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A patient with granulomatosis with polyangiitis and focal pulmonary lesions – challenges in differential diagnosis: a case report

Chory z ziarniniakowatością z zapaleniem naczyń oraz ze zmianami ogniskowymi w płucach – trudności w diagnostyce różnicowej: opis przypadku

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Abstract

Objective: Vasculitis is an increasingly prevalent condition, often characterised by an insidious and multifaceted clinical course, which delays accurate diagnosis and treatment. **Case Report:** A 63-year-old male diagnosed with granulomatosis with polyangiitis (GPA), who demonstrated pulmonary disease progression after six months of remission-induction therapy with cyclophosphamide. Imaging studies revealed new cavitating infiltrates in the upper lobe of the left lung, along with numerous satellite nodules in both lungs. A thorough differential diagnosis ruled out infectious aetiologies. **Summary:** Despite extensive diagnostic efforts, including invasive procedures and positron emission tomography–computed tomography scanning, exclusion of malignancy remained challenging. Establishing an accurate diagnosis and excluding infectious or neoplastic diseases enables timely and appropriate treatment, which can be life-saving in patients with GPA. Delayed treatment increases the risk of GPA-related organ complications.

Keywords: immunosuppression, smoking, neoplasms, granulomatosis with polyangiitis, lung mass

Streszczenie

Cel: Coraz częściej występujące zapalenie naczyń ma bardzo podstępny i wielowymiarowy przebieg, co opóźnia ustalenie trafnego rozpoznania i leczenie. **Opis przypadku:** 63-letni mężczyzna z rozpoznaniem ziarniniakowatości z zapaleniem naczyń (*granulomatosis with polyangiitis*, GPA) oraz progresją w obrębie płuc po pół roku leczenia indukującego remisję cyklofosfamidem. W badaniach obrazowych nowe zmiany naciekowe z rozpadem w górnym polu płuca lewego oraz liczne guzki satelitarne w obu płucach. Diagnostyka różnicowa pozwoliła wykluczyć proces swoisty. **Podsumowanie:** Pomimo wielu badań, w tym inwazyjnych oraz pozytonowej tomografii emisyjnej połączonej z tomografią komputerową, wykluczenie choroby nowotworowej może być trudne. Postawienie trafnej diagnozy, wykluczenie chorób infekcyjnych i rozrostowych pozwala na wdrożenie szybkiego, odpowiedniego leczenia i ratuje życie chorych z GPA. Opóźnione leczenie prowadzi do większej liczby powikłań narządowych GPA.

Słowa kluczowe: immunosupresja, nikotynizm, nowotwory, ziarniniakowatość z zapaleniem naczyń, guz płuca

INTRODUCTION

Granulomatosis with polyangiitis (GPA) is a systemic disorder classified as a type of anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV). It is characterised by the presence of necrotising inflammation of small arteries, veins, and capillaries in the affected organs, usually the upper and lower airways, kidneys, skin, joints, eyes, and nervous system[1–4].

Complex immune abnormalities trigger the production of anti-neutrophil cytoplasmic antibodies (ANCA) that target specific proteins, most commonly proteinase 3 (PR3) and myeloperoxidase (MPO). These antibodies are responsible for neutrophil-mediated vascular damage[5,6]. This, in turn, leads to ischaemia, followed by impaired function of the affected organs.

Imaging often reveals multiple nodules, whereas nodular masses or cavities are less common. In cases of high pulmonary disease activity, 5–15% of GPA patients may experience alveolar bleeding and respiratory failure, with a mortality rate of approximately 20%[7].

The paper discusses a case of active multi-organ GPA in a patient with long-term nicotine addiction, infiltrative lesions with disintegration in the upper segments of the left lung and multiple nodular lesions in both lungs.

CASE REPORT

A 63-year-old patient with retroperitoneal fibrosis treated for one year with glucocorticoids (GCSs) and methotrexate, and with a smoking history of approximately 30 pack-years was admitted to the Department of Nephrology due to acute kidney injury.

For the past month, the man had experienced deterioration in general condition, weight loss, low-grade fever, and joint pain. Physical examination showed elevated blood pressure, clear lung fields on auscultation, a clear nasal cavity without pathological discharge, scabbing, or bleeding, lower leg oedema, absence of joint inflammation, and skin without pathological eruptions.

Laboratory workup revealed creatinine of 3.0 mg/dL and an estimated glomerular filtration rate (GFR) of 19 mL/min/1.73 m^2, compared with creatinine of 1.0 mg/dL two months earlier. Urinalysis demonstrated haematuria occupying the entire field of view and proteinuria.

Complete blood count revealed mild anaemia with haemoglobin of 10.8 g/dL. Inflammatory markers were not elevated, with C-reactive protein at 0.5 mg/dL. Antinuclear antibodies (ANAs) and anti-dsDNA were negative, complement levels were within the normal range, but anti-neutrophil cytoplasmic antibodies against proteinase 3 (PR3-ANCA) were detected at 9.8 IU/mL.

Ultrasound revealed kidneys measuring up to 130 mm with increased parenchymal echogenicity, without focal lesions or urinary stasis in the calyceal–pelvic system.

Chest computed tomography (CT) demonstrated minor fibrotic scarring changes in both apices and isolated pulmonary nodules measuring up to several millimetres, the largest located in segment 3 of the right lobe (9 mm) and pericardially in segment 8 of the right lobe (10 mm).

A kidney biopsy was performed, revealing pauci-immune necrotising glomerulonephritis with secondary glomerular sclerosis.

Based on the clinical presentation, laboratory (positive PR3-ANCA antibodies) and histopathological findings, GPA was diagnosed. The patient was put on intravenous and then oral GCSs in combination with cyclophosphamide administered based on the CYCLOPS regimen.

The treatment course was initially uneventful, with clinical and laboratory improvement.

However, the patient's condition deteriorated after six months of cyclophosphamide therapy. Apart from the recurrence of fever, joint pain, increased creatinine and PR3-ANCA antibodies up to 32 IU/mL, highly dynamic pulmonary changes was observed. However, the patient denied dyspnoea or haemoptysis, with oxygen saturation (SaO_2) within normal limits.

Another follow-up chest CT revealed an infiltrative lesion with calcifications measuring 50 × 35 mm in segments 1 and 2 of the left lung, as well as a 40 × 40 mm nodular lesion with central necrosis located in the upper lobe of the left lung, adjacent to the aortic arch. Additionally, multiple nodular lesions were identified in both lungs, the largest measuring 15 × 17 mm and 10 × 16 mm located subpleurally in segments 1 and 3 of the right lung, and 14 × 14 mm in segment 8 of the left lung. Several enlarged lymph nodes, up to 11 mm in size, were observed in the aortopulmonary window, paratracheally, and in the right hilar regions. According to the radiologist's report, these findings suggested a proliferative process with metastatic involvement of both lungs.

Since the progression of pulmonary changes occurred during initially effective remission-inducing treatment with cyclophosphamide, and given that the patient belonged to a high-risk group for cancer (long-term nicotine use, immunosuppression), an urgent differential diagnosis was undertaken.

Although bronchoscopy showed no invasive lesions, features of subglottic stenosis typical of GPA were detected (histopathology of specimens from this area showed intense, predominantly eosinophilic inflammatory infiltration). No cancer cells were found in the bronchoalveolar lavage (BAL). Cultures were negative. All tests for TB and atypical mycobacteria, as well as were also negative. QuantiFERON test result negative.

The patient underwent percutaneous needle biopsy of the left lung. Histopathology revealed multiple macrophages, red blood cells, small patches of "atypical epithelial cells", but no cancer cells.

Ultimately, the patient underwent positron emission tomography combined with computed tomography (PET-CT), which identified metabolically active (SUV_{max} 16–11.5) lesions adjacent to the descending aorta in the left

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lung (as in CT) and a spiculated lesion in the apex of the right lung, 24 × 22 mm (SUV_{max} 11.7), which was not visible on previous scans. Additionally, multiple nodules with increased 18F-FDG metabolism and moderately metabolically active lymph nodes were described in both lungs (reactive activity). No suspicious changes were found in other organs, including the central nervous system, liver and skeleton. Although the examination provided no additional data for differential diagnosis, it enabled a more precise assessment of the size and extent of the inflammatory infiltrate, while excluding inflammatory activity within the adjacent aortic wall and the presence of potential metastases.

In the absence of data confirming the neoplastic nature of detected lesions, and after excluding infectious foci, rituximab therapy was started, initially as induction treatment, and then as maintenance therapy, and has been continued to date.

Currently, the patient remains in clinical and radiological remission.

A follow-up PET-CT showed a significant reduction of lung lesions, regression of the largest lesion from 47 × 31 mm to 26 × 10 mm, and a decrease in the number and metabolic activity of the remaining pulmonary nodules.

However, he still struggles with advanced CKD, with creatinine of 3.5 mg/dL and GFR of 18 mL/min/1.73 m^2, although these values have remained stable over an extended period. General urinalysis shows no presence of red blood cells, and no PR3-ANCA antibodies were detected.

Despite many attempts, the patient has still not managed to permanently discontinue smoking. Due to the presence of risk factors, he requires close monitoring for both cancer and cardiovascular complications.

DISCUSSION

Lung involvement in GPA occurs in 25–80% of cases. Granulomatous inflammation, which can be detected in the lungs in up to 50% of patients as single or multiple nodules that tend to form cavities due to central necrosis, is a key feature of GPA[8].

The clinical picture of systemic vasculitides overlaps with other conditions, which often leads to diagnostic errors, delays in diagnosis and treatment, and consequently may contribute to increased mortality[9].

As reported by Sreih et al., the initial diagnosis was incorrect in 73% of cases; systemic vasculitis was misdiagnosed as an infection, malignancy, and another autoimmune disorder in 33%, 5%, and 19%, respectively[9]. In our clinical practice, we have encountered patients who were initially treated for pulmonary tuberculosis, with the diagnosis later revised to GPA, as well as patients in whom the progression of pulmonary lesions during immunosuppressive therapy confirmed concomitant mycobacterial infection overlapping with vasculitis. The same may be seen for lung cancer, where patients are often initially diagnosed with this malignancy, and only further diagnostic workup confirms the diagnosis. Lung cancer is common in the general population due to the high prevalence of tobacco smoking and occupational exposure. Long-term immunosuppression used in GPA can promote the progression of proliferative diseases.

GPA requires a complex diagnostic and therapeutic approach, especially in patients with multiple comorbidities. As pointed out by Luqmani et al., early diagnosis and treatment lead to clinical remission in 75% of patients and are a key strategy in reducing permanent organ damage and mortality[10].

Imaging modalities, particularly chest radiography and, most importantly, computed tomography, play a crucial role in detecting pulmonary involvement in GPA, especially when respiratory symptoms are mild or absent[8].

Bronchoscopy with BAL is also an important diagnostic technique. BAL allows for detecting malignant cells, performing nonspecific cultures, and testing for both atypical mycobacteria and tuberculosis (Ziehl–Neelsen stain, BACTEC MGIT, GeneXpert MTB/RIF). Transbronchial or surgical biopsies may be indicated to exclude malignancies or infectious diseases that may mimic vasculitis, or to confirm the diagnosis in cases of isolated pulmonary nodules without evidence of involvement of other organs[11].

In the case of our patient, the diagnostic tests were negative. Before further treatment decisions were made, a PET-CT scan was performed in the hope of obtaining additional data. PET-CT is not a well-established tool in the diagnosis of GPA, and only a limited number of clinical studies have evaluated its use. Available data suggest that PET-CT may allow for a more accurate assessment of disease extent and help detect clinically silent yet potentially dangerous inflammatory changes, such as aortic wall infiltration. However, PET-CT has not been demonstrated to be an effective modality for differentiating AAV-related from hyperplastic lesions, although it would probably be most readily used for this purpose[12–14].

In the described patient, PET-CT helped to more precisely determine the extent of lesions and exclude disease activity in other organs and systems.

Although cyclophosphamide initially yielded very good outcomes, there was a rapid relapse. Rituximab proved effective in inducing and maintaining remission, as confirmed by clinical assessment, as well as imaging and laboratory findings (PR3-ANCA negative). Rituximab shows an advantage in relapsing disease, and when used for both induction and maintenance of remission, it increases the chances of achieving antibody negativity. Once remission is reached, a booster dose is administered every 6 months for a minimum of 18–24 months (or longer depending on the risk of disease relapse).

Regular monitoring of overall health, renal function, and complications of chronic immunosuppression is a key aspect of patient care. Due to remaining risk factors, the patient still requires high levels of vigilance, both in terms of oncology and cardiovascular complications.

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CONCLUSIONS

GPA requires broad, immediate differential diagnosis, particularly when the clinical presentation includes one or multiple pulmonary nodules. The presented case illustrates the complexity of GPA and its management in the elderly population. Accurate diagnosis with exclusion of infectious and proliferative diseases enables timely initiation of appropriate therapy, which is often lifesaving in GPA patients. Delayed treatment, in contrast, increases the risk of GPA-related organ complications.

Conflict of interest

The authors do not report any financial or personal associations with other persons or organisations that might affect the content of this publication of claim any rights hereto.

Author contribution

Original concept of study: MM. Collection, recording and/or compilation of data: NAP, MFK, BTR, WD, SK. Analysis and interpretation of data: NAP, MFK, MD, AR. Writing of manuscript: NAP, MFK. Critical review of manuscript; final approval of manuscript: MM, SN.

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