CASE REPORT

When pulmonary nodules, epistaxis and renal lesion do not add up to Wegener’s granulomatosis?

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ABSTRACT

Wegener’s granulomatosis usually presents with clinical features of systemic vasculitis affecting lung, upper respiratory tract, kidney and even a nervous system. Yet, invasive pulmonary aspergillosis is characterised by invasion of blood vessels in the lungs, but the infection often spreads to kidneys, skin and central nervous system. We report a case of a 46-year old male patient with no prior medical history. Clinical presentation included epistaxis, hemoptysis, hematuria and proteinuria, along with pulmonary nodular infiltrates. Differential diagnosis included invasive aspergillosis and Wegener’s granulomatosis, but the diagnosis was only confirmed after autopsy. Establishing diagnosis of invasive aspergillosis remains a challenge for clinicians in acute care setting.

Key words: Aspergillus, bronchoalveolar lavage, galactomannan

INTRODUCTION

Invasive pulmonary aspergillosis (IPA) is a rapidly progressive infection caused by Aspergillus spp. mold that usually occurs in immunocompromised patients. This infectious process is characterized by invasion of blood vessels, resulting in multifocal infiltrates, often wedge-shaped, pleural-based, and cavitary (1). Dissemination to other organs, particularly the central nervous system, kidneys, skin, heart and liver may occur. Reported mortality rates are as high as 90% (1,2). On the other hand, Wegener’s granulomatosis is a rare autoimmune disease that presents with clinical features of systemic vasculitis affecting upper respiratory tract, lung and kidney, but it may also affect nervous system and spleen (3). It is not always possible to get a histopathological diagnosis early in the course of disease, and patients with acute onset of nonspecific clinical features have a broad differential diagnosis (1). The essential dilemma for a clinician is: infectious or autoimmune and, consequently, antimicrobials or immunosuppressants?

CASE REPORT

We report the case of a 46-year old male patient who was admitted to Vojvodina Institute for Pulmonary Diseases with the following symptoms: productive cough, exertional dyspnea, fever and inappetence. The immediate reason for referral to the Institute was occurrence of a blood-tinged sputum. The patient was a welder with poor socio-economic status and no prior medical history. Clinical presentation included epistaxis, hemoptysis, hematuria and proteinuria, along with pulmonary nodular infiltrates. Differential diagnosis included invasive aspergillosis and Wegener’s granulomatosis, but the diagnosis was only confirmed after autopsy. Establishing diagnosis of invasive aspergillosis remains a challenge for clinicians in acute care setting.

Figure 1. Initial chest radiograph showing bilateral patchy opacities (Stojanović M, 2011)

A preliminary diagnosis was bilateral pneumonitis. Since blood count showed marked leucopenia and neutropenia, this was first interpreted as a sign of sepsis. All inflammatory markers were elevated. Blood gases reflected moderate type I respiratory insufficiency. Initial therapy included oxygen and broad spectrum antibiotics. Both sputum and blood cultures came back negative.
Chest CT was performed, and it showed multiple, well demarcated nodular lesions in various segments of both lungs. There were no signs of cavitation within the nodules. Also, there were bilateral areas of lung consolidation with clearly visible „air bronchogram“ (Figure 2).

Figure 2. Chest CT scan showing bilateral nodular infiltrates (Stojanović M, 2011)

When new symptoms appeared, epistaxis and crusted lesions around nostrils, along with proteinuria and hematuria, we suspected Wegener’s. Yet, ANCA was negative. Bronchoscopy was requested but it was postponed by bronchologists due to thrombocytopenia. Otolaryngologist still took a biopsy of nasal mucosa – pathologist’s response was inconclusive: nonspecific inflammation. Since borderline exophthalmos was noted, we checked thyroid hormones: TSH was low and fT4 mildly elevated. Since patient was febrile despite broad-spectrum antibiotic therapy, parenteral fluconazole was introduced. This intervention was followed by a 20-hour period without fever. Galactomannan test was scheduled for next Thursday, since that test is performed only once a week in the central laboratory. Fever came back the next day and a change in mental status was noted. The patient was intubated and transferred to ICU where lethal outcome ensued in the next 24 hours.

Preliminary autopsy findings read, “Vasculitis necroticans pulmonum et renum granulomatosis sec.Wegener?””. However, final autopsy findings confirmed multiple infarctions of the lungs and pleura caused by *Aspergillus fumigatus*, along with mycotic emboli of the kidneys, thyroid gland, spleen and cerebrum.

Invasive fungal disease has been considered by clinicians somewhat of a rarity, mainly “reserved” for immunocompromised hosts (1). Major risk factor for IPA is neutropenia, followed by hematopoietic stem-cell and solid organ transplantation, cytotoxic therapy, corticosteroid therapy, malignancy, AIDS and chronic granulomatous disease (1-3). However, critically-ill may develop IPA even without classic risk factors. In one study, 89 cases (70%) of invasive aspergillosis were found in patients without malignancy admitted to ICU (2). In another study of 172 critically-ill patients who had positive sputum for *Aspergillus*, 83 had invasive disease, whereas 60% of these patients had no classic risk factors (4). In our case, we did not initially suspect IPA, since the patient had no prior medical history. Chest radiograph is usually of little use in early stages of the disease, because of the nonspecific findings, which was also the case here. Chest CT scan can be more useful, given that it includes typical findings such as multiple nodules and the halo sign, which appears as a zone of low attenuation due to hemorrhage surrounding the pulmonary nodule (5). Another late radiological sign is the air crescent sign - crescent-shaped lucency in the region of original nodule secondary to necrosis (3,5). Neither sign is sensitive or pathognomic of IPA (5). Cavitary lesions may also point to Wegener’s granulomatosis, and there is a number of cases where patients with ANCA-associated vasculitis were also diagnosed with IPA (3). Histopathological diagnosis, by examining lung tissue remains the ’gold standard’ in the diagnosis of IPA (6).

Blood cultures are rarely positive in patients with IPA (7). As for galactomannan assay, its negative predictive value is 92–98% and positive predictive value is 25–62% (8). Bronchoscopy with bronchoalveolar lavage (BAL) is generally helpful in the diagnosis of IPA, especially in patients with diffuse lung involvement – it is not necessary to take transbronchial biopsies since they are associated with increased risk of bleeding (7). It is important to send samples such as sputum, BAL fluid, or lung tissue both for culture and for histological examination. In our case, sputum and blood cultures were negative, while galactomannan assay was not performed since the patient died before the scheduled test. Detection of Aspergillus DNA by PCR is a significant tool for early diagnosis, but is not widely available (9). Therapy should be considered as soon as there is a clinical suspicion of IPA, and the antifungal drug of choice is voriconazole, which long replaced amphotericin B. Other effective antifungals in-
clude posaconazole and echinocandin derivatives (10). In our case, fluconazole was the only readily available parenteral antifungal agent, however, it has not proven efficient in IPA treatment. Even with the appropriate antifungal therapy, reported mortality rates range from 60 to 90% (1,2).

In conclusion, clinical signs and symptoms of invasive pulmonary aspergillosis are often non-specific in those critically ill, who are prone to invasive fungal disease independent of the classic risk factors. Targeted diagnostic evaluation and appropriate early antifungal therapy should be employed as soon as invasive pulmonary aspergillosis is suspected.

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**TRANSPARENCY DECLARATIONS**

Competing interests: none to declare.

**REFERENCES**


**Kada nodularne promene u plućima, epistaksa i bubrežna lezija ne ukazuju na Wegenerovu granulomatozu?**

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**SAŽETAK**

Wegenerova granulomatoza obično se prezentuje kliničkim znacima sistemskog vaskulitisa koji zahvata pluća, gornji respiratorni trakt, bubrege, pa čak i nervni sistem. Invazivna pluća aspergiloza, s druge strane, zahvata krvne sudove pluća, ali se infekcija često širi i u bubrege, kožu i centralni nervni sistem. U ovome radu je prikazan slučaj 46-godišnjeg pacijenta, bez ranijih obolenosti. U kliničkoj slici bili su prisutni epistaksa, hemoptizije, hematurija i proteinurija, uz nodularne infiltrate u plućima. Diagnostikovanje invazivne aspergilose i dalje predstavlja izazov za kliničare koji rade na odeljenjima poluintenzivne i intenzivne nege.

**Ključne reči:** *Aspergillus*, bronhoalveolarna laža, galaktomanan.