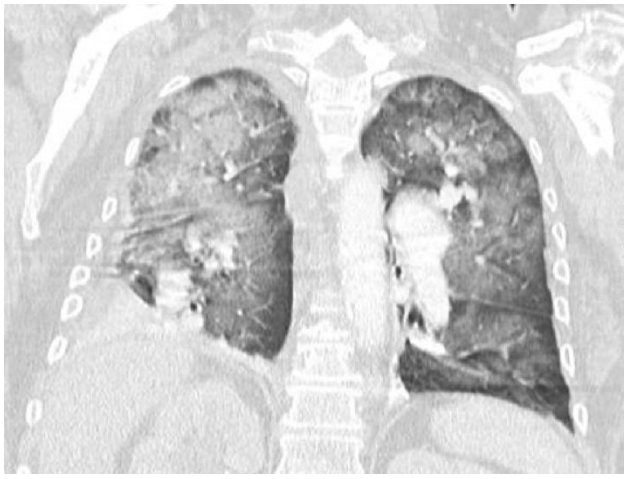

Figure 2: HRCT chest coronal reformatted image shows ground glass opacity with interlobular septal thickening in bilateral lung fields predominantly on right side.

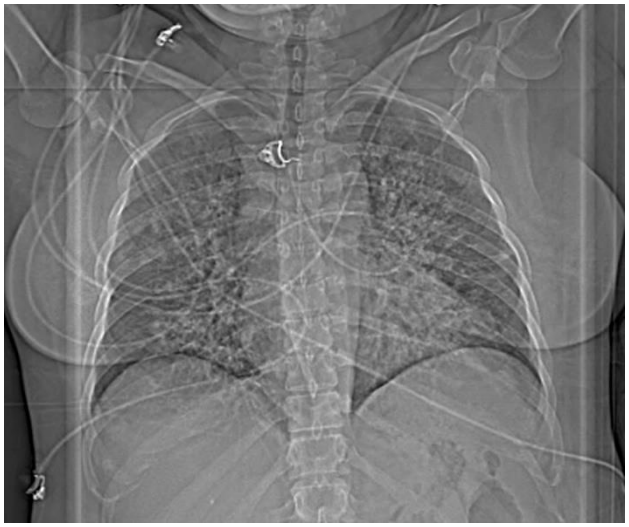

Figure 3: Pretreatment chest X ray showed diffuse infiltrate in mid and lower lung fields with some blunting of the left costophrenic angle.

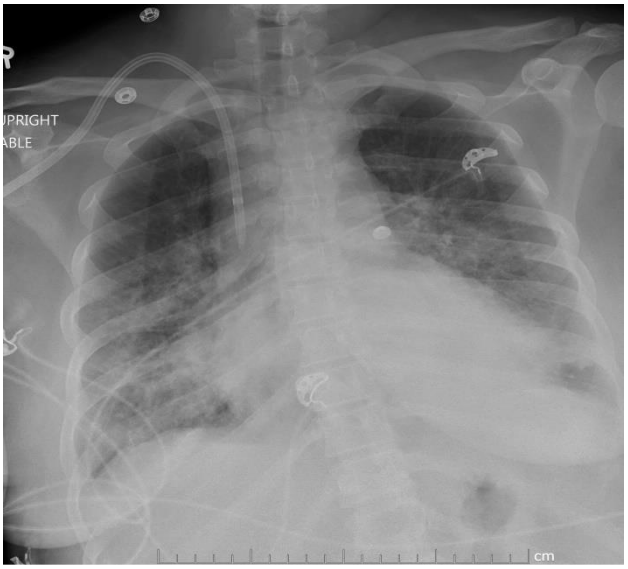

Figure 4: Post treatment chest X ray showed resolution after the treatment.

Treatment

On admission, patient was started on dialysis for acute renal failure. She was placed on plasmapheresis for 4L exchange, pulsed methyl prednisone (1 mg/kg) for 5 days and immunosuppression (cyclophosphamide-2 mg/kg/day).

Outcome and follow-up

Patient came first time in 2013 and then she was followed up every 3-4 weeks. Initially, she was on plasmapheresis for 4 L exchange for 4 weeks (initially consecutive and later alternate days) for possible removal of all circulating antibodies. Later on discharge, she was given oral prednisone and cyclophosphamide for 8 months which successfully induced remission. After 8 months of therapy, she had near normal proteinuria and no blood in urine with 2.8 mg/dL serum creatinine. There was substantial improvement in the overall clinical status of the patient during her four weeks of stay in the hospital. Patient was maintained on amlodipine, carvedilol, cyclophosphamide, hydralazine, ondansetron, prednisone, trimethoprim-sulfamethoxazole, oxycodone, and acetaminophen. Patient experienced no complications after discharge with resolved clinical symptoms at follow up after 8 months.

DISCUSSION

Acute worsening of flank pain and glomerular hematuria points towards glomerulonephritis. Pulmonary renal syndrome is a life threatening condition that involves worsening of renal function and pulmonary function simultaneously. Goodpasture disease can be differentiated from microscopic polyangitis and Wegener's granulomatosis from anti-GBM and ANCA, which are positive in a former disease.[1] The gold standard for the diagnosis of pulmonary renal syndrome is kidney biopsy. Kidney biopsy is often performed to identify histology and immunofluorescence studies. Goodpasture disease most commonly presents with progressive glomerulonephritis and hemoptysis while rest presents with renal symptoms only, which is also known as anti-GBM disease.[2] In our patient, goodpasture disease was confirmed by the presence of anti-GBM antibody with linear deposit of IgG with kidney biopsy.

Cigarette smoking is associated with development and progression of the goodpasture disease.[3,4] Goodpasture disease is thought be associated with pneumocystis carini pneumonia which initially thought to be associated with influenza infection.[5,6] That is the reason our patient was on prophylaxis for this on Trimethoprim sulphamethoxazole after discharge. Increasing evidence showed that genetic factors are associated with goodpasture disease. Human leukocyte antigen DRB1-1501 and goodpasture are associated with each other and are present in 1/3rd of the white population but lakes data for other ethnicity.[7] Damage to lung from cigarette smoking, infections, urinary tract infection might trigger an autoimmune response to the alpha-3 chain of type IV collagen and might lead to goodpasture disease.[8]

Our patient had presented with acute renal injury with anti-GBM antibodies and ANCA antibodies present. Goodpasture disease can rapidly progress to end stage renal disease and can lead to death if therapy is not guided properly according to disease severity.Anti-GBM antibodies and serum creatinine are important prognostic factors to guide the therapy. Anti-GBM is directly proportional to renal outcome.[9,10] That means, if one is going up/down so will be the other.ANCA positivity also considered as an important prognostic factor in recurrent renal disease as in our case. Dual antibody (anti-GBM and ANCA) have worse outcome as compared to ANCA only.[11]

These days, patient is treated with cycles of plasmapheresis and pulsed steroids therapy. American Society of Apheresis published guidelines on the use of plasmapheresis. It has shown that every patient without the need of dialysis should undergo plasmapheresis for 14 days or it becomes undetectable in serum.[12,13] Few patients might require immunosuppressive therapy (cyclophosphamide as in our case) depending on the severity of the disease.[14] Those who did not responded well to these therapies or had shown adverse reactions might need to put on rituximab or mycophenolate mofetil.[15,16]

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Doshi RP, Patel V, Patel K, Patel M. Pulmonary renal syndrome: treatment of acute renal failure secondary to double positive goodpasture syndrome. Int J Res Med Sci 2016;4:322-5.