THE ROLE OF PULMONARY BIOPSY IN THE DIAGNOSIS OF INTERSTITIAL LUNG DISEASES

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Abstract
Background. Granulomatosis with polyangiitis (GPA) is a rare autoimmune disease characterized by diverse clinical symptoms and radiological presentations, which often make diagnosis challenging. Pulmonary nodules associated with GPA can mimic malignancies or other pulmonary conditions, necessitating thorough evaluation to achieve a definitive diagnosis.
Case Report. A 45-year-old female presented with a two-month history of systemic symptoms and respiratory issues. Initially followed in the infectious diseases department, she was referred to our service with suspicion of lung cancer after inconclusive laboratory and imaging studies. Contrast-enhanced computed tomography (CT) revealed two opacities in the right lung with significant enhancement. Subsequent endoscopic biopsy confirmed the diagnosis of granulomatosis with polyangiitis. Treatment with corticosteroid and immunosuppressant was initiated, leading to clinical improvement.
Conclusion. The differential diagnosis of pulmonary nodules encompasses a wide range of conditions, including malignant tumors, infectious or non-infectious granulomas, and other entities such as bronchiolitis obliterans organizing pneumonia (BOOP), pulmonary infarction, or arteriovenous malformations. In patients without risk factors for malignancy, such as non-smokers, systemic symptoms can guide alternative diagnostic pathways. Pulmonary biopsy remains a cornerstone in cases where clinical, laboratory, and imaging findings are inconclusive. This case highlights the importance of multidisciplinary evaluation in diagnosing complex pulmonary conditions and tailoring appropriate treatment strategies.

Key words: pulmonary biopsy, ILD, granulomatous polyangitis

ROLI I BIOPSISË PULMONARE NË DIAGNOZËN E SËMUNDJES INTERSTICIALE PULMONARE

Hyrje. Poliangiti granulomatoz (GPA) është një sëmundje autoimune e rrallë, e karakterizuar nga simptoma klinike dhe paraqitje radiologjike të ndryshme, të cilat shpesh e bëjnë diagnostikimin të vështirë. Nodujt pulmonarë të lidhur me GPA mund të imitojnë malinje ose kushte të tjera pulmonare, duke kërkuar një vlerësim të plotë për të arritur një diagnozë përfundimtare.
Rasti Klinik. Një paciente 45-vjeçare u paraqit me një histori 2-mujore të simptomave sistemike dhe problemeve respiratore. Fillimisht e ndjekur në departamentin e sëmundjeve infektive, ajo u referua në shërbimin tonë me dyshimin për kancer të mushkërive pas studimeve laboratorike dhe imazherike të pasakta. Tomografia e kompjuterizuar (CT) me kontrast zbuloi dy opacitete në mushkërinë e djathtë me përmirësim të dukshëm. Biopsia endoskopike pasuese konfirmoi diagnozën e Poliangiti granulomatoz. Trajtimi me kortikosteroide dhe imunosupresantë u nis, duke çuar në përmirësim klinik.
Konkluzion. Diagnoza diferenciale e nodujve pulmonarë përfshin një gamë të gjerë kushtesh, si tumoret malinje, granulomat infektive ose jo-infektive, dhe entitete të tjera si bronchioliti

obliterans me pneumoni organizuese (BOOP), infarkti pulmonar, ose malformimet arterio-venoza. Tek pacientët pa faktorë rreziku për malinje, si mos-pirësit e duhanit, simptomat sistemike mund të drejtojnë shtigje diagnostikuese alternative. Biopsia pulmonare mbetet një gur themeli në rastet kur gjetjet klinike, laboratorike dhe imazherike janë të pamjaftueshme. Ky rast nënvizon rëndësinë e vlerësimit multidisiplinar në diagnostikimin e kushteve komplekse pulmonare dhe përshtatjen e strategjive të duhura të trajtimit.

Fjalë kyçe: biopsi pulmonare, ILD, poliangiti granulomatose.

Introduction

Pulmonary nodules are small abnormal areas (less than 3 cm) sometimes discovered incidentally during routine chest CT scans. They are usually non-malignant, and based on a scoring system, they are monitored with follow-up CT scans after 3–6 months to assess for size changes over time. However, nodules detected during lung cancer screening are typically considered malignant and are managed differently. Granulomatosis with polyangiitis (GPA), also known as Wegener's granulomatosis, is a necrotizing systemic vasculitis (1). Although diagnosing GPA remains challenging in clinical practice, non-pulmonary manifestations, serological tests, and histopathology obtained via endobronchial, transbronchial, or transthoracic approaches can aid in reaching a diagnosis (2,3). This article presents a clinical case diagnosed and treated in our service, following a multidisciplinary approach and based on available literature from online databases, regarding the challenges of diagnostic processes and disease management.

Case presentation

This clinical case involves a 45-year-old female patient referred to our service from the Infectious Diseases Department, where she had been hospitalized for a prolonged febrile condition initially considered a viral infection. During her stay, she underwent a pulmonary CT scan, which revealed two pulmonary opacities in the right lung, raising suspicion of a malignant process, specifically lung cancer. Her two-month clinical history included various symptoms such as jaw pain, nasal congestion, and a feeling of ear blockage accompanied by hearing loss. She also reported recurrent episodes of high fever, reaching up to 39°C over the previous two weeks, which did not respond to different antibiotic treatments, either outpatient or during hospitalization. Laboratory examinations showed microcytic hypochromic anemia and elevated inflammatory markers, including CRP, D-dimer, fibrinogen, and ferritin. A urinalysis was normal, while total IgE levels were within acceptable limits. Tests for anti-echinococcus antibodies, direct sputum analysis, and GeneXpert for tuberculosis were all negative, ruling out common infectious causes. To refine the diagnostic process, the patient underwent a contrast-enhanced CT scan, which revealed a spiculated peripheral opacity in the third segment of the right lung, measuring 21x16 mm. This opacity demonstrated increased density after contrast injection, rising from 24 HUI to 45 HUI, further reinforcing suspicions of a malignant process.

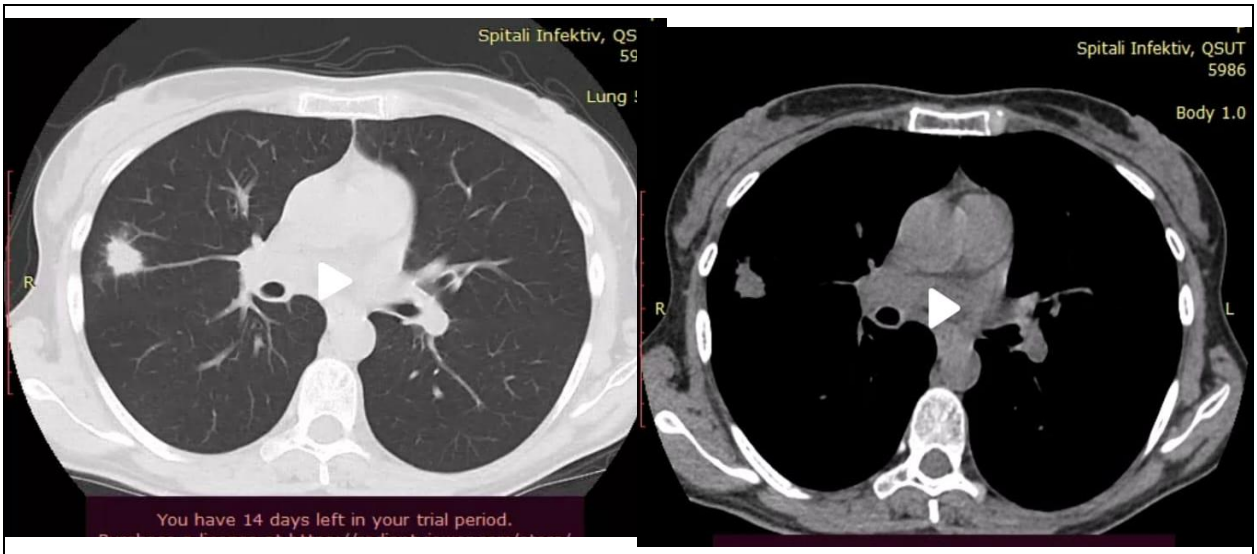

Figure 1. Under computerized tomography two opacities where noticed on the right lung

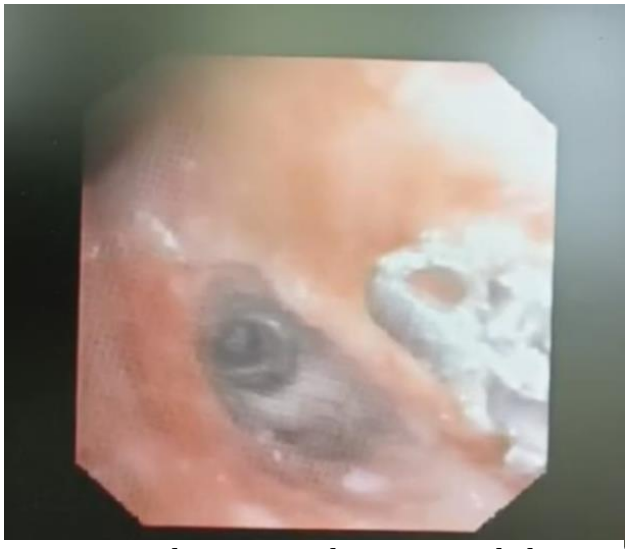

Figure 1. Endoscopic evaluation revealed infiltration of tracheal carina and right primary bronchus with necrotic elements on the surface.

Endoscopic evaluation identified infiltration of the tracheal carina extending toward the primary right bronchus, accompanied by visible necrotic elements on the mucosal surface. A biopsy was taken during this procedure and subsequently analyzed histopathologically. Concurrently, the patient was assessed by a rheumatologist, who requested a complete autoimmune panel. Meanwhile, treatment with Cefuroxime (750 mg), Prednisolone (50 mg daily), and supportive therapy was initiated. Within two days of starting treatment, the patient's febrile condition improved, and the fever did not recur.

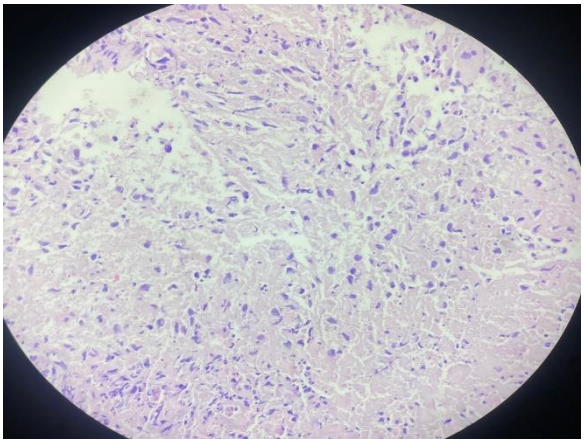

Figure 2 Pathological evaluation resulted as granulomatous necrotic inflammation with giant multinuclear cells.

The autoimmune panel was negative for ANA, RF, anti-CCP, ENA screen, anti-dsDNA, C3, and C4. However, PR3-ANCA tested positive, with a very high level of 356.09 RU/mL (normal value <20), suggesting the presence of an autoimmune pathology. Ten days later, histopathological analysis of the biopsy material revealed necrotizing granulomatous inflammation with multinucleated giant cells. These findings confirmed the diagnosis of Granulomatosis with Polyangiitis (GPA). The patient was treated with a corticosteroid regimen (75 mg daily, with a gradual dose tapering weekly) and immunosuppressants (Cyclophosphamide). Following an intensive treatment period, she was discharged from the hospital with significant improvement in her clinical and radiological condition. This case underscores the importance of a multidisciplinary approach and advanced diagnostic procedures in identifying and accurately treating rare pathologies such as Granulomatosis with Polyangiitis.

Discussion

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis, is a rare systemic vasculitis that primarily affects small and medium-sized blood vessels, often involving the upper respiratory tract, lungs, and kidneys. It is characterized by the presence of necrotizing granulomas, vasculitis, and autoantibodies against proteinase 3 (PR3), known as anti-neutrophil cytoplasmic antibodies (ANCA). This case highlights the clinical, diagnostic, and therapeutic challenges associated with GPA, particularly in patients with overlapping characteristics that mimic malignancy (4).

Clinical Presentation and Challenges

The patient's presentation with prolonged fever, jaw pain, nasal congestion, and hearing loss posed an initial diagnostic dilemma. Such symptoms are nonspecific and can overlap with many conditions, including chronic infections, malignancies, or other systemic autoimmune diseases (5). GPA often manifests with upper respiratory tract symptoms that can mimic chronic sinusitis or middle ear infections, as seen in this case. Fever and systemic symptoms are also common and may lead to a misdiagnosis of infectious diseases in the early stages (6). Pulmonary involvement, as observed in this case with pulmonary nodules and infiltrates, further complicates the diagnostic process. Pulmonary nodules in GPA are usually bilateral and cavitary, but they may appear solid or spiculated, raising suspicion for malignancy, especially in patients without other risk factors for lung cancer (7). The radiological findings in this patient—spiculated opacities with contrast enhancement—highlight the overlap between the imaging characteristics of GPA and malignancies, often necessitating a tissue biopsy for a definitive diagnosis.

Diagnostic Approach.

The diagnostic evaluation in this case was comprehensive and systematic, involving laboratory, imaging, and histopathological investigations. Initial laboratory findings revealed anemia and elevated inflammatory markers (CRP, D-dimer, fibrinogen, ferritin), which are consistent with active inflammation but nonspecific. Notably, the autoimmune panel was crucial in narrowing the differential diagnosis. While most markers were negative, the highly elevated PR3-ANCA level (356.09 RU/mL, normal <20) strongly suggested GPA as the underlying etiology (8). Pulmonary biopsy remains the gold standard for diagnosing GPA, particularly when imaging and serological findings are inconclusive. The histopathological findings of necrotizing granulomatous inflammation and multinucleated giant cells confirmed the diagnosis in this case. The biopsy findings not only supported the diagnosis but also ruled out malignancy and infections such as tuberculosis, which were initially considered based on the patient's clinical presentation.

Therapeutic Considerations

The management of GPA involves immunosuppressive therapy aimed at inducing and maintaining remission. In this case, the patient was treated with high-dose corticosteroids (Prednisolone 75 mg daily) combined with Cyclophosphamide, a standard induction regimen for severe GPA (9). The patient responded well to this regimen, with rapid resolution of fever and improvement in clinical and radiological findings. Long-term management would involve transitioning to a maintenance regimen with less toxic agents, such as azathioprine or methotrexate, to minimize the risk of relapse (10).

Importance of a Multidisciplinary Approach

This case underscores the critical role of a multidisciplinary approach in diagnosing and managing complex cases of GPA. Collaboration among pulmonologists, rheumatologists, radiologists, and pathologists facilitated an accurate and timely diagnosis, allowing for the initiation of appropriate treatment. The involvement of a rheumatologist in the diagnostic process was particularly valuable, as it prompted the autoimmune panel testing that revealed the characteristic PR3-ANCA positivity.

Differential Diagnosis and Broader Implications

Pulmonary nodules and systemic symptoms require a broad differential diagnosis, including infections (e.g., tuberculosis, fungal infections), malignancies, and other autoimmune conditions such as sarcoidosis and eosinophilic granulomatosis with polyangiitis (EGPA). In this case, the absence of risk factors for malignancy (e.g., smoking history) and the presence of systemic symptoms (e.g., fever) directed clinicians toward a non-malignant etiology, further supported by PR3-ANCA positivity.

This case also highlights the need for heightened clinical suspicion for GPA in patients with unexplained systemic symptoms and multi-organ involvement. Delayed diagnosis can lead to significant morbidity, including permanent organ damage, particularly renal involvement, which fortunately was absent in this patient.

Conclusions

This case demonstrates the diagnostic and therapeutic challenges of GPA, particularly when presenting with features that mimic malignancy. Early recognition, multidisciplinary collaboration, and a systematic diagnostic approach were critical in achieving a favorable outcome. Future efforts should focus on improving diagnostic algorithms for systemic vasculitides to minimize delays in diagnosis and optimize patient outcomes.

Conflict of interest: None

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