Tumor-like lung lesion revealing Goodpasture's syndrome in an elderly patient: a case report

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ABSTRACT

Background: Pulmonary involvement in Goodpasture's syndrome is exceptionally isolated without the renal impairment. Usual lung damage includes alveolar hemorrhage resulting in pulmonary-renal syndrome. Isolated and atypical lung involvement can precede kidneys damage.

Case presentation: We report a case of an 80 year-old man admitted for dyspnea related to a tumor-like lung lesion and we were unable to confirm the malignant nature. Three months later, the patient presented acute renal failure with rapidly progressive glomerulonephritis leading to the diagnosis of anti-glomerular basement membrane disease, while the lung lesion remained stable. He received corticosteroid and immunosuppressive therapy with partially favorable renal outcome and complete regression of the lung lesion.

Conclusion: Slight modifications of the urinary sediment should be sought in the case of lung abnormalities. Anti-glomerular basement membrane antibodies must be considered in case of any kidney damage associated with pulmonary involvement even if atypical.

Keywords: Goodpasture's syndrome, pulmonary alveolar hemorrhage, rapidly progressive glomerulonephritis, crescentic glomerulonephritis, lung mass, case report.

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Background

Goodpasture syndrome or anti-glomerular basement membrane (anti-GBM) disease is an immune-complex small vessels vasculitis according to the most recent Chapel Hill classification of vasculitis [1]. It mainly affects glomerular capillaries and pulmonary capillaries with anti-GBM deposition at different basement membranes. Pulmonary involvement usually manifests as pulmonary hemorrhage, while renal involvement causes necrotizing and crescentic glomerulonephritis [2], while isolated renal involvement is observed in 30% of cases, pulmonary involvement with normal renal function is far more exceptional [2]. We report the case of an 80-year-old man with an anti-GBM vasculitis revealed by a tumor-like lung lesion. This case illustrates the difficulty of early diagnosis when pulmonary involvement is atypical or isolated, especially at an age when neoplastic diseases tend to be dominant.

Case Presentation

Eighty-year-old male with a 180 pack-year smoking history presented basithoracic pain and dyspnea requiring his admission in the Department of Pneumology.

Clinical examination showed a dyspneic, afebrile patient, blood pressure of 110/70 mmHg, heart rate at 100 bpm. He was properly hydrated and had a normal diuresis. The auscultation of the cardiac and respiratory systems was without abnormalities.

Routine laboratory tests showed evidences of the inflammation (erythrocyte sedimentation rate at 112 mm and C reactive protein at 156 mg/l). Full blood count revealed microcytic anemia (hemoglobin: 10.5 g/dl). Renal function tests were within the normal range: urea and creatinine serum level, respectively, at 9 and 91 µmol/l. Blood gas test was normal (pH at 7.38, PaO_2: 88.5 mmHg, $PaCO_2$: 44 mmHg, and SaO_2: 95.4%).

Chest X-ray revealed an ill-defined round basilar opacity of the left lung (Figure 1). Chest computed tomography (CT) highlighted the presence of a mass with irregular contours on the lower lobe of the left lung. It obstructed the anterior and lateral segmental branches of the basal pyramid. Chest CT also revelaed the presence of multiple nodules and micro nodules over both lungs (Figure 2). Abdominal and pelvic CT was without abnormalities, especially absence of enlargement of lymph nodes or hepatosplenomegaly. Bronchial endoscopy showed signs of bronchial mucosa inflammation without obstruction. Bronchoalveolar lavage showed inflammatory fluid with no isolated neoplastic cells. Tuberculin skin test was negative. Sputum examination did not objectify Koch bacillus. Legionella pneumonea and aspergillosis serology was

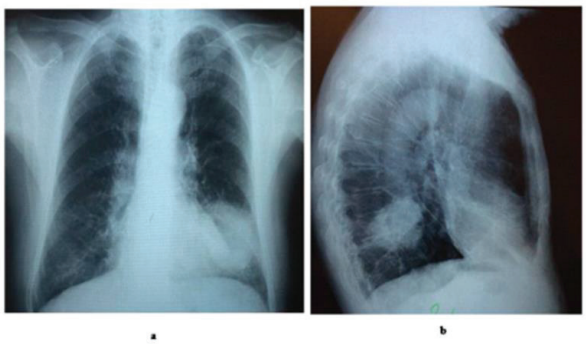

Figure 1. *Chest X-ray showing basilar opacity of the left lung: (a) antero-posterior view and (b) lateral view.*

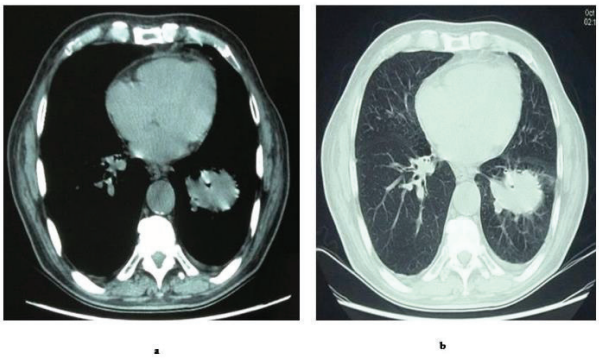

Figure 2. *Chest CT axial view: (a) mediastinal window and (b) pulmonary window showing a mass with irregular contours of the left lung.*

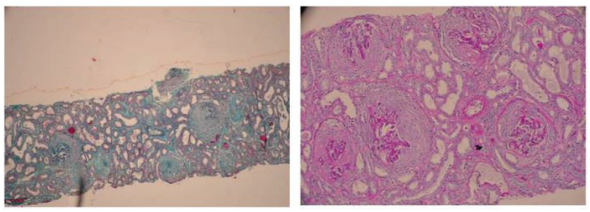

Figure 3. *Fibro-cellular circumferential crescentic glomerulonephritis: (a) Masson's trichrome stain and (b) Periodic acid–Schiff stain (PAS) stain.*

negative. Tumor markers were negative: carcinoembryonic antigen was at 3.1 µg/l (<5 µg/l) and CA 19-9 was at 17 U/ml (<30 U/ml).

A CT-scan guided biopsy was proposed, but refused by the patient who left the hospital against medical advice.

Three months later, the patient was referred to the Internal Medicine Department for oliguria. Clinical examination found an afebrile patient, hemodynamically stable with no edema. The auscultation of the respiratory system objectified an abolition of the respiratory murmur on the lower zone of the left lung. Urine test strip noted the presence of both proteinuria +++ and hematuria +++. Otherwise, general examination was essentially normal.

Kidney function tests showed acute renal failure: blood urea nitrogen at 37.9 mmol/l and serum creatinine at 1,143 µmol/l. Calcium serum level was 2.25 mmol/l (normal range: 2.25–2.6). Full blood count objectified anemia (hemoglobin: 7.9 g/dl) with normal leucocyte and platelet count. Laboratory evidences of inflammation were also found (C-reactive protein: 228 mg/l, erythrocyte sedimentation rate: 100 mm H1, elevated alpha2globulinemia: 9.4 g/l and polyclonal hypergammaglobulinemia: 15.2 g/l). Serum protein immunofixation did not show monoclonal gamma globulin.

Urinalysis showed proteinuria of 1.2 g/24 hours, hematuria: 7,500 elements/ mm^3, with natriuresis at 62 mmol/24 hours, kaliuresis at 38 mmol/24 hours, and urinary urea at 117 mmol/24 hours.

The same lung lesion was found on chest X-ray.

Given the rapid progression of acute renal failure, immunologic work-up was requested revealing the presence of anti-GBM antibodies. Anti-neutrophil cytoplasmic antibodies, anti-nuclear antibodies, and cryoglobuline testing were negative. Renal biopsy was performed. Histological examination showed fibro-cellular circumferential crescentic glomerulonephritis affecting all glomeruli (Figure 3). Immunofluorescence study highlighted the linear immunoglobulin G deposits along the glomerular basement membrane.

Bronchoalveolar lavage revealed the presence of 27% siderophages with a positive GOLD score. There were no malignant cells.

Diagnosis of anti-GBM vasculitis was established given the finding of renal biopsy, bronchoalveolar lavage, and immunological workup with probable tumor-like lung involvement.

Treatment was immediately initiated using plasmapheresis (three exchanges per week for 2 weeks), corticosteroid therapy with three intravenous boli followed by 1 mg/kg/day of oral Prednisone and boli of Cyclophosphamide (800 mg every 3 weeks).

Patient gradually recovered normal diuresis with residual renal failure (serum creatinine: 700 µmol/l) requiring hemodialysis. Hemoglobin improved reaching 8.9 g/dl and regression of laboratory sings of inflammation was noted with C-reactive protein at 29 mg/l. Chest X-ray showed disappearance of the lung lesion (Figure 4).

Discussion

Our patient presented respiratory symptoms linked to a lung mass which was followed 3 months later by the acute renal failure pointing to the diagnosis of anti-GBM disease. Although we did not obtain histological examination of the lung mass as the patient refused biopsy, positive GOLD score in the bronchoalveolar lavage and the outcome after immunosuppressive therapy is greatly in favor of specific lung involvement related to anti-GBM disease.

Anti-GBM disease, although rare, is the main cause of pulmonary-renal syndrome (30%) [3]. Incidence of this disease is estimated to 0.5–1 case per million inhabitants per year [3].

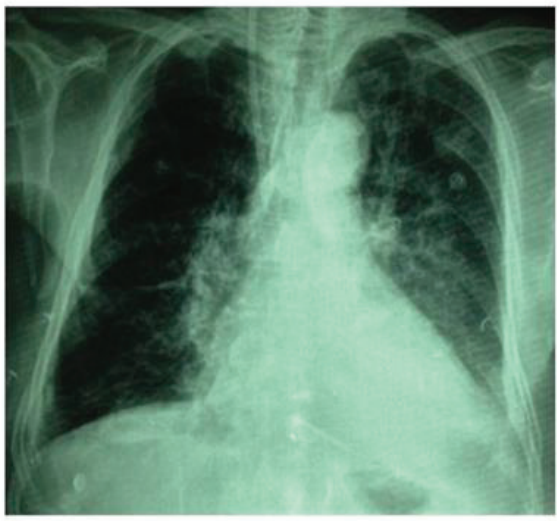

Figure 4. *Chest X-ray antero-posterior view showing the regression of the lung mass.*

Two incidence peaks have been reported between the second and third decade of the life. Prevalence of the disease is higher among men in the younger patients while women are more affected at an older age [4]. Our patient was 88-year-old making clinical suspicions mostly directed toward neoplastic disease given the nature of lung involvement.

Anti-GBM disease is an autoimmune disease that could be favored by exposure to toxins as tobacco or hydrocarbons [3]. Our patient had a long history of smoking. This disease is strongly associated with HLA DRB1 * 1501 [5].

This disease is characterized by the presence of circulating antibodies directed against an antigen normally present in the glomerular basement membrane and alveolar basement membrane. These antibodies activate the complement system, resulting in tissue damage. This is a typical type II reaction in the Gell and Coombs classification of antigen–antibody reactions. Immunofluorescence techniques allow visualizing antibodies deposition as a linear deposit along the glomerular basement membrane and, more rarely, alveolar basement membrane. Although basement membranes are ubiquitous, only alveolar and glomerular basement membrane are clinically affected. Preferential binding to glomerular and alveolar basement membranes appears to be due to greater accessibility of epitopes [6]. Pulmonary-renal syndrome is usually the sole clinical feature of anti-GBM disease [7].

In our patient, the diagnosis of anti-GBM disease could not initially be established given the isolated and atypical pulmonary involvement. Isolated pulmonary involvement represents only 4% of anti-GBM disease and can reach 20% if minimal renal damage (hematuria or proteinuria) is taken into account [8]. Typically, it is an alveolar hemorrhage which can be suspected in case of hemoptysis, anemia, and nonspecific radiological infiltrate.

Other less typical radiological aspects have been described such as diffuse infiltrate in both lungs, asymmetric unilateral forms, spontaneously resolving opacities, and pseudo-pneumonic systematized forms. Our patient presented a tumor-like lung injury which evolved favorably on specific treatment.

Pulmonary biopsy is risky, especially if presence of alveolar hemorrhage. It may provide insight in the diagnosis in only 25% of cases [8].

Renal involvement is rarely absent in anti-GBM disease and may occur later during the course of the disease, such as with our patient [9]. Renal involvement usually manifests as rapidly progressive glomerulonephritis. Histological examination shows necrotizing crescentic glomerulonephritis most of the time. Linear deposits of anti-GBM antibodies are always found in immunofluorescence.

Diagnosis of anti-GBM disease requires the detection of anti-MBG antibodies. These antibodies can be detected both in circulation and in the kidney by immunofluorescence on renal biopsies [3].

Combination of high dose corticosteroid therapy, Cyclophosphamide and plasma exchange is the corner stone for treatment of anti-GBM disease. Such treatment, although effective, present a large variety of adverse effects such as metabolic and infectious diseases. Elderly patient are more prone to such complications. These adverse effects need to be monitored and managed without discontinuing therapy in life-threatening condition. Treatment is more effective if started early. Duration of immunosuppressive therapy is not well established. In patients with complete remission, Cyclophosphamide should be maintained for 2–3 months and corticosteroids for 6 months. Patients with clinically active disease or persistent positivity of anti-GBM antibodies after 3 months require longer therapy. Plasma exchanges are daily for a minimum of 14 days, until disappearance of anti-GBM antibodies. Use of fresh frozen plasma (300–600 ml) at the end of session is strongly recommended in cases of active alveolar hemorrhage, coagulopathy, or recent invasive action (renal biopsy). It is also important to mention that Cyclophosphamide should be given after and not before exchange sessions to avoid apheresis [2–9].

Rituximab has been proposed as a second-line agent in patients whose treatment with cyclophosphamide has failed [8].

At the stage of renal failure, renal transplantation should be delayed until anti-GBM antibodies are undetectable in serum for 12 months and the disease has been in remission for at least 6 months without the use of cytotoxic agents. Five-year survival rate exceeds 80% due to immunosuppressive therapies and less than 30% of patients require long-term dialysis. For elderly patients, creatinine serum level higher than 500 µmol/l, oliguria, the presence on renal biopsy of more than 50% affected glomeruli, and the presence of intra-alveolar hemorrhage have been reported as poor prognosis factors [2].

Conclusion

In conclusion, with this report, we draw attention to the possibility of anti-GBM disease manifesting as a lung lesion with no obvious renal abnormality occurring in an elderly patient making differential diagnosis with neoplastic disease as a challenging task. However, anti-GBM with normal renal functions tests may just be an early form of the disease since abnormalities of the urinary sediment may occur later during the disease course.

List of Abbreviations

Anti-GBM	Anti-glomerular basement membrane
CT	Computed tomography

Consent for publication

Informed consent was obtained from the patient for publication of this case report and any accompanying images.

Ethical approval

Not required.

Author's contributions

All authors contributed to the writing and correction of this manuscript as well as being involved in the patient treatment.

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Summary of the case

Patient (gender, age)	1	Male, 80-year old
Final diagnosis	2	Anti-glomerular basement membrane disease
Symptoms	3	Dyspnea, renal failure
Medications	4	Corticosteroid, cyclophosphamide, plasma exchange
Clinical Procedure	5	Computed tomography, renal biopsy
Specialty	6	Nephrology