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GOODPASTURE SYNDROME. A CASE REPORT

Keywords: Anti-Glomerular Basement Membrane Disease; Glomerulonephritis; Interstitial Lung Diseases.
Palabras clave: Enfermedad por Anticuerpos Antimembrana Basal Glomerular; Diálisis; Hemorragia Alveolar.

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ABSTRACT

Introduction: Goodpasture syndrome, also known as anti–glomerular basement membrane disease, is a very rare small vessel vasculitis that may be limited to the kidneys, with manifestations ranging from relatively mild kidney failure to rapidly progressive glomerulonephritis (RPG). It may also appear as a pulmonary-renal syndrome, including RPG and diffuse alveolar hemorrhage (DAH).
Case report: A 49-year-old man with no significant medical history was admitted to a quaternary care center in Bogotá (Colombia) due to fatigue, muscle weakness, loss of appetite, multiple episodes of vomiting, black stools, and anuria over the previous week. Admission labs showed active sediment in urianalysis and presence of anti-glomerular basement membrane antibodies (anti-GBM). A high-resolution computed tomography of the chest showed bilateral multilobar alveolar involvement, while a kidney biopsy revealed findings compatible with linear deposits of immunoglobulin G (IgG) in the glomerular basement membrane. Considering these results, as well as the presence of DAH, Goodpasture syndrome was diagnosed, leading to treatment with 3 doses of methylprednisolone (500 mg intravenously) for 3 days, followed by prednisolone at 0.5 mg/kg/day orally for 30 days, and 7 sessions of plasmapheresis (1 per day). Given that DAH persisted, intravenous cyclophosphamide was indicated 7 days after admission. Although pulmonary involvement was resolved, kidney function was not recovered, so the patient was discharged with dialysis requirement.
Conclusion: Anti-GBM disease is a rare small vessel vasculitis with fairly high morbidity and mortality, so early diagnosis is crucial to achieve a good prognosis. The diagnosis is confirmed by performing anti-GBM antibody tests and a kidney biopsy, as the results of these tests allow establishing the treatment in accordance with recommendations based on current evidence.

RESUMEN

Introducción. La enfermedad de anticuerpos antimembrana basal glomerular es una vasculitis de vasos pequeños de muy baja prevalencia que puede presentarse como una enfermedad limitada a los riñones, cuyas manifestaciones varían desde insuficiencia renal relativamente leve hasta glomerulonefritis rápidamente progresiva (GRP), o como un síndrome pulmonar-renal (síndrome de Goodpasture), que incluye GRP y hemorragia alveolar difusa (HAD).
Presentación del caso. Hombre de 49 años sin antecedentes médicos de importancia, quien ingresó a una institución de cuarto nivel de atención de Bogotá (Colombia) por fatiga, debilidad muscular, pérdida de apetito, múltiples episodios de vómito, evacuación de heces negras y anuria durante la última semana. Los laboratorios de ingreso mostraron sedimento urinario activo y presencia de anticuerpos antimembrana basal glomerular (anti-MBG). Se realizó una tomografía

computarizada de alta resolución de tórax en la que se observó compromiso alveolar multilobar bilateral y una biopsia renal cuyos hallazgos fueron compatibles con depósitos lineales de inmunoglobulina G (IgG) en la membrana basal glomerular y anticuerpos positivos contra la membrana basal glomerular. Teniendo en cuenta estos resultados y la presencia de HAD, se realizó diagnosticó de síndrome de Goodpasture y se instauró manejo con 3 dosis de metilprednisolona (500 mg vía intravenosa) por 3 días, seguido de prednisolona a 0.5 mg/kg/día oral por 30 días y 7 sesiones de plasmaféresis (1 diaria). Debido a la persistencia de HAD, a los 7 días del ingreso se indicó manejo con ciclofosfamida vía intravenosa. Aunque la afectación pulmonar fue resuelta, la función renal no se recuperó, por lo que el paciente egresó con requerimiento de diálisis.
Conclusión. La enfermedad anti MBG es una vasculitis de vasos pequeños poco frecuente con una morbimortalidad marcadamente alta, por lo que su diagnóstico temprano es determinante para lograr un buen pronóstico. El diagnóstico se confirma con la realización de pruebas de anticuerpos anti MBG y biopsia renal, cuyos resultados, además, permiten establecer el tratamiento según recomendaciones basadas en la evidencia actual.

INTRODUCTION

Anti-glomerular basement membrane antibody disease (anti-GBM disease) is a rare small vessel vasculitis that can affect the capillary beds of the kidneys and lungs (1,2). It presents either as a disease limited to the kidneys, with manifestations ranging from relatively mild renal insufficiency to rapidly progressive glomerulonephritis (RPGN), or as a pulmonary-renal syndrome known as Goodpasture syndrome, which includes RPGN and diffuse alveolar hemorrhage (DAH) (80-90% and 40-60% of cases, respectively) (3,4). Its age distribution is bimodal, occurring in the third decade of life, with a slight male predominance, and between the sixth and seventh decades of life, mainly affecting women (4,5).

Although the triggers that induce the autoimmune response are not fully understood, it has been established that anti-GBM disease is caused by the development of directly pathogenic autoantibodies directed against a well-characterized autoantigen expressed in the basement membranes of these organs (1). According to the literature, the prevalence of anti-GBM disease is estimated to be 1 to 2 cases per million inhabitants in Europe, being even rarer in African populations (1,2). In Colombia, the exact prevalence is unknown.

Without treatment, anti-GBM disease is associated with a very high morbidity because almost all patients develop renal insufficiency (6), with 50% of these patients requiring dialysis (3); therefore, early detection is essential to achieve a good prognosis. To diagnose GBM, it is necessary to correlate the clinical presentation with the results of serological tests for anti-GBM antibodies and to

perform a renal biopsy that shows a linear deposit of immunoglobulin G (IgG) along the GBM (1,5,6).

Treatment is established depending on the stage of renal and pulmonary disease. It is recommended to initiate immunosuppression with glucocorticoids and cyclophosphamide, plus plasma exchange therapies (plasmapheresis) in all patients, excluding those who are undergoing dialysis or who have more than 50% global glomerulosclerosis in the biopsy and do not have pulmonary hemorrhage (6).

The following is the case of a patient with Goodpasture syndrome who, due to the consequences arising from renal involvement, required dialysis.

CASE PRESENTATION

A 49-year-old man, with no relevant family or personal medical history, was admitted to the emergency department of a quaternary care hospital in Bogotá D.C. (Colombia) due to fatigue, muscle weakness, loss of appetite, multiple episodes of vomiting, black stools (melena), and anuria over the past week.

On admission physical examination, the general condition of the patient was poor, with altered consciousness, tachypnea (36rpm), and rales in the lung bases. A complete blood count, ionogram, arterial blood gases, and renal function test were requested (Table 1), as well as a chest X-ray that showed interstitial infiltrates in all 4 lung fields. Given the X-ray findings, a high-resolution computed tomography (HRCT) scan of the chest was performed on the same day of admission, revealing interstitial infiltrates and ground-glass opacities (Figures 1 and 2). As a result, it was established that the patient had bilateral multilobar alveolar involvement.

Table 1. Laboratory tests on admission.

Test		Result	Reference values
Arterial blood gases	Arterial pH	7.00	7.38-7.42
	Bicarbonate (HCO_3^-)	8mEq/L	18-22mEq/L
	Excess base	-16mEq/L	+2/-2 mEq/L
Blood count	White blood cell count	13 000µL	4 500-11 000µL
	Hemoglobin analysis	6.7g/dL	13.2-16.6g/dL
Electrolytes and renal function	Potassium blood test (K^+)	6.8mEq/L	3.5-5.5mEq/L
	Creatine blood test	23mg/dL	0.8-1.0mg/dl
	Blood urea nitrogen (BUN)	160mg/dL	6-20mg/dl

Source: Own elaboration.

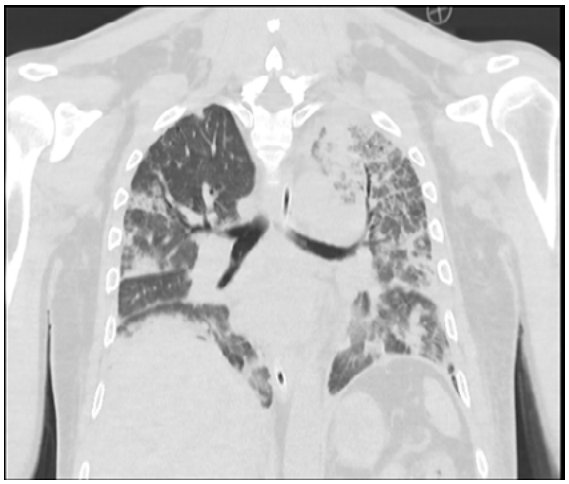

Figure 1. High resolution tomography of the thorax, coronal view. Evidence of bilateral multilobal alveolar involvement with interstitial infiltrate and ground-glass opacities in all lung fields.

Source: Image obtained while conducting the study.

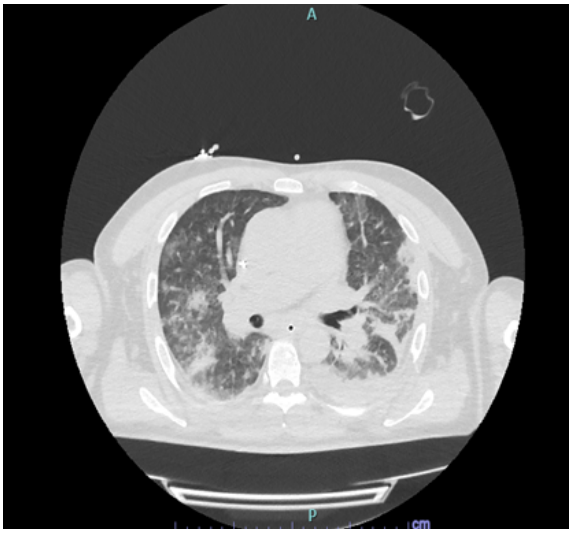

Figure 2. High-resolution tomography of the thorax, cross-sectional view. Interstitial infiltrates, ground-glass opacities, and free pleural effusion are observed.

Source: Image obtained while conducting the study.

In addition, an endoscopy was performed, but no active bleeding was observed. During his stay in the emergency department, the patient presented with respiratory distress and hemoptysis, so it was considered that the digestion of hematic secretions caused tarry stools due to hemoptysis. Due to the hemodynamic instability shown in the admission laboratories (Table 1), the patient was immediately transferred to the intensive care unit (ICU), where

he underwent invasive mechanical ventilation. Likewise, renal replacement therapy (RRT) was initiated since the admission laboratories showed severe renal compromise, severe metabolic acidosis, and hyperkalemia (Table 1).

Two days after admission to the ICU, a urinary tract ultrasound was performed, revealing normal-sized kidneys (right: 100x48x45mm [13mm parenchyma], left: 96x47x39mm [16mm parenchyma]). A follow-up urinalysis was also performed, and the results are presented in Table 2.

Table 2. Urinalysis results.

Test		Result	Reference values
Urinalysis	Urine pH	7.0	5-8
	Urine density	1.001	1.005-1.030
	Urine protein	100mg/dL	0
	Urine leukocytes	39 per field	5-10 per field
	Urine red blood cells	365 per field	3-5 per field

Source: Own elaboration.

Immunological tests were also performed on admission, revealing a regular complement test and positive results for antinuclear antibodies (ANA) and anti-GBM antibodies (Table 3). Based on these results, and due to the presence of DAH, Goodpasture syndrome was established as a diagnosis.

Table 3. Immunological tests.

Test	Result	Reference values
Anti-double stranded DNA (Anti-dsDNA)	Negative	Negative
Antinuclear antibodies (ANA)	Positive: 1:320	Negative
Complement test	C3: 114.2mg/dL (normal) C4: 33.6mg/dL (normal)	C3: 88-201mg/dl C4: 15-45mg/dl
Anti-neutrophil cytoplasm antibodies (ANCA) ELISA test	Anti-MPO: 1.7 (negative) Anti-PR3: 1.7 (negative)	Negative <2
Anti-glomerular basement membrane antibodies (Anti-GBM)	Day 1: 177.2UI/mL Day 15: 41.6UI/mL Day 22: 42UI/mL	Negative <20UI/mL

Anti-MPO: anti-myeloperoxidase antibodies; Anti-PR3: anti-proteinase 3 antibodies.
Source: Own elaboration.

In view of the findings, it was decided to initiate therapeutic management with 3 doses of methylprednisolone (500mg intravenously) for 3 days, followed by prednisolone at 0.5mg/kg/day orally for 30 days, and 7 sessions of plasmapheresis

(1 daily). Anti-GBM antibodies were rechecked after 15 and 22 days (Table 3), while hemoglobin was monitored after 6, 20, and 40 days (Figure 3).

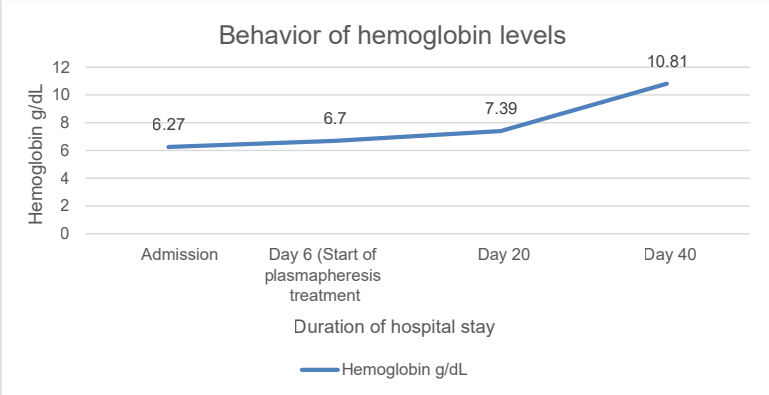

Figure 3. Curve of hemoglobin levels as measured on days 1, 6, 20, and 40 of hospital stay.
Source: Own elaboration.

On the third day of ICU stay, a renal biopsy was performed, and the results confirmed focal segmental glomerulosclerosis (FSGS) in 58 out of 63 glomeruli, as well as glomerular capillary wall retraction, basement membrane fragmentation, fibrosis, and tubular atrophy greater than 50%. Immunofluorescence staining showed linear IgG-positive antibodies in the basement membrane, while electron microscopy showed deposits of mesangial immune complexes (Figures 4 and 5).

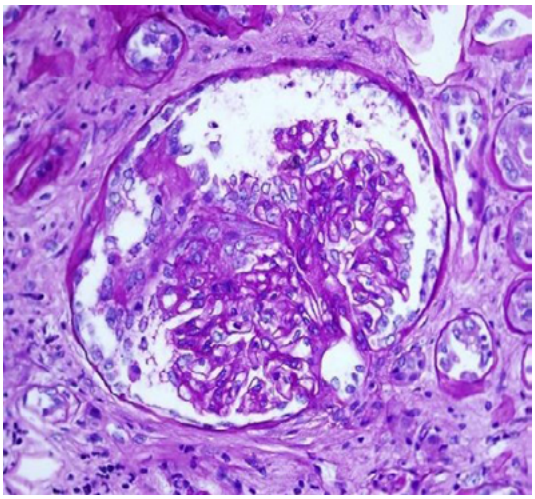

Figure 4. Renal biopsy. Periodic acid-Schiff stain at 40X. Capillary wall retraction is observed.
Source: Image obtained while conducting the study.

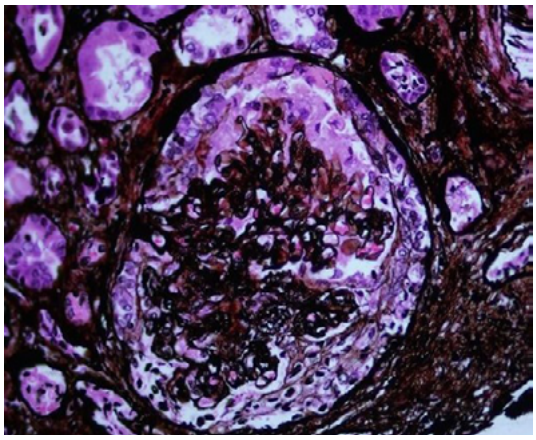

Figure 5. Renal biopsy. Grocott's methenamine silver stain at 10X. Collapsed glomerulus, Bowman's capsule rupture, scarring, and collapse of capillary walls.
Source: Image obtained while conducting the study.

As DAH persisted, intravenous cyclophosphamide (single dose of 12mg/kg) was indicated after 7 days in the ICU. To complete the treatment, oral cyclophosphamide was suggested; however, due to the unavailability of this drug in the institution, it was indicated to start it on an outpatient basis after discharge and maintain it for 3 months at a dose of 2mg/kg/day (150mg: 2 tablets in the morning and 1 tablet in the afternoon).

After 40 days of hospital stay, the patient was discharged with a prescription of oral prednisolone 0.5mg/kg/day for 6 months. Furthermore, as kidney function was not restored, renal replacement therapy (hemodialysis) was prescribed. The patient continued to receive follow-up care at his dialysis center.

DISCUSSION

Anti-GBM disease is a small vessel vasculitis that can affect glomerular and pulmonary capillaries (1,2). Its prevalence is 1 to 2 cases per million inhabitants. It exhibits a bimodal distribution in the third and sixth to seventh decades of life, with the former being more common in men, affecting the lungs and kidneys, and the latter being more common in women, primarily affecting the kidneys (5).

In anti-GBM disease, the autoantibody is a polyclonal IgG (predominantly of the IgG1 and IgG3 subclasses) that targets the epitopes EA and EB of the noncollagenous (NC1) domain of the α3 chain of type IV collagen (α3(IV) NC) (4). This disease may involve only the kidneys, with manifestations ranging from relatively mild renal failure to RPGN, or involve both the kidneys and lungs in Goodpasture syndrome with RPGN and DAH (3,4). In the present case, the patient presented with RPGN resulting in renal failure and severe life-threatening DAH. Furthermore, anti-GBM antibodies were detected in immunological tests, leading to the diagnosis of Goodpasture syndrome.

The prognosis of classic anti-GBM disease is closely correlated with the rapid reduction of anti-GBM antibody levels (7). Therefore, anti-GBM antibody levels must be monitored, as in the present case, in which it was found that they went from 177.2IU/mL on day 1 to 41.6IU/mL on day 15 and to 42IU/mL on day 22.

Diagnosis can be supported by the following renal biopsy findings: basement membrane rupture, Bowman's capsule rupture, IgG deposits, presence of fibrinoid necrosis, crescents, tubular necrosis, and interstitial fibrosis (1), most of which were observed in the biopsy taken from the patient in this case. It should be noted that the presence of extracapillary proliferation, capsular rupture, and interstitial fibrosis is associated with poor renal prognosis (8), resulting in a high percentage of patients with anti-GBM antibody disease requiring RRT (8).

Treatment focuses on reducing inflammation and autoantibody formation with immunosuppressants, such as cyclophosphamide, which should be maintained for up to 3 months, and glucocorticoids, which are initially administered with intravenous loading doses of methylprednisolone, followed by oral prednisolone for at least 6 months, as recommended in the KDIGO 2021 guideline (6). Plasma exchange is used to eliminate circulating antibodies and is indicated for 14 days or until antibodies are no longer detectable (2). If the antibody is not detected after 6 months, it is not necessary to continue maintenance treatment, unless relapses occur, although they are rare (0% to 6% of cases) and are often associated with smoking (6).

Anti-GBM disease is a rare disease that should be considered as a differential diagnosis in the context of lung-kidney syndrome, as early diagnosis and treatment have a significant impact on the prognosis and quality of life of patients, as well as on the costs incurred by the health care system due to unfavorable outcomes such as chronic kidney disease, which was recorded in the case presented.

CONCLUSIONS

Anti-GBM disease is a rare small vessel vasculitis with high morbidity and mortality, so its early diagnosis is crucial to achieve a good prognosis. Diagnosis is confirmed by performing anti-GBM antibody tests and a renal biopsy, and the results of these tests are used to establish a treatment plan based on recommendations derived from current evidence.

ETHICAL CONSIDERATIONS

The patient's informed consent and the approval of the hospital's ethics committee were obtained for the preparation of this case report. Patient anonymity was guaranteed at all times.

CONFLICTS OF INTEREST

None stated by the authors.

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