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An 80-year-old female with double positive disease: Case report and brief review of literature

Tarek Almouradi[1], Peter Hart[2], Talia Muram-Zborovski[3]

[1] Department of Medicine, John H Stroger Hospital of Cook County, Chicago, IL, U.S.A.
[2] Department of Nephrology, John H Stroger Hospital of Cook County, Chicago, IL, U.S.A.
[3] Department of Pathology, John H Stroger Hospital of Cook County, Chicago, IL, U.S.A.

Summary

Background: Goodpasture's syndrome is a triad of alveolar hemorrhage, Glomerulonephritis and circulating anti Glomerular basement membrane antibodies, 25% of cases test positive for ANCA antibodies, this association is known as Double positive disease. This article describes a rare presentation of this entity and reviews available literature.

Case Report: 80 year old female presented with hemoptysis and renal failure, she tested positive for both p ANCA and anti glomerular basement membrane antibodies, and despite aggressive medical treatment, she suffered a frustrating outcome.

Conclusions: Double positive disease accounts for 25% of cases of Goodpasture's syndrome, a suggested Pathophysiology of this association is the renal involvement in ANCA Vasculitis leading to the exposure of antigens from the basement membrane and the formation of antibodies.

This entity is believed to carry better prognosis when compared to isolated anti glomerular basement membrane disease.

key words: goodpasture syndrome • p-ANCA • pulmonary renal syndrome • double positive disease

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Author's address: Tarek Almouradi, Department of Medicine, John H Stroger Hospital of Cook County, Chicago, IL, U.S.A., e-mail: tarekmuradi@hotmail.com

Background

Goodpasture's syndrome is a triad of alveolar hemorrhage, Glomerulonephritis and circulating anti Glomerular basement membrane antibodies, 25% of cases test positive for ANCA antibodies, this association is known as Double positive disease.

Case Report

An 80 year-old Hispanic female with history of hypertension, presented to our institution with one month of fatigue, weight loss, and two weeks of hemoptysis with blood streaks and clots, patient denied pain, fever or chills, she denied recent travels, chronic cough, night sweats, sick contacts.

Her Social history was remarkable for 30 pack year of smoking.

Upon presentation to emergency department, her vital signs were: Heart rate of 96, Blood pressure of 175/77, respiratory rate of 22, and Oxygen saturation of 88% on room air, improved to 96% on non rebreather mask.

Her initial exam was remarkable for Cachexia, multiple ecchymoses over upper and lower extremities.

Heart exam revealed for 2/6 systolic murmur best heard over the apex, she had bibasilar crackles on lung examination, her abdominal exam was unremarkable, she did not have any lower extremities edema, no palpable lymph nodes, and her neurologic exam revealed asterixis.

Initial blood work is shown in Tables 1–3, initial urinalysis results are shown in Table 4.

Her initial chest x radiograph is showed moderate cardiomegally and bilateral pulmonary edema (Figure 1).

Overnight, patient was admitted to the intensive care unit, started on hemodialysis using a femoral Quinton catheter, she was also started on antibiotics for possible urinary tract infection.

The following morning, patient continued to have hemoptysis, continued to require non rebreather mask, serologic markers for autoimmune diseases were sent.

On the third day of hospitalization, patient had bilateral kidney ultrasound, showed normal sized kidneys with increased echogenicity suggestive of chronic renal insufficiency.

On day four, preliminary autoimmune panel results came back, with positive ANCA antibodies, so patient was started on Intra venous Methylprednisolone 500 mg/day along with plasmapheresis.

Autoimmune panel results shown in Table 5.

The same evening, due to respiratory distress, patient was intubated and mechanical ventilation was started, over the following few days, her clinical course deteriorated, she expired one week after.

Table 1. Basic metabolic panel.

Sodium	121
Potassium	7.5
Chloride	91
Bicarbonate	10
Blood urea nitrogen	112
Creatinin	14.2
Calcium	8
'Phosphorus	7.5
Magnesium	2.8

Table 2. Complete blood count.

WBC	9.8
Hemoglobin	7.3
MCV	73
Platelets count	287

Table 3. Coagulation panel.

PT	14.6
PTT	40
INR	1.1

Table 4. Urinalysis.

Color	Red
Specific gravity	1.013
RBC	2170
WBC	882
Glucose	70
Protein	200

Anti-glomerular basement membrane came back positive with titer above 100 (normal 0–3).

Patient's family agreed with autopsy, which showed diffuse alveolar hemorrhages, severe glomerulosclerosis associated with acute glomerulonephritis (Figures 2–4).

Discussion

We report a case of an 80 year-old female with pulmonary-renal syndrome that tested positive for both anti Glomerular basement membrane and anti-neutrophil cytoplasmic antibodies, a syndrome known as "double positive disease".

In 1989, O'Donoghue et al. reported three patients with ANCA-positive serum and anti-GBM disease, all of them

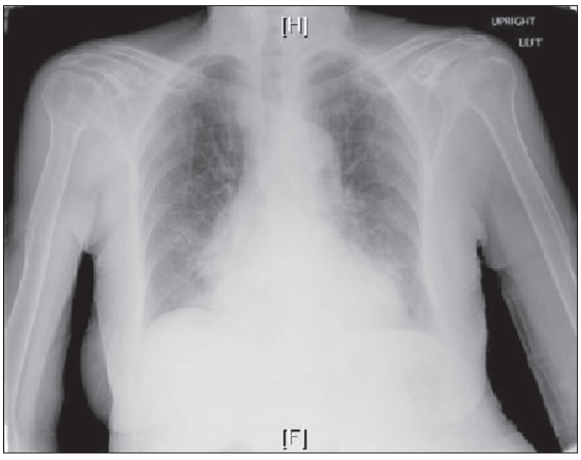

Figure 1. Chest x-ray.

Table 5. Autoimmune panel.

Marker	Result
Anti nuclear antibodies ANA titer	Positive 1:160
Double stranded DNA	Negative
Anti Smith antibodies C3 level C4 level	Negative 96 19
C ANCA	Negative
P ANCA	Positive
P ANCA Titer MPO titer	1:160 56

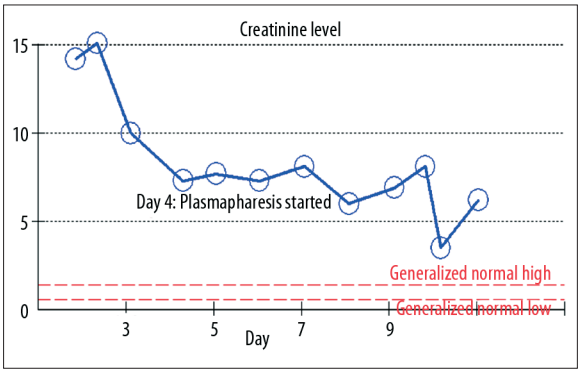

Figure 2. Creatinin level during hospital stay.

had severe renal involvement and alveolar hemorrhage, in one case c-ANCA were initially absent but subsequently developed concurrently with the clinical appearance of systemic Vasculitis as the anti-GBM antibody titer was falling, the report suggested that c-ANCA can complicate anti-GBM disease [3].

In 1990, Jayne DR et al studied the incidence of anti glomerular basement membrane and/or anti-neutrophil cytoplasmic antibodies in patient with suspected rapidly progressive glomerulonephritis; found that 2% of those patients had both antibodies [1].

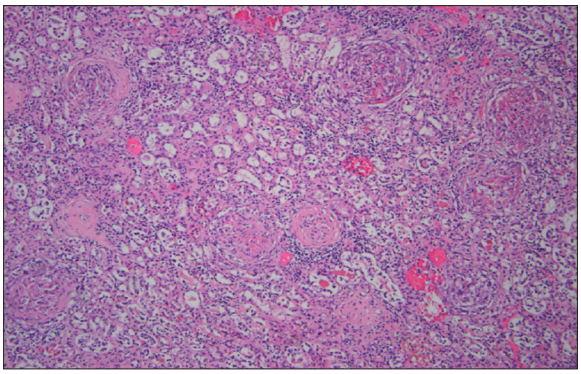

Figure 3. Representative photomicrograph of the kidney cortex exhibiting glomeruli with parietal cell proliferation and glomerular tuft compression (crescentic glomerulonephritis), sclerotic crescent formation impinging on glomerular tufts, and completely sclerotic glomeruli. Within the interstitum, there is mild fibrosis and a chronic inflammatory infiltrate. (100×, H&E stain).

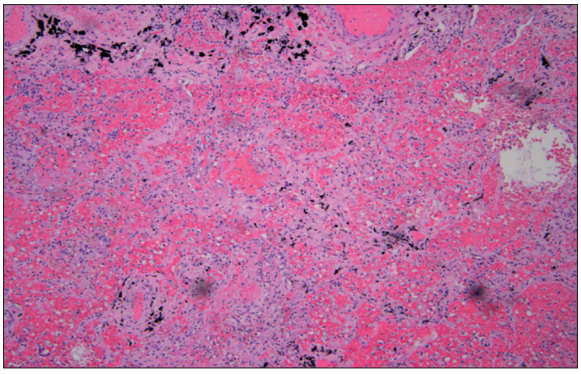

Figure 4. Representative photomicrograph of the lung parenchyma with abundant intraalveolar hemorrhage, numerous pulmonary macrophages, and perivascular and intraseptal hemosiderin laden macrophages. (100×, H&E stain).

Later reports described the presence of anti-neutrophil cytoplasmic antibodies in approximately one third of patient with Goodpasture's syndrome.

A suggested Pathophysiology of this association is the damage to glomerular basement membrane that occurs as part of ANCA associated Vasculitis involving the glomerular capillaries leading to uncovering "hidden antigens" from the membrane, inducing the formation of antibodies, in another word, the underlying etiology is ANCA Vasculitis, and the production of anti GBM is a secondary phenomenon.

This theory could not be proven since in all reported cases anti GBM antibodies and ANCA antibodies were evident simultaneously at the time of diagnosis.

But in 2004, a case report from France (2) described the development of Anti GBM glomerulonephritis in a patient who was diagnosed with ANCA associated Vasculitis three years earlier [2].

The prognosis of double positive disease compared to isolated antiglomerular basement membrane disease is controversial.

In 1991, Bosch X et al. suggested that among patients with both antibodies, those with highest ANCA titers recovered renal function despite being initially on hemodialysis, as opposed to those with lowest ANCA titers or Anti GBM alone [4].

A Swedish study published in 2003, reported a better outcome in patients with both anti-GBM antibodies and P-ANCA. These patients had better overall survival, and more chance of recovering renal function compared to those with only anti-GBM antibodies, in fact, all six patients who recovered renal function were double positive [5,8].

In the other hand, a case series from China, published in 2005, was not able to show any correlation between the presence of ANCA and the outcome of Goodpasture's disease [6].

As for treatment, it is suggested that all patients with anti-GBM antibody disease and severe renal failure who do not require immediate dialysis should be considered intensive plasma exchange and intensive immunosuppression, including steroids and cyclophosphamide [7].

Patients who present with dialysis-requiring renal failure are less likely to recover renal function but may occasionally do so with intensive, early treatment.

Immunosuppression and plasma exchange should also be considered in patients with pulmonary hemorrhage, regardless of the severity of the renal failure, since pulmonary hemorrhage responds in most patients.

Conclusions

Double positive disease accounts for 25% of cases of Goodpasture's syndrome, a suggested Pathophysiology of this association is the renal involvement in ANCA Vasculitis leading to the exposure of antigens from the basement membrane and the formation of antibodies.

This entity is believed to carry better prognosis when compared to isolated anti glomerular basement membrane disease.

Our patient is the oldest Goodpasture's syndrome patient reported in literature; her clinical presentation (hemoptysis and renal involvement) is unique for her age group, and despite the early aggressive treatment, the presence of possible good prognostic factor (positive p-ANCA), she suffered a frustrating outcome.

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