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GOODPASTURE SYNDROME: A BIBLIOGRAPHIC REVIEW OF CLINICAL-THERAPEUTIC ASPECTS

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Abstract: **Introduction:** Goodpasture syndrome (GS) is a severe inflammatory process caused by the development of specific autoantibodies against type IV collagen of the glomerular basement membrane. Lung injury is characterized by hemorrhagic pneumonitis and, in the glomeruli, diffuse endo and extracapillary proliferative injury is observed. Mortality, therefore, approaches 30% of cases, with pulmonary hemorrhage being the main cause – although glomerulonephritis can rapidly progress to chronic renal failure (NUNES et al, 2003). As it is a syndrome relatively little described in the scientific literature and with a very serious prognosis in morbidity and mortality, the current study aims to review clinical and therapeutic aspects of the disease published in recent years **Methodology:** This article is a bibliographic review with a descriptive character, whose collection of scientific articles was carried out in the SCIELO, Google Scholar, PubMed and LILACS system. After selection, an analysis of the clinical-therapeutic aspects of the syndrome was constructed. **Results:** For a clinical diagnosis, the presence of renal and pulmonary manifestations must be identified. The renal picture is manifested with hematuria (stigma of the syndrome), subnephrotic proteinuria (< 3.5g in 24h), oliguria, generalized edema (anasarca) and arterial hypertension. In the complementary exams for glomerulonephritis, it is possible to detect in the urine sediment exam: casts due to erythrocyte dysmorphism (indicating glomerular lesion), pyuria and leukocyte casts. Patients with a suggestive clinical picture must be referred for renal biopsy. For the pulmonary condition, imaging tests can be performed. In very rare cases, lung biopsy will be indicated. Bronchoscopy can be useful to document diffuse alveolar hemorrhage and to rule out an infection, but it is not an initial test. Treatment is performed from

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daily plasmapheresis or every other day until inactivation of anti-GBM in serum, corticosteroids and the immunosuppressant.

Conclusions: In recent years, studies on GS are still incipient. For the most part, a series of punctual old case reports predominate in the scientific literature. In this sense, considering that it is a syndrome of poor prognosis, it is essential that new research be developed in order to deepen the pathophysiological aspects that interfere in the clinical manifestations and in the best therapy for the disease.

Keywords: Goodpasture Syndrome. Anti-GBM glomerulonephritis. Diagnosis. Treatment.

INTRODUCTION

Goodpasture syndrome (GS) is a severe inflammatory process caused by the development of specific autoantibodies against type IV collagen in the glomerular basement membrane. When patients have only the glomerular syndrome, it is characterized as anti-GBM glomerulonephritis, present in up to 30-50% of cases. On the other hand, when a pulmonary hemorrhagic syndrome is associated with a renal condition, in 50-70% of cases, OS is established. The term was introduced in 1958 by Santon & Tange under the analysis of a case report carried out by Ernest Goodpasture about a young man who manifested the disease after an Influenza infection.

In epidemiology, this syndrome is characterized as the first reported case: it affects mainly young men (20-30 years old) with a sex prevalence of 6:1 and is related to the genetic marker HLA-DR2, in addition to lifestyle habits linked to smoking, recent respiratory infection or exposure to volatile hydrocarbons.

The mechanism of kidney and lung injury is complex. In the kidney, antibodies bind to the basement membrane, activate the complement and protease cascade, such activation causes disruption of the glomerular barrier and Bowman's capsule, causing proteinuria, hematuria and facilitating the formation of crescents. The cell sector with CD4 and CD8+ T lymphocytes, macrophages and neutrophils participate in the aggression producing, among others, interleukin 12 and interferon gamma that mediate the formation of crescents (BALDA et al, 2004).

The lung lesion is characterized by hemorrhagic pneumonitis and, in the glomeruli, there is a diffuse proliferative endo and extracapillary lesion (Figure 1). Mortality, therefore, approaches 30% of cases, with pulmonary hemorrhage being the main cause – although glomerulonephritis can rapidly progress to chronic renal failure (NUNES et al, 2003).
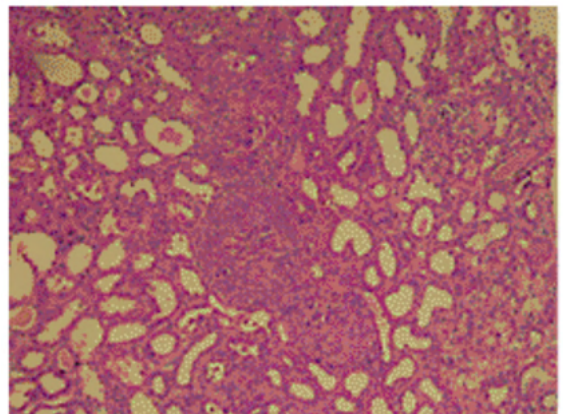

Figure 1: Renal biopsy (HE 400x) showing necrotizing exudative proliferative glomerulonephritis with cellular and fibrocellular crescents in all viable glomeruli, in addition to global glomerular sclerosis of about 30% of the sampled glomeruli, degenerative and necrotic changes in the tubules.

Source: BALDA et al, 2004.

Unlike other ANCA-positive vasculitis, histologically the disease pattern is typically monophasic, with glomerular lesions of similar stage of evolution. In the

immunofluorescence exam almost all the patients present linear deposits of IgG in the basement membrane, C3 and, occasionally, IgA and IgM (BALDA et al, 2004).

As it is a syndrome that is relatively little described in the scientific literature and has a very serious prognosis in terms of morbidity and mortality, the current study aims to review clinical and therapeutic aspects of the disease published in recent years.

METHODOLOGY

This article is a bibliographic review with a descriptive character, whose collection of scientific articles was carried out in the SCIELO, Google Scholar, PubMed and LILACS system. Descriptors defined by DeCs were: Goodpasture Syndrome, Anti-GBM Glomerulonephritis, diagnosis, treatment. Inclusion criteria were articles published between 2004 and 2022, provided that the full text was available and was useful for the clinical and therapeutic description proposed by the topic. There was no need to determine the source language. For exclusion, older articles or articles with little additional information were discarded. After selection, an analysis of the clinical-therapeutic aspects of the syndrome was constructed.

RESULTS

Clinically, pulmonary hemorrhage usually precedes glomerulitis by weeks to months, with hemoptysis as the predominant symptom. Chest radiography (Figure 2) shows diffuse bilateral alveolar infiltrate corresponding to generalized alveolar hemorrhage.
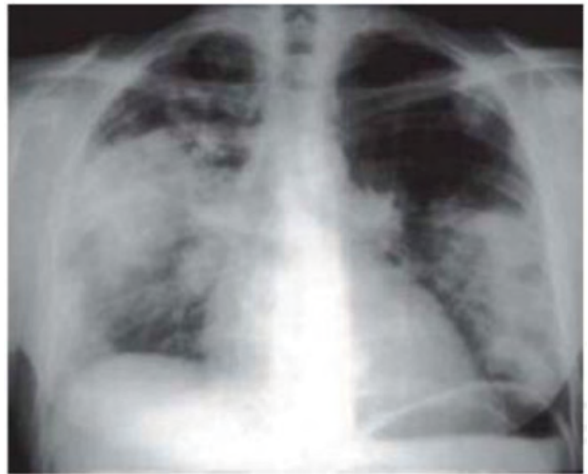

Figure 2. Chest X-ray showing bilateral and asymmetric infiltrates compatible with alveolar hemorrhage.

Source: OTERO et al, 2006.

Hemoptysis can be minimal or massive, although its absence does not exclude pulmonary hemorrhage. When moderate, it may resolve spontaneously or progress to massive hemorrhage in a short period with fulminant respiratory failure. Other manifestations include continuous or episodic dyspnea - a result of compromised ventilation-perfusion secondary to alveolar filling -, fatigue - a significant loss of blood to the lungs can determine a decrease in circulating hemoglobin with the development of anemia - and cough - which is usually acute, but occasionally subacute and recurrent.

Physical examination is usually normal, although lung crackles may be heard. From the heart, there may be a systolic murmur suggestive of mitral stenosis or evidence of pulmonary hypertension. On complementary exams, blood gas analysis shows decreased PO2 and, on bronchoscopy, bleeding can be observed. clearly observe bleeding. As stated, chest radiography shows bilateral, diffuse infiltrates, predominantly central in the lung, and pleural effusion is

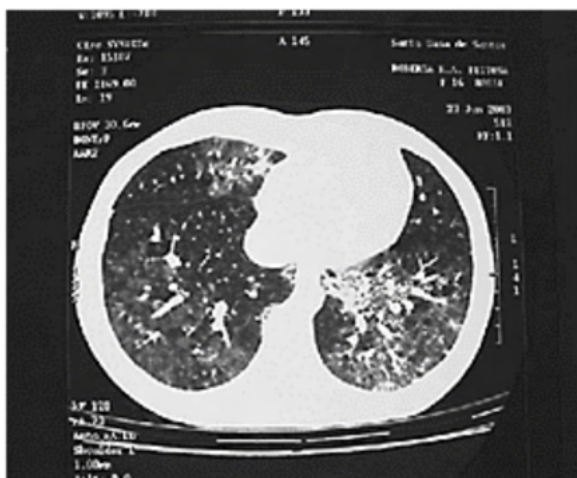rare. Computed tomography (CT) provides higher definition images (Figure 3).

Figure 3. Chest tomography showing ground-glass opacification, diffuse involvement of both lung fields with a more accentuated process at the bases and sparing apexes.

Sourve: OTERO et al, 2006.

For a clinical diagnosis, the presence of renal and pulmonary manifestations (proliferative glomerulonephritis, diffuse pulmonary hemorrhage and the presence of anti-MB antibodies) must be identified. The renal picture is manifested with hematuria (stigma of the syndrome), subnephrotic proteinuria (< 3.5g in 24h), oliguria, generalized edema (anasarca) and arterial hypertension.

Complementary tests for glomerulonephritis can detect: casts due to erythrocyte dysmorphism (indicative of glomerular injury), pyuria and leukocyte casts in the urine sediment test. Epithelial casts are also almost always pathological. Patients with a suggestive clinical picture must be referred for renal biopsy. For the pulmonary condition, imaging tests can be performed. In very rare cases, lung biopsy will be indicated. Bronchoscopy can be useful to document diffuse alveolar hemorrhage and to rule out an infection, but it is not an initial test.

The CO (carbon monoxide) diffusion test can distinguish alveolar hemorrhage from other causes of infiltrate (pneumonia, edema). In hemorrhage, there is increased diffusion of this gas due to the presence of red blood cells in the alveoli, unlike other causes of alveolar occupation.

The differential diagnosis (Table 1) must be made with the other causes of Lung-Kidney Syndrome (hemoptysis + glomerulitis), such as leptospirosis and some systemic vasculitis. 40% of patients may have, in addition to positive anti-GBM, also positive ANCA due to coexistence with systemic vasculitis. It is worth remembering that in anti-GBM glomerulonephritis and in OS there is no drop in complement, unlike what occurs in lupus and cryoglobulinemia.

Lung-Kidney Syndromes
Leptospirosis
Systemic lupus erythematosus
Wegener's granulomatosis
Henoch-Schonlein Syndrome
Polyarteritis Nodosa
Cryoglobulinemia

Table 1. Differential diagnoses of Goodpasture Syndrome.

Treatment is performed from daily plasmapheresis or every other day until inactivation of anti-GBM in serum, corticosteroid (Prednisone 1 mg/kg/day) and immunosuppressant (Cyclophosphamide 2 mg/kg/day or Azathioprine 1-2 mg). /kg/day), the latter being used mainly after remission, in maintenance therapy.

If treatment is started before plasma creatinine exceeds 5 mg/dL, the prognosis will improve, with renal survival of up to 90%. However, it is less than 10% for patients who required dialysis before starting therapy

(ie, those with plasma creatinine values greater than 5 mg/dL). In this sense, kidney transplantation is feasible, but there is the possibility of recurrence of the disease in the graft, and it is recommended to perform it only after the anti-GBM has become negative for at least 2-3 months. This patient's diet will be restricted to sodium - whose intake must be less than 2g per day - and to liquids - which will depend on the renal function of each patient and the use of Cyclophosphamide.

Three months of treatment is usually sufficient to suppress the production of anti-GBM antibodies. After this suppression, cyclophosphamide can be discontinued and the corticosteroid can be gradually weaned. If the treatment is completed, the percentage of relapses is lower. Without treatment, anti-GBM antibodies can remain in the blood for a year or more before disappearing. Patients with an association of ANCAs and anti-GBM antibodies are generally treated for a period longer than three months.

CONCLUSIONS

Among the main clinical aspects of the syndrome, the association between hemoptysis and signs of glomerulonephritis, such as hematuria, hypertension, edema and oliguria, stands out. For definitive diagnosis, imaging tests help in the recognition of alveolar hemorrhage and renal biopsy identifies the diffuse proliferative lesion.

Treatment is based on the plasmapheresis-corticosteroid-immunosuppressive triad and normally lasts around 3 months – enough time for anti-GBM antibody suppression, except for refractory cases, such as in the co-presence of positive ANCAs.

In recent years, however, studies on GS are still incipient. For the most part, a series of punctual old case reports predominate in the scientific literature. In this sense, considering that it is a syndrome of poor prognosis, it is essential that new research be developed in order to deepen the pathophysiological aspects that interfere in the clinical manifestations and in the best therapy for the disease.

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