Case report – Kidney-Lung Syndrome (*Goodpasture Syndrome*) when to think

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ABSTRACT

Lung-kidney syndrome is an anti-glomerular basement membrane (anti-GBM) disease, which is often characterized by pulmonary hemorrhage and renal dysfunction. To date, no specific trigger for the development of anti-GBM antibodies has been identified, and exposure of the alveolar capillaries to these antibodies requires an initial attack on the pulmonary vasculature, resulting in a typical picture of glomerulonephritis. As it is a disease of low prevalence, clinical reasoning associated with an effective investigation for early detection is essential for a satisfactory evolution. Good results are seen when treatment is started immediately. Thus, the present case report aims to discuss, through a literature review in databases such as Scielo and PubMed, the efficacy of an early intervention in a patient with initially unexplained respiratory failure and renal dysfunction, associated with alterations in laboratory and imaging tests. In addition, it aims to demonstrate the importance of quick clinical reasoning to avoid sequelae and increase the chances of a good prognosis.

Keywords: Kidney-Lung Syndrome, Goodpasture Syndrome, Pulmonary Hemorrhage, Glomerulonephritis, Glomerular Basement Membrane.

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INTRODUCTION

Goodpasture syndrome refers to an anti-glomerular basement membrane (anti-GBM) disease that involves the lungs and kidneys, often presenting as pulmonary hemorrhage and glomerulonephritis. (HELLMARK; SEGELMARK, 2014) It seems to be the result of environmental insults in a person with a genetic predisposition, so far, no triggering stimulus for the development of anti-glomerular basement membrane antibodies has been identified. (PHELPS; REES, 1999)

Exposure of the alveolar capillaries to these autoantibodies requires an initial insult to the pulmonary vasculature. These environmental factors include: Drugs, such as alemtuzumab, which cause lymphocyte depletion; Cocaine inhalation; Infections, such as influenza A2; Smoke; Exposure to metal dust; organic solvents or hydrocarbons; Extracorporeal shock wave lithotripsy. (CRANFIELD; MATHAVAKKANNAN, 2014)

Autoantibodies activate the complement system in the basement membrane, causing tissue injury. This autoantibody binding can be seen as a linear deposition of immunoglobulins along the basement membrane and the inflammatory response in this area results in the typical picture of glomerulonephritis. Although Goodpasture syndrome is considered an autoantibody-mediated disease, a vital role is played by T cells in the initiation and progression of the disease, T cells cause B cells to increase antibody production and play a direct role in kidney and lung injury. (CUI et al., 2011)

Up to 80-90% of patients have features of rapidly progressive glomerulonephritis, characterised by active urine sediment analysis, subnephrotic proteinuria, and reduced urine output. 40-60% of patients will have pulmonary hemorrhage concomitant with hemoptysis and varying degrees of dyspnea. A small minority of patients may have isolated lung disease. In a few cases, patients present with severe acute kidney injury that requires dialysis treatment. (REGGIANI et al,. 2023).

In a retrospective study conducted in the United States, about 93 million hospitalizations found in the national database between 2003 and 2014 were analyzed, among these 964 patients were hospitalized with the diagnosis of Goodpasture's syndrome. Thus, the prevalence was approximately 10 hospitalizations per 1,000,000. (KAEWPUT et al., 2020) Other studies show that among European and Asian populations, there is a frequency of 0.5 to 1.8 cases per million inhabitants per year. A recent paper from Ireland reported a national incidence of Goodpasture Syndrome of 1.64 per million population per year. (GULATI; MCADOO, 2018).

Good renal outcomes can be achieved with immediate initiation of treatment. However, when patients have severe renal impairment requiring dialysis or with a high proportion of glomerular crescents on biopsy, renal outcomes are poor. Relapses are rare, and when renal involvement is

present, concomitant diseases such as ANCA-associated vasculitis and membranous nephropathy should be suspected. (REGGIANI et al,. 2023).

In the study by Reggiani (2023), patients treated with the combination of plasma exchange, cyclophosphamide, and corticosteroids have a 1-year survival of 80-90% and the efficacy of treating pulmonary hemorrhage is greater than 90%. The degree of renal involvement directly affects renal survival. In patients with creatinine values equal to or less than 5.65 mg/dL, renal survival varies between 94-95% in up to 5 years. Creatinine values higher than 5.65 mg/dL and that do not require immediate dialysis have renal survival of 82% and 50% at 1 and 5 years, respectively. However, when immediate dialysis is required, it has renal recovery in only 8% in 1 year. Along with renal function, the proportion of glomeruli affected by crescents was also correlated with renal survival. (REGGIANI et al,. 2023).

CASE REPORT

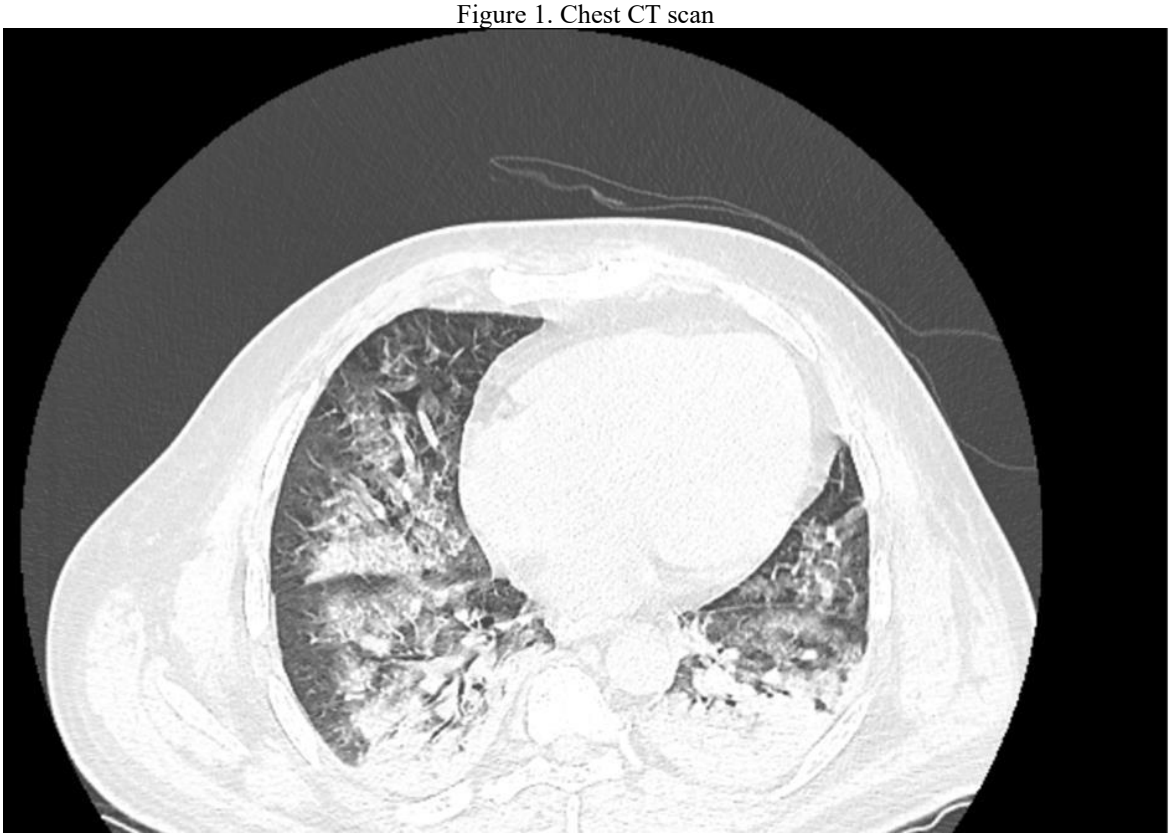
S.R.H., 58 years old, hypertensive. The patient was admitted to the emergency department with a drop in general condition, hemoptysis, cough and chills that began 5 days ago and worsened in the last 24 hours, arrives in respiratory failure associated with a lower level of consciousness, and orotracheal intubation is performed and antibiotics (ampicillin + sulbactam) are started due to the initial suspicion of community-dwelling bacterial pneumonia.

Initial tests were performed and severe renal dysfunction was identified with dialysis urgency with creatinine 18 (CKD-EPI 3 ml/min/1.73m2), urea 332 , K 7.6 and metabolic acidosis (arterial blood gas analysis PH 6.38, PCO2 57 PO2 157, HCO3 9.9 BE -23 and SatO2 96%, on mechanical ventilation with FiO2 100%). At this time, the patient had no evidence of shock or poor tissue perfusion with lactate 0.6, with BP 168x90 mmhg, HR 80 bpm, and no other organ dysfunctions, except renal and pulmonary. Other tests were not compatible with infection or septic shock, including: hemoglobin 10.3, hematocrit 28.6, leukocytes 17450, rods 2%, platelets 215,000, creatinine 22.10, urea 431, potassium 7.2, sodium 123, CRP 3.10. At 07h: haemoglobin 9.3, haematocrit 26.8, leukocytes 15180,

platelets 210,000, INR 1.16, creatinine 21.80, urea 430, potassium 8.1, sodium 136, ionic calcium 0.69, magnesium 2.5, glutamic-oxaloacetic transaminase (GOT) 25, pyruvic transaminase (TGP) 33, total bilirubins 0.70, CRP 2.90, non-reactive VDRL and urine test with no signs of infection but bleeding with dysmorphic red blood cells (protein+++, hemoglobin++++, negative nitrite, leukocytes 300,000, hyaline casts +, bacteria).

After 48 hours in the hospital, the patient was transferred from the emergency room to the intensive care unit (ICU) undergoing a chest tomography (Fig. 1) during transport, which showed alveolar hemorrhage and thought of kidney-lung syndrome.

Figure 1. Chest CT scan



Chest CT scan, where areas compatible with alveolar hemorrhage (hemoptoic report, hemoglobin drop, bilateral alveolar consolidations with central predominance).

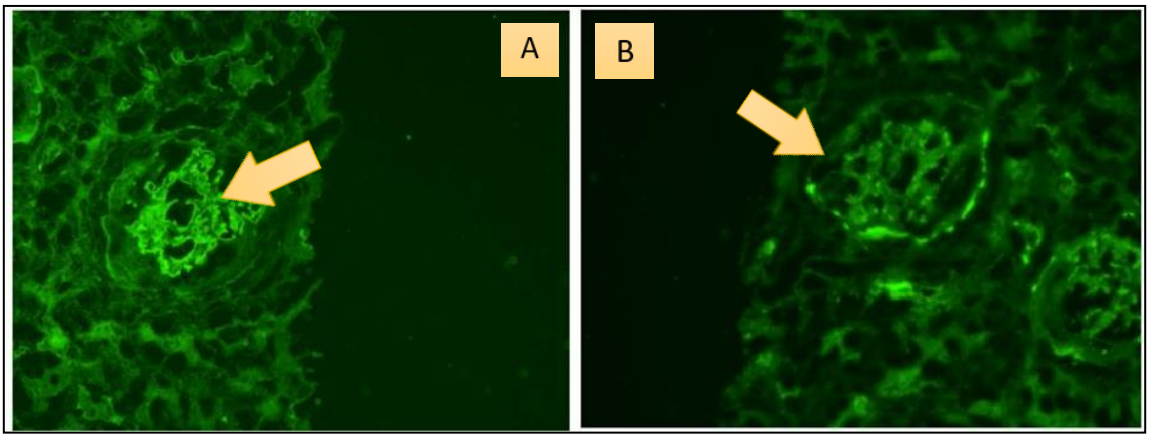
Upon arrival at the ICU, antibiotics were withdrawn, albendazole and ivermectin were given a dose to treat worms, and pulse therapy was discussed with the pulmonology and nephrology team in groups.

After 5 days of hospitalization, we received additional tests performed to investigate Goodpasture's Syndrome, including: serology for hepatitis B and C, ANA, ANCA, ASCA, complement, ESR, cryoglobulin and NEGATIVE immunoglobulins, glomerular basement membrane antibodies: 156.00 U/mL (compatible with Goodpasture's Syndrome) (Fig. 2). Pulse therapy was then started with methylprednisolone 01 gram/day for 3 days and intravenous cyclophosphamide 01 gram single dose, with a schedule to administer a new dose after 4 weeks.

After completion of methylprednisolone, performed for 3 days, the first plasmapheresis was performed, with subsequent extubation within 48 hours, after improvement of the pulmonary condition, still requiring dialysis, without recovery of diuresis or renal function.

For better investigation, a renal biopsy was performed, with results received about 7 days after discharge from the ICU and in an inpatient unit already in the hospital discharge plan.

Figure 2. Renal biopsy



A. IgG: POSITIVE in glomerular loops, linear pattern (4+/4+); B. C3: POSITIVE in glomerular loops (2+/4+).

DISCUSSION

The patient studied arrived at the hospital with hemoptysis, bronchospasm and asthenia, which was clinically unstable. However, without a definitive diagnosis, due to the complexity of the condition and severity, some suspicions were raised, since he was being treated for pneumonia.

Laboratory and imaging tests were performed to better elucidate the case and raise some diagnostic hypotheses, because with the results it was possible to find some worsening factors even with the optimized treatment. An electrocardiogram was performed, in which an apiculated T wave was revealed, and laboratory tests showed drastically reduced renal function, proteinuria, and hematuria.

In patients with renal and pulmonary involvement, leptospirosis, Goodpasture's syndrome, heart failure, and rapidly progressive glomerulonephritis may be suspected. According to Devrieze and Hurley (2022), some physical examination findings related to Goodpasture's syndrome are: Increased respiratory rate; Basilar inspiratory crackles; Cyanosis; Hepatosplenomegaly; Hypertension; Oedema.

Some differential diagnoses can also be thought of in patients with these renal and pulmonary symptoms, they are: granulomatosis with polyangiitis (Wegener's granulomatosis); systemic lupus erythematosus; microscopic polyangiitis; Henoch-Schonlein purple; IgA nephropathy; Acute glomerulonephritis; community-acquired pneumonia; granulomatosis with polyangiitis; pneumonia caused by Pneumocystis jiroveci; Churg-Strauss syndrome.

Careful physical examination should be performed of patients presenting with findings suspicious of anti-glomerular basement membrane disease. Patients with Goodpasture syndrome initially present similarly to other forms of rapidly progressive glomerulonephritis with acute renal failure. Pulmonary symptoms are typically present at or shortly after the initial encounter. Haemoptysis of various grades is typical of pulmonary involvement, ranging from severe, life-threatening bleeding to mild diffuse haemorrhage.

It is more common for younger patients affected by the disease to have concurrent renal and pulmonary symptoms and to be critically ill at presentation and patients over 50 years of age tend to have only glomerulonephritis and follow a less severe course. And in this patient, even at 57 years old, he was affected by the severe form of the disease.

Some tests help guide treatment decisions, such as: urine test that is characteristic and usually demonstrates low-grade proteinuria, macroscopic or microscopic hematuria, and red cell casts; a complete blood count may reveal anaemia secondary to intrapulmonary haemorrhages, and leukocytosis is usually present; in renal function tests they can be altered secondary to renal dysfunction; Chest X-ray shows irregular parenchymal opacifications, which are usually bilateral and bibasal. Costophrenic apices and angles are usually spared; pulmonary function tests show high carbon monoxide diffusing capacity (DLCO) secondary to carbon monoxide binding to intra-alveolar hemoglobin.

Subsequently, a computed tomography scan was performed in this patient, which revealed bilateral alveolar consolidations with central predominance, and after discussing the case with a nephrologist to request renal biopsy, pulse therapy was initiated with methylprednisolone 500mg/day for 3 days, ivermectin for 2 days, and albendazole for 5 days.

Patients who present with Goodpasture's syndrome (both glomerulonephritis and pulmonary hemorrhage) may be critically ill at presentation. Urgent hemodialysis is often necessary, and intubation for respiratory failure as well. When the clinician suspects the diagnosis, a renal biopsy should be done as soon as the clinical situation permits. After diagnosis, patients should be started on prednisone, cyclophosphamide, and daily plasmapheresis to improve overall mortality in general and renal survival in particular. (JOHNSON et al., 1985)

Renal biopsy is the gold standard for diagnosis, but it is not required to initiate treatment or continue therapy if biopsy is not feasible. When performed, biopsy provides important information about the activity and chronicity of renal involvement that can guide therapy. Renal biopsy is preferable to lung biopsy as it provides a much higher yield, but lung biopsy can be performed when renal biopsy is contraindicated for any reason.

Light microscopy will show increasing glomerulonephritis. Over time, the crescents become fibrotic, and frank glomerulosclerosis with interstitial fibrosis and tubular atrophy may be seen. Immunofluorescence will show linear deposition of IgG and complement (C3) along the basement membrane. Predominantly, the IgG-1 subclass is present. (ZHAO et al., 2009)

Typically, daily plasmapheresis is performed until anti-glomerular basement membrane antibodies are undetectable, with steroids and cyclophosphamide continuing thereafter for 3 to 6 months until complete remission is achieved. This can be assessed by checking for repeated titers after plasmapheresis, as well as any time new symptoms develop that may be a harbinger of relapse.

Overall, relapse remains rare. The initial dose of cyclophosphamide is 2 mg/kg orally, adjusted to maintain a white blood cell count of approximately 5,000. (SYEDA et al., 2013)

Even with proper treatment, kidney function can be impaired to the point of failure. Although renal failure is a relatively common complication for patients with Goodpasture syndrome, less than 30% of surviving patients require long-term dialysis. In severe cases, a kidney transplant may be necessary.

The prognosis of Goodpasture syndrome with the development of aggressive therapies such as plasmapheresis, corticosteroids, and immunosuppressive agents has improved significantly. With these therapies, the 5-year survival rate has exceeded 80% and less than 30% of patients require long-term dialysis. However, delayed administration of cyclophosphamide has been found to be associated with a fatal prognosis. (WEBER et al., 1992)

CONCLUSION

Lung-Kidney Syndrome is a disease that is difficult to diagnose and needs to be remembered in cases of alveolar hemorrhage and renal dysfunction. Many patients have unexplained pulmonary and kidney symptoms, so whenever possible, the syndrome should be diagnosed and treated early in order to avoid sequelae, disease progression, and increase the chances of a good prognosis. The patient will also require an intensive care setting for better outcome and outcome. Kidney biopsy is essential to confirm the diagnosis, but it should not delay the start of treatment, and can be done at a later time, when the patient is stable.

REFERENCES

1. Apaydin, S. (2018). The treatment of ANCA-associated rapidly-progressive glomerulonephritis and Goodpasture syndrome with therapeutic apheresis. *Transfusion and Apheresis Science*, 57(1), 8-12. https://doi.org/10.1016/j.transci.2018.02.007

2. Cranfield, A., & Mathavakkannan, S. (2014). Goodpasture's disease following extracorporeal shock wave lithotripsy: A case report & literature review. *Clinical Case Reports*, 3(3), 160-164. https://doi.org/10.1002/ccr3.190

3. Cui, Z., Zhang, L., Chen, X., & Wu, Y. (2011). Clinical features and outcomes of anti–glomerular basement membrane disease in older patients. *American Journal of Kidney Diseases*, 57(4), 575-582. https://doi.org/10.1053/j.ajkd.2010.09.022

4. Devrieze, B. W., & Hurley, J. A. (2022). Goodpasture syndrome. Retrieved August 15, 2023, from https://www.ncbi.nlm.nih.gov/books/NBK459291/?report=reader#_NBK459291_pubdet_

5. Gulati, K., & McAdoo, S. P. (2018). Anti–glomerular basement membrane disease. *Rheumatic Disease Clinics of North America*, 44(4), 651-673. https://doi.org/10.1016/j.rdc.2018.06.011

6. Hellmark, T., & Segelmark, M. (2014). Diagnosis and classification of Goodpasture's disease (anti-GBM). *Journal of Autoimmunity*, 48-49, 108-112. https://doi.org/10.1016/j.jaut.2014.01.024

7. Johnson, J. P., Ecker, R., & Miskulin, D. (1985). Therapy of anti-glomerular basement membrane antibody disease. *Medicine*, 64(4), 219-227. https://doi.org/10.1097/00005792-198507000-00003

8. Kaewput, W., Vannaprasit, K., & Kanya, W. (2020). Inpatient burden and mortality of Goodpasture's syndrome in the United States: Nationwide inpatient sample 2003–2014. *Journal of Clinical Medicine*, 9(2), 455. https://doi.org/10.3390/jcm9020455

9. Levy, J. B., & et al. (2001). Long-term outcome of anti–glomerular basement membrane antibody disease treated with plasma exchange and immunosuppression. *Annals of Internal Medicine*, 134(11), 1033. https://doi.org/10.7326/0003-4819-134-11-200106050-00009

10. Nunes, A. J. F., & et al. (2003). Relato de caso: Síndrome de Goodpasture. *Brazilian Journal of Nephrology*, 25(2), 104-107. https://bjnephrology.org/wp-content/uploads/2019/11/jbn_v25n2a06.pdf

11. Phelps, R. G., & Rees, A. J. (1999). The HLA complex in Goodpasture's disease: A model for analyzing susceptibility to autoimmunity. *Kidney International*, 56(5), 1638-1653. https://doi.org/10.1046/j.1523-1755.1999.00720.x

12. Reggiani, F., & et al. (2023). Goodpasture syndrome and anti-glomerular basement membrane disease. *Clinical and Experimental Rheumatology*, 41, 964-974. https://doi.org/10.55563/clinexprheumatol/tep3k5

13. Syeda, U. A., & et al. (2013). Anti-glomerular basement membrane antibody disease treated with rituximab: A case-based review. *Seminars in Arthritis and Rheumatism*, 42(6), 567-572. https://doi.org/10.1016/j.semarthrit.2012.10.007

14. Zhao, J., & et al. (2009). The immunoglobulin G subclass distribution of anti-GBM autoantibodies against rHα3(IV)NC1 is associated with disease severity. *Human Immunology*, 70(6), 425-429. https://doi.org/10.1016/j.humimm.2009.04.004

15. Weber, M. F., & et al. (1992). Antineutrophilcytoplasmic antibodies and antiglomerular basement membrane antibodies in Goodpasture's syndrome and in Wegener's granulomatosis. *Journal of the American Society of Nephrology*, 2(7), 1227-1234. https://doi.org/10.1681/asn.v271227