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DIAGNOSTIC AND THERAPEUTIC MEANDERS IN A WEGENER DISEASE - CASE REPORT AND THERAPEUTIC CHALLENGES

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Abstract

Granulomatosis with polyangiitis (GPA), previously known as Wegener's granulomatosis, is a vasculitis that primarily affects the respiratory tract and kidneys(1). Known as a rare disease, predominantly affects Caucasian adults aged between 45 and 60 years(2). While the specific cause remains unclear, it is believed that environmental factors play a role in triggering the condition in individuals who are genetically predisposed(3).

There is a wide range of clinical manifestations, comprising both general nonspecific symptoms(4) and organ-specific symptoms, with lung involvement in nearly 90% of patients(5). The diagnosis relies on clinical and imaging criteria, along with histopathological confirmation(2). Treatment consists of an induction phase, followed by a maintenance phase, utilizing glucocorticoids and immunosuppressants, which has greatly enhanced the prognosis for these patients(6).

The objective of this paper is to illustrate the complexity of GPA through the presentation of a clinical case. The patient is a 59-year-old man with a professional background involving exposure to respiratory toxins who presented to the clinic with intermittent mucopurulent cough, episodes of hemoptysis, nonspecific chest pain, bilateral knee pain, weight loss, and excessive nocturnal sweating. The imaging findings indicated significant polymorphic lesions in the lungs, and the diagnosis of GPA was confirmed via transthoracic biopsy.

Using a therapeutic strategy of immunosuppression and oral corticosteroid therapy, the patient's clinical condition showed a modest improvement. The particularity of this case lies in the need to revise the treatment strategy for a patient identified as a non-responder to cyclophosphamide, given the imaging, functional and biological decline observed under the initial immunosuppressive therapy.

Keywords: *granulomatosis with polyangiitis, Wegener, vasculitis.*

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Rezumat

Granulomatoza cu poliangeită (GPA), cunoscută anterior sub numele de granulomatoză Wegener, este o vasculită granulomatoasă rară care afectează în principal tractul respirator și rinichii[1]. Cu o incidență de 7-12 cazuri la un milion de persoane anual, GPA afectează predominant adulții caucazieni cu vârste între 45 și 60 ani[2]. Etiologia exactă este necunoscută, dar se consideră că debutul este determinat de influența factorilor de mediu la persoane susceptibile genetic[3].

Manifestările clinice variază considerabil, incluzând simptome generale (fatigabilitate, febră, scădere ponderală)[4] și simptome specifice organului afectat, plămânul fiind implicat în până la 90% dintre pacienți[5]. Diagnosticul se bazează pe criterii clinice și imagistice, precum și pe confirmarea histopatologică[2]. Tratamentul implică o fază de inducție și una de întreținere, cu administrare de glucocorticoizi și imunosupresoare, ceea ce a îmbunătățit semnificativ prognosticul acestor pacienți[6].

Obiectivul acestei lucrări este de a prezenta un caz clinic prin care este ilustrată complexitatea GPA. Pacientul, un bărbat în vârstă de 59 de ani, cu istoric de expunere profesională la noxe respiratorii, s-a prezentat în clinică pentru tuse cu expectorație mucopurulentă, asociind ocazional hemoptizie, gonalgii bilaterale și transpirații nocturne profuze. Investigațiile imagistice au identificat un polimorfism lezional important la nivel pulmonar, iar biopsia transtoracică a confirmat diagnosticul. Sub tratament cu imunosupresoare și corticoterapie, pacientul a evoluat clinic favorabil, însă progresia imagistică a impus reconsiderarea terapiei, care a condus ulterior la ameliorări clinice și funcționale.

Cuvinte cheie: *granulomatoză cu poliangeită, Wegener, vasculită.*

Introduction

Granulomatosis with polyangiitis, also known as Wegener's granulomatosis, is a granulomatous vasculitis characterized by involvement of the upper and lower respiratory tracts, as well as the kidneys[1]. It was first described in 1931 by Klinger and later detailed as a syndrome by Wegener in 1936 and 1939. In 1954, Godman and Churg first referred to it as Wegener's granulomatosis. Since November 2010, the condition has been renamed "granulomatosis with polyangiitis"[7].

GPA is a rare condition, with an incidence ranging from 7 to 12 new cases per million per year, which has increased in recent years, likely due to improved diagnostic methods. Individuals are typically diagnosed between the ages of 45 and 60, with a higher occurrence in Caucasians and no significant gender-related differences in prevalence[2].

While the etiology remains unclear, it is thought that immune processes play a role. Since the respiratory system is most commonly affected, it is believed that granuloma formation is triggered by the inhalation of an antigen and an altered immune response[3].

The clinical picture includes either general symptoms (weight loss, fever, myalgia, arthralgia, fatigue)[4], or organ-specific symptoms. Pulmonary involvement occurs in up to 90% of cases and is clinically expressed as dyspnea, cough, hemoptysis, or chest pain[5].

According to the American College of Rheumatology, the diagnosis of GPA is confirmed by the presence of at least two of the following criteria: sinus involvement, chest X-ray showing opacities with or without cavitation, urinary sediment with hematuria or red cell casts, and histopathological evidence of granulomas either in an artery or in the perivascular region[2]. The prognosis of the disease is unfavorable in the absence of treatment; however, with the advent of new therapeutic regimens, survival rates can reach 80% at 10 years post-diagnosis[2]. Treatment includes an induction phase followed by a maintenance phase and is based on immunosuppression.

The most commonly used agents in therapy are glucocorticoids, cyclophosphamide, rituximab, azathioprine, and methotrexate[6]. Thanks to advances in therapy, GPA has become a chronic, relapsing condition, and maintenance therapy to prevent relapses remains the primary challenge[2].

Case Presentation

We present the case of a 59-year-old male patient, a non-smoker, with occupational exposure to multiple respiratory toxins due to 13 years of work in an industrial environment characterized by dust, paint vapors, and exhaust gases. His medical history includes grade II hypertension with a high-risk profile and type II diabetes, which is managed with oral antidiabetic medications, without the need for insulin.

The patient presented to our clinic for a pulmonary evaluation, referred by a pulmonologist from a regional medical service, where the etiological diagnosis of a polymorphic lesion identified by CT imaging could not be established. Both the imaging findings and clinical progression were unfavorable despite dual antibiotic therapy with second-generation cephalosporins and fluoroquinolones.

CT evaluations revealed two pseudonodular areas: one with a tendency to cavitate, located subpleurally in the anterior segment of the right upper lobe (RUL), and another described as a cavitary lesion with a thick wall

in contact with a bronchial branch, located in the anterior segment of the left upper lobe (LUL). Slight dimensional progression was noted after antibiotic therapy. It is important to note that the CT images are not available at the time of this writing.

At the time of presentation in our clinic, the patient reported a clinical history with onset one year earlier, characterized by intermittent mucopurulent cough, episodes of hemoptysis, nonspecific posterior chest pain, bilateral knee pain, weight loss, and profuse nocturnal sweating. Upon clinical examination, the patient was stable from a respiratory perspective, normoxemic, with bilateral vesicular breath sounds present and no added pulmonary rales. Nevertheless, the assessment revealed minimal bilateral oedema in the lower extremities, noticeable superficial venous patterns in the lower limbs, and a body mass index of 29 kg/m^2, indicating a status of overweight.

Pulmonary functional testing, performed through spirometry and carbon monoxide diffusing capacity test, showed results within normal limits.

The imaging investigation consisting in a posteroanterior chest X-ray, revealed multiple pseudonodular opacities, some of which were poorly defined and relatively inhomogeneous, with an apparent outline of air bronchograms. These opacities were located in both lung fields, primarily in the upper two-thirds, including a cavitary lesion with a thick wall in the middle third of the left lung field (Figure 1).

Additionally, a fiberoptic bronchoscopy was performed, revealing moderate mucosal congestion with minimal blood-tinged streaks in the left bronchial tree; however, no evident proliferative elements were visible in the examined areas. The bronchoalveolar lavage from the left upper segment did not yield significant diagnostic information, as there was no evidence of an infectious or neoplastic process.

Since the etiology of the polymorphic lesion responsible for the patient's symptoms could not be established despite exhaustive investigations, the next step in the diagnostic process was a CT-guided biopsy of the lesion located in the right upper lobe. Given that the immunohistochemical results indicated chronic granulomatous inflammation without specific characteristics, a week later, a second CT-guided biopsy was performed on the lesion in the left upper lobe, followed by a rapid histological examination of the biopsy fragment, which confirmed a diagnosis of granulomatosis with polyangiitis.

At that time, the posteroanterior chest X-ray revealed multiple nodular opacities of moderate intensity and variable sizes, which were poorly defined, with irregular margins, distributed throughout both lung fields (Figure 2). Notably, there was a significantly

	T1	T3	T7	T14
FVC%	94.5	95	94.5	98
FEV1%	91.5	91.7	86.4	92.6
TI%	76.71	76.34	72.24	74.46
MEF50%	79.1	69.6	50.6	71.9
DLCO%			82	88.7
Interpretation	N	N	Distal obstructive syndrome	N

Table 1. *Respiratory functional tests. T1 - Month 1 from the time of presentation in our clinic, T7 - At 6 months after the initiation of treatment, T14 - Last functional evaluation, at 7 months from the reassessment of therapy. N - Normal values.*

Laboratory test	Values	Normal range
ESR (mm/h)	57	2 - 20
CRP (mg/L)	84.08	0 - 5
Fibrinogen (mg/dL)	503	238 - 498
WBC (*10^3/µL)	13.85	3.9 - 10.9
Neutrophils (*10^3/µL)	10.43	1.8 - 6.98
Hemoglobin (g/dL)	12.2	13.5 - 16.9
MCV (fL)	81.5	81.8 - 95.5
MCHC (g/dL)	32.2	32.4 - 35
Glucose (mg/dL)	145	74 - 106

Table 2. *Laboratory blood test*

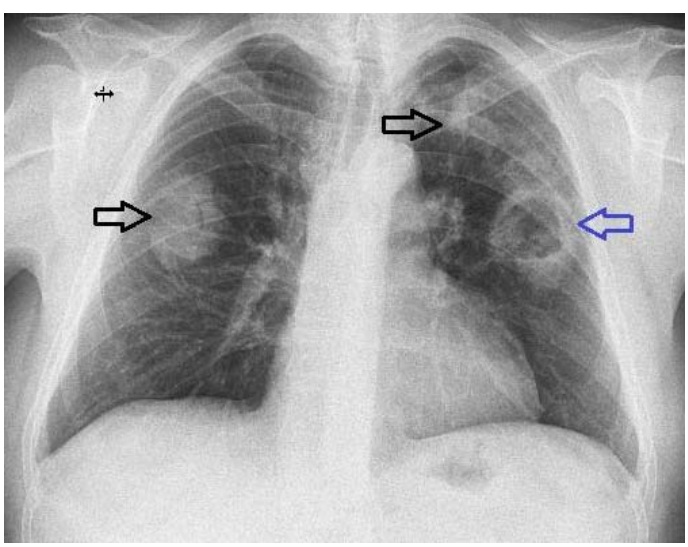

Figure 1. *Chest X-ray PA - Multiple pseudonodular opacities, some poorly defined and relatively heterogeneous, with an apparent outline of an air bronchogram, located in both upper lung fields (black arrows), including a cavitary image with a thick contour in the middle third of the left lung field (blue arrow)*

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elevated titre of cANCA antibodies (>100 UI/mL) along with a pronounced inflammatory syndrome.

The chest CT scan further described areas of pulmonary consolidation in the bilateral upper segments, although with dimensional regression, associated with satellite nodular lesions, some of which were cavitated and had thick walls. Moreover, sequelae were noted, characterized by the presence of fibrotic bands and bronchiectasis (Figure 3).

The diagnosis of granulomatosis with polyangiitis, involving both pulmonary and joint manifestations, was supported by a correlation of clinical and paraclinical data, including the patient's symptoms, significant inflammatory syndrome, elevated cANCA titre, imaging findings, and, most importantly, histopathological results.

In this context, first-line therapy was initiated, consisting of immunosuppression with cyclophosphamide and corticosteroid therapy with prednisone, followed by an augmentation of the treatment regimen through the introduction of mycophenolate mofetil. Six months after the initiation of the recommended treatment, the patient returned for pulmonary reevaluation. Although there was a noted improvement in symptoms under the treatment, with persistent episodes of mucopurulent cough, the evaluation indicated an unfavorable clinical progression, as evidenced by the presence of hypoxemia (O2 = 88% in room air at rest) as well as paraclinical findings. Functionally, a distal obstructive syndrome developed (Table 1 – T7), most likely secondary to bronchial distortions caused by the disease. Imaging revealed a numerical progression of cavitary lung lesions and the acquisition of endobronchial features, changes identified both on the plain chest X-ray (Figure 4) and on the chest CT scans (Figure 5, Figure 6).

At that time, from a biological standpoint (Table 2), the blood tests revealed a nonspecific inflammatory syndrome (CRP = 84.08 mg/L, ESR = 57 mm/h, fibrinogen = 503 mg/dL), along with markers of infection (WBC = 13.85 × 10^3/µL, neutrophils = 10.43 × 10^3/µL), mild normochromic normocytic anemia (Hb = 12.2 g/dL), and hyperglycemia (glucose = 145 mg/dL).

The complete urine examination revealed leukocyturia and proteinuria, findings suggestive of renal involvement due to GPA, particularly considering that the urine culture excluded a possible urinary infection that could account for these changes.

On one hand, in the context of the infection markers identified in the blood tests, as well as the described clinical status, the possibility of a bacterial superinfection of the pulmonary lesions was considered. This led to the decision to initiate a short course of empirical antibiotic therapy with an oral fluoroquinolone, under

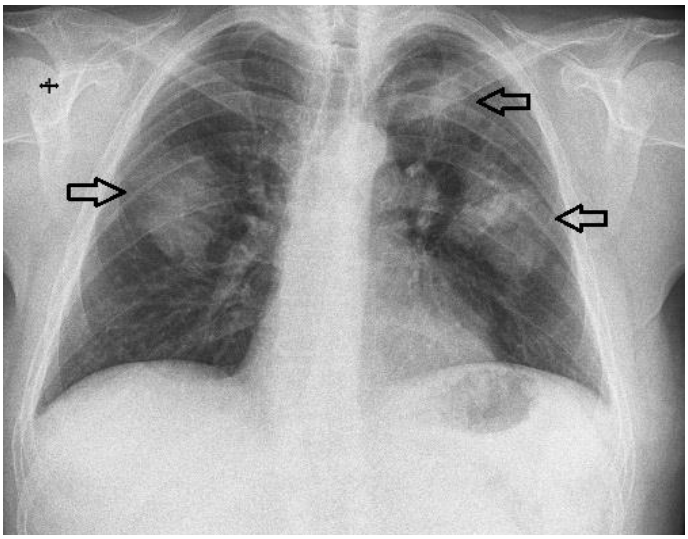
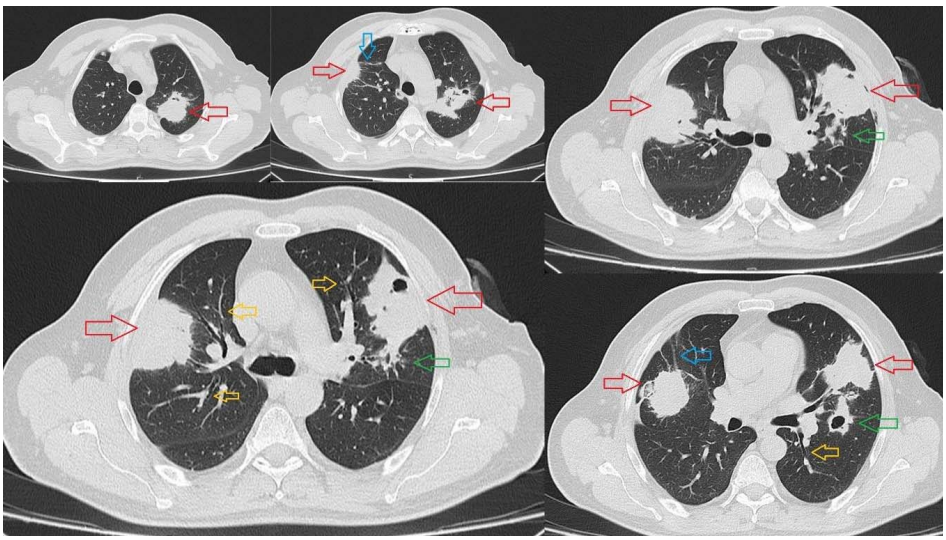


Figure 2. *Chest X-ray PA - Multiple nodular opacities of medium intensity and variable sizes, poorly defined, located in both lung fields (black arrows)*



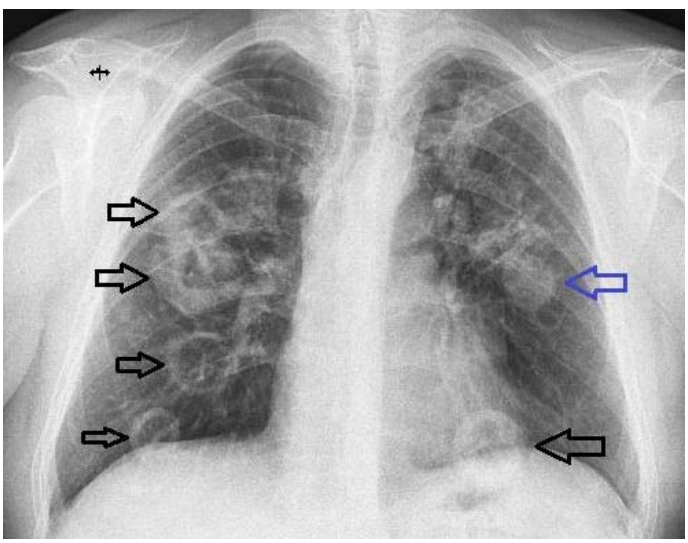


Figure 3. *CT scan - Areas of pulmonary consolidation in the bilateral upper lobes (red arrows), satellite nodular lesions, some cavitary and with thick walls (green arrows), fibrotic bands (blue arrows), and bronchiectasis (yellow arrows)*

Figure 4. *Chest X-ray PA - Nodular opacities (blue arrows), some with a tendency to cavitation (black arrows), diffusely distributed bilaterally*

which significant clinical progress was noted.

On the other hand, given the negative functional and imaging progression, it was decided to suspend the administration of cyclophosphamide and to initiate biological therapy with rituximab, combined with an oral treatment regimen that included mycophenolate mofetil and prednisone. Seven months after the treatment modification, the patient presented for reevaluation, exhibiting complete remission of symptoms and a normal clinical examination, including normoxemia. Additionally, favorable paraclinical evolution was observed, as evidenced by the numerical and dimensional reduction of the previously described pulmonary lesions (Figures 7, 8, 9), biological parameters (blood tests with normal values), and functional parameters, demonstrated by the normalization of pulmonary volumes (Table 1 – T14).

Notably, the urine examination revealed leukocyturia and microscopic hematuria, findings that further support the renal involvement in the context of GPA, subject for further investigation.

Discussion

GPA is considered a multisystem autoimmune condition[8] that affects small blood vessels[9] through necrotizing granulomatous inflammation and pauci-immune vasculitis. The disease was first described in detail in 1936, following an autopsy on a 38-year-old patient, performed by Wegener, assistant professor in the Department of Pathology at the University of Kiel, at that time. The patient had died after a prolonged febrile syndrome, associated with uremia and a saddle-shaped deformity of the nose. Autopsy findings revealed destruction of the nasal septum, inflammation of the nasal mucosa and cartilage, as well as involvement of the entire upper respiratory system and kidneys. Histopathological examination identified necrotizing granulomatous inflammation and necrotizing glomerulonephritis.

Wegener was aware of a report presented by his friend Heinz Klinger, a former colleague from the Faculty of Medicine, who had identified a similar case in 1931, along with other relevant cases. This familiarity led him to recognize the importance of a thorough study of this condition. The significance of Wegener's work was fully appreciated for the first time in 1954 when Godman and Churg published an article titled "Wegener's Granulomatosis". Notably, during his lifetime, Wegener witnessed studies demonstrating the significant impact of cyclophosphamide on the disease's course - once considered fatal - as well as the identification of anti-neutrophil cytoplasmic antibodies (cANCA) as a marker of the disease[8]. However, it is important to note

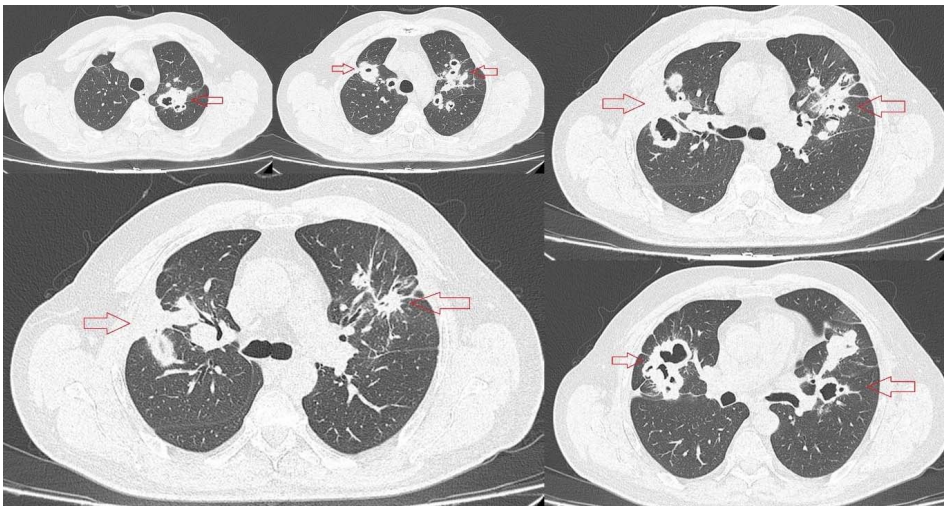


Figure 5. *CT scan - Dimensional regression of nodular lesions in the right and left lower lobes, currently with cavitary images (red arrows)*

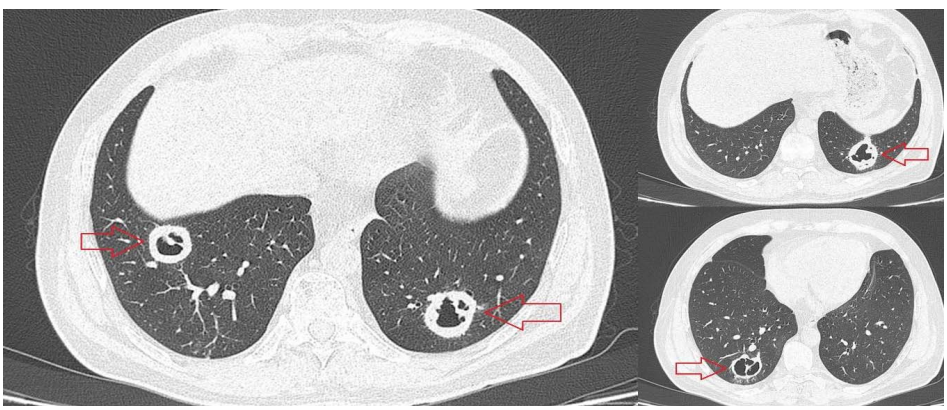


Figure 6. *CT scan - Cavitary images in the bilateral lower lobes*

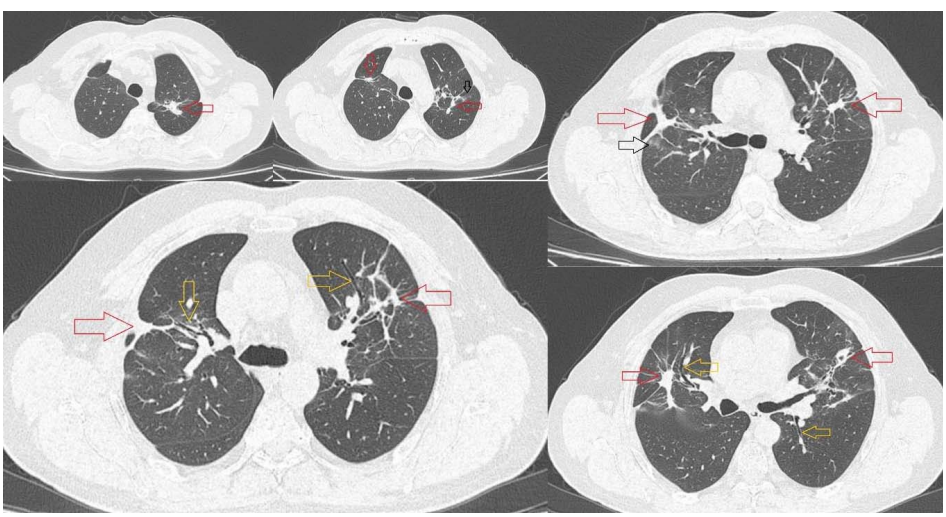


Figure 7. *CT scan - Bilateral spiculated pseudonodular consolidations (red arrows), cylindrical bronchiectasis (yellow arrows), and minimal areas of ground-glass opacity adjacent (black arrows)*

that since November 2010, Wegener's granulomatosis has been renamed granulomatosis with polyangiitis, reflecting a transition to a nomenclature for vasculitis that avoids eponyms[7].

Epidemiology

GPA is a rare condition, with an estimated incidence ranging from 0.4 to 11.9 cases per million per year[4]. It is diagnosed in Caucasians aged between 9 and 78 years, with an average age of 41[3], and no gender predominance is observed. In Europe, it is most commonly found in Nordic countries[2]. The prevalence of GPA has likely increased in recent years, attributed to the widespread use of cANCA testing[4].

Etiology

The exact etiological factor is not known, but it is believed to be non-specific[2]. The onset of the disease may be influenced by environmental exposure to infectious, chemical, toxic, and pharmacological factors[4] in genetically and epigenetically susceptible individuals[10]. Genetic elements that have shown some influence on the etiology of GPA include HLA-DPB1*0401 and HLA-DPB4. Additionally, the association with HLA-DP, SERPINA1, and PRTN3 is characteristic of PR3-ANCA specificity. Furthermore, the aberrant expression of proteinase 3 (PR3) and myeloperoxidase (MPO), which are proteins specific to neutrophils (10), leads to the formation of cANCA and pANCA antibodies identified in patients with GPA[11]. cANCA antibodies directed against PR3 are present in 65% to 75% of patients, while pANCA antibodies directed against MPO are found in 20% to 30%[4].

Exposure to dust or silica is noted in 10% of patients with GPA[2]. The concept of seasonality has also been discussed, with many case reports suggesting an increased incidence during the colder months (29.8%)[12]. The production of ANCA can be induced by certain drug agents; antibiotic, oncological, biological therapies, and cocaine may potentially play a role in the onset of GPA[10]. Evidence of potential involvement is closely associated with Staphylococcus aureus[4], as patients often present with nasal carriage of this infectious pathogen, which also influences the recurrence rate of the disease. Additionally, other studies have shown a strong association between GPA and the presence of IgG antibodies against cytomegalovirus (CMV)[13].

Pathophysiology

The formation of cANCA antibodies against PR3 and MPO leads to an immune-mediated vasculitis that affects small and medium

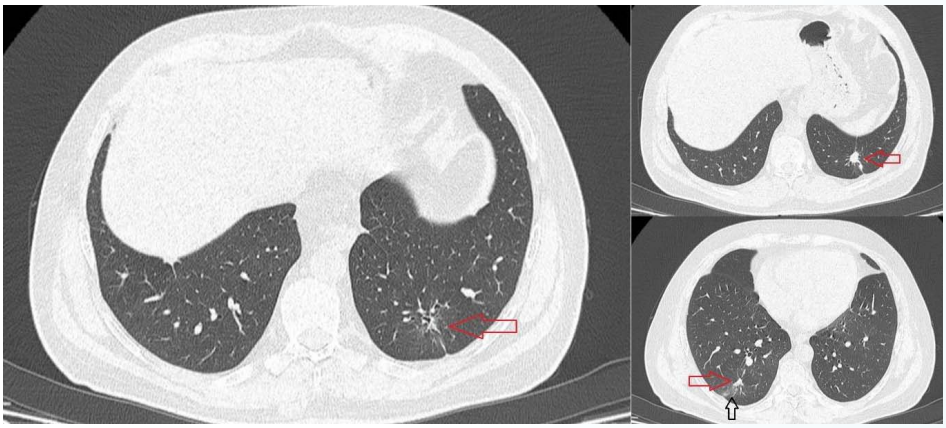


Figure 8. *CT scan - Bilateral spiculated pseudonodular consolidations (red arrows), minimal areas of ground-glass opacity adjacent (black arrow)*

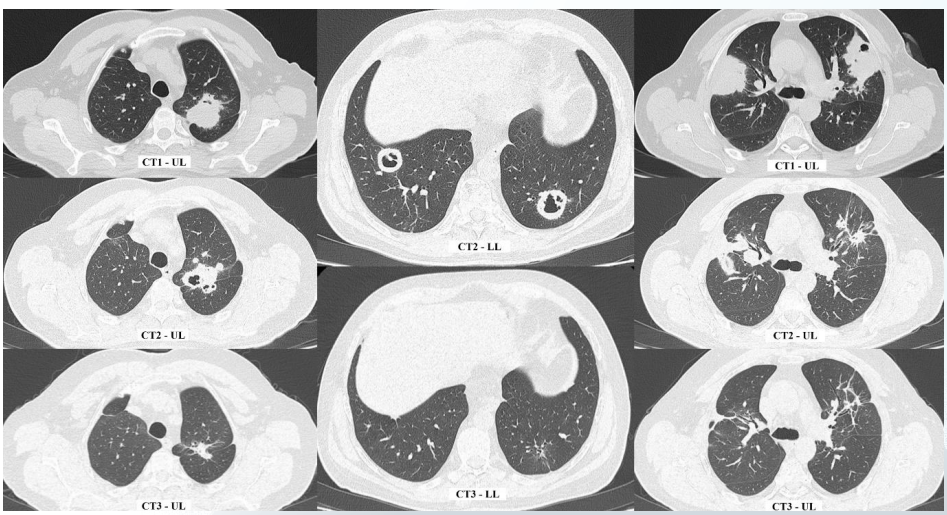


Figure 9. *CT scan - Favorable imaging evolution with a numerical and dimensional reduction of the lesions. CT1 - CT performed at the time of diagnosis. CT2 - CT performed post-therapy with cyclophosphamide. CT3 - CT performed post-therapy with rituximab. UL - upper lobes. LL - lower lobes*

blood vessels. This vasculitis most commonly involves the auditory system, nose, pharynx, larynx, trachea, lungs, and kidneys[6]. If renal involvement occurs, GPA has a mortality rate of 21.5% at 5 years[14]; however, significant morbidity is also associated with necrotizing sinusitis or pulmonary capillaritis that may arise. Granuloma formation begins with the presence of neutrophilic microabscesses. These microabscesses contain plasma cells, lymphocytes, and dendritic cells arranged circumferentially, with a center composed of giant cells. Granulomas can cause partial or total obstruction of blood vessels, leading to tissue necrosis and deformation[6].

Clinical and Paraclinical Picture

Typically, GPA manifests through symptoms characteristic of upper and lower respiratory tract involvement, systemic vasculitis, and renal impairment. From the onset of the disease, a patient with GPA may report nonspecific general symptoms such as fatigue, fever, loss of appetite, weight loss, myalgias, and arthralgias[6], which occur in approximately 50% of cases.

Since the clinical case presented is based on respiratory manifestations, which are the most common, we will focus on pulmonary involvement, which occurs in 50-90% of patients with GPA[2]. Thus, the patient may either be asymptomatic[3] or report episodes of cough, with or without hemoptysis, dyspnea, and chest pain characterized by discomfort or a pleuritic nature[6].

Imaging findings in GPA may present as pulmonary infiltrates, pulmonary nodules, or pleural effusion[6], which can be identified both on plain radiographs and chest CT scans in 85% of patients with GPA[4]. Pulmonary infiltrates may be unilateral or bilateral[6], predominantly located in the upper lobes[3]. Pulmonary nodules can be singular or multiple[2], typically round to oval in shape[4], with a tendency to cavitate[3] and can reach a diameter of up to 10 cm. Cavitary lesions may have either thin or thick walls and are observed in 25% of cases when the nodules exceed 2 cm[4]. These nodular opacities may be surrounded by a "ground-glass" appearance on high-resolution computed tomography, also known as the "halo sign", which suggests the presence of alveolar hemorrhage that occurs following necrotizing capillaritis.

Less frequently, GPA may present radiologically as pleural involvement, mediastinal or hilar lymphadenopathy, or interstitial lung disease[4]. A major cause of morbidity in this context is diffuse alveolar hemorrhage[6], which can lead to respiratory failure. Endobronchial involvement occurs less often in GPA, affecting 16% of cases[2], and it was also observed during the pharmacological treatment of the case discussed in this paper.

In terms of laboratory analyses, the cANCA titer is of great importance, serving as a marker with high sensitivity and specificity for GPA. It is positive in 90%-95% of cases of generalized acute GPA and in 60% of localized GPA cases. A negative cANCA titer does not exclude the diagnosis of GPA[3]. Other biological changes may include normochromic, normocytic anemia, leukocytosis, eosinophilia, and significant inflammatory syndrome characterized by increased erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels. Additionally, depending on the extent of the disease, serum tests may reveal hypoalbuminemia, microhematuria, proteinuria, or the presence of hematic casts in urine tests. Rheumatoid factor may be positive, and gamma-globulins may exceed normal upper values[3]. Functionally, obstructive syndrome of varying degrees may be evidenced by airway involvement due to disease-specific changes.

The three histopathological elements that establish the diagnosis of GPA are vasculitis of small and medium vessels, necrotizing granulomas, and inflammatory infiltrates[15]. Microscopy reveals parenchymal necrosis in the form of neutrophilic microabscesses or an extensive area of necrosis[4], as well as granulomas and vasculitis[3], with infiltration of neutrophils, lymphocytes, plasma cells, histiocytes, and/or eosinophils[4]. Although pulmonary tissue can be obtained through bronchoscopy, positive diagnostic criteria are most frequently met through surgical approaches. Bronchoscopy may reveal the presence of a superimposed infection, alveolar hemorrhage, or eosinophilia in bronchoalveolar lavage fluid. Nevertheless, surgical lung biopsy via video-assisted thoracoscopy often provides a definitive pathological diagnosis[15]. It is important to note renal involvement, which leads to a high mortality rate in patients with GPA, most commonly expressed as glomerulonephritis, manifested by proteinuria and microhematuria. Renal biopsy establishes both the diagnosis and prognosis of the disease[2].

Joint involvement, also mentioned in the presented clinical case, manifests as symmetrical polyarthralgias or arthritis, with predominant involvement of the knees and talocrural joints[3].

Positive Diagnosis

The diagnosis of GPA is suspected in patients presenting with multisystem involvement, including the upper and lower respiratory systems, glomerulonephritis, or vasculitis affecting any organ. Historically, the gold standard for diagnosis was defined by the identification of necrotizing granulomatous inflammation in the histopathological examination of a pulmonary specimen. However, this may yield false-negative results, as the lungs are not affected in 100% of cases, especially at the onset of the disease[3].

According to the American College of Rheumatology, the diagnosis of GPA is defined by the presence of at least two of the following criteria established since 1990: nasal or oral involvement, modified chest radiography, pathological values in urinary sediment, and histopathologically confirmed granulomatous inflammation. Thus, the diagnosis is based on correlating clinical findings (oral ulcers, purulent nasal discharge, epistaxis), pulmonary imaging (nodules, infiltrates, and cavitary opacities), urinary findings (microhematuria or hematic casts), and histopathological results (granulomatous inflammation in the walls of arteries or perivascular areas)[16].

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Differential Diagnosis

Differential diagnosis may include other forms of cANCA-positive vasculitis, such as Churg-Strauss syndrome, Goodpasture syndrome, MPA, and Henoch-Schönlein purpura, as well as infections caused by mycobacteria or fungi, malignant conditions (including lymphomas, lymphomatoid granulomatosis, and carcinomatosis), and autoimmune diseases (such as systemic lupus erythematosus, rheumatoid arthritis, and amyloidosis)[6].

In the case presented, infections were initially ruled out through a therapeutic test with empirical antibiotic therapy. The absence of clinical and imaging responses to the antibiotic treatment, along with bronchoalveolar lavage results that lacked diagnostic significance, excluded infection as the primary etiology.

Sarcoidosis, a systemic condition with similar imaging findings, is generally associated with normal cANCA levels and was definitively excluded based on the histopathological results specific to GPA. Additionally, the microscopic appearance, along with the absence of proliferative tumor elements observed during the fibrobronchoscopy examination, significantly contributed to the exclusion of pulmonary neoplasms.

Moreover, in the context of exposure to respiratory irritants, the diagnosis of hypersensitivity pneumonitis was considered; however, this hypothesis was refuted by the incompatible imaging findings and histopathological examination.

Treatment

Immunosuppressive treatment with cyclophosphamide and corticosteroids has been the first-line therapy for patients with GPA for many years. Although it has yielded very good results, achieving complete remission in 70% of patients and significant improvement in 90% of cases, it has been associated with important adverse events, primarily due to the effects of cyclophosphamide, such as cystitis, bladder cancer, and myelodysplasia[5]. Currently, a structured two-phase treatment approach is recommended: induction of remission lasting 3-6 months, followed by maintenance therapy for 12-24 months. Corticosteroids are included in all induction regimens and are typically tapered off gradually once remission is achieved[1]. The induction phase is recommended to be based on a combination of corticosteroids and immunosuppressants. For mild forms of the disease, oral prednisone is administered at a dose of 1 mg/kg/day, which may be preceded in severe cases by intravenous bolus methylprednisolone for 1-3 days[2]. For less severe forms of the disease, methotrexate is the preferred immuno-suppressant[1]. Treatment with rituximab, a

monoclonal anti-CD20 antibody, has shown favorable results, demonstrating in studies to be non-inferior to cyclophosphamide in inducing remission in severe ANCA-associated GPA[17]. Additionally, rituximab has been shown to be a safe option for pregnant women. For maintenance therapy, a combination of oral corticosteroids with azathioprine or methotrexate may be utilized[2].

Mycophenolate mofetil, a purine synthesis inhibitor, is considered for both inducing remission and maintenance therapy, although it has yielded suboptimal results. Other agents have also been explored, but they have not significantly influenced disease progression and likely require further studies[18].

Prognosis

Although recent studies on GPA have resulted in improved diagnostic and therapeutic management, a high degree of morbidity and mortality persists due to potential irreversible organ dysfunctions, such as respiratory failure and chronic kidney disease, as well as adverse events associated with the long-term use of immunosuppressive agents and corticosteroids. Patients may experience significant complications, including hearing loss or complete deafness, blindness, multiple mononeuropathy, and an increased cardiovascular risk due to vascular processes[6]. In terms of mortality, patients with GPA have a 2.6 times higher risk of death compared to the general population. The survival rate is 60% to 70% ten years after diagnosis; however, in patients with renal involvement, it drops to only 40%[19].

Conclusions

This particular case highlights a pathology that continues to garner significant interest in both the diagnostic process and therapeutic approach. The peculiarity of this case lies in the complexity of managing a patient with GPA, which required multiple evaluations and therapeutic adjustments in the context of a rare condition associated with substantial morbidity.

A thorough medical history and well-developed clinical intuition remain fundamental elements in establishing diagnostic accuracy. A comprehensive evaluation is essential to exclude other potential pathologies. Access to high-quality paraclinical investigations has been a crucial factor, necessitating extensive assessments, including CT-guided biopsy and histopathological examination. In addition to pulmonary and joint involvement, renal involvement in GPA, indicated by changes in urinalysis, necessitates ongoing monitoring and further evaluation.

Although the treatment of granulomatosis with polyangiitis has evolved in recent years, an inconsistent therapeutic response remains a possibility. While this is less commonly encountered at the onset of the disease, it can negatively impact its progression. In this context, a multidisciplinary approach and a rigorous selection of optimal therapeutic strategies are essential for achieving remission and improving patients' quality of life.

Conflict of interest

There was no conflict of interest.

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