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# Necrotizing pulmonary aspergillosis caused by anorexic syndrome - a case report

**Case report**

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**Abstract:** The patient presented is a 44-year-old female treated for cavitary changes in the lung apexes. Due to suspected tuberculosis, treatment began with anti-tuberculosis (AT) drugs, despite negative sputum smears for acid-fast bacilli. During hospitalization, the patient was febrile (up to 38˚C), hypotensive, extremely cachectic (32 kg), had a dry cough, increased nitrogen products, hypokalemia and anemia. Because of poor response to the applied AT therapy, bronchoscopic tests were repeated and spores of aspergillus fungus were discovered in the pathohistological findings of transbronchial lung biopsy. The appropriate treatment with amphotericin B and voriconazole was initiated. A psychiatric opinion was requested because we suspected that the patient suffered from the anorexic syndrome (anorexia nervosa). This diagnosis was confirmed by a psychiatrist; her psychiatric treatment began simultaneously with the treatment in our facility. Anorexia was the cause of the cachexia, immunodeficiency and invasive pulmonary aspergillosis. The disorder was not recognized before the manifestation of the somatic disorder. There is little data in the available literature on the association between these two diseases.

**Keywords:** *Pulmonary aspergillosis • Anorexia nervosa*

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## 1. Introduction

Aspergillosis refers to the spectrum of diseases caused by *Aspergillus* (A) species (*A. fumigatus, A. flavus, A. niger, A. terreus*, and others). The spectrum of pulmonary diseases ranges from a non-invasive disease form, such as the colonization of the organism or the presence of a fungus ball (aspergilloma), an allergic response that produces the syndrome of allergic bronchopulmonary aspergillosis, to an semi-invasive or invasive infection such as the chronic necrotizing pneumonia and invasive pulmonary aspergillosis [1,2].

Invasive aspergillosis is a rare, but serious, form of pulmonary mycosis. The mycotic infection spreads through lungs, producing granuloma, necrotizing and/or suppurative lesions. Invasive aspergillosis can be acute, triggering progressive and extensive pulmonary damage (necrotizing aspergillosis) that causes death in a matter of days. Predisposing factors include neutropenia, especially in patients with leukemia; bone marrow transplant; the application of corticosteroid therapy; chemotherapy in patients with cancer; AIDS or chronic granulomatous diseases. The radiological results may be non-specific [3-5]. Even more frequent are indolent forms of this disease, which occur when the pulmonary invasion happens slowly and can last for weeks, months, or even years. This is referred to as chronic necrotizing aspergillosis. Extensive pulmonary cavities may occur inside the lungs, most often bilaterally. The indolent form of the disease is often fatal if not treated in its early phases, but subacute and chronic invasive aspergillosis may have a more optimistic prognoses [6-8].

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## 2. Case Report

A 44-year-old female was hospitalized at our clinic for dry cough, stabbing chest pain and hemoptysis, an elevated temperature up to 38°C, serious weight loss, pain in the joints and exhaustion. In her medical history, she mentioned chronic renal failure of unclear etiology that occurred several months prior to admission, sideropenic anemia and lumbar vertebrae osteopathy. Her menopause started early, at 38 years of age. She also mentioned a frequent use of laxatives for constipation problems. On admission, she was subfebrile (37.9°C), extremely cachectic (weight 32 kg, body mass index 12.3), adynamic, hypotensive (90/60, 80/60 mmHg), and had a breathing frequency 22/min and SaO2 94%.

Initial and follow-up laboratory blood tests revealed anemia (red blood cells 3.38 and 3.2 T/L; hemoglobin 7.3, 5.2 and 5.1 mmol/L; hematocrit 32% and 28%); hypokalemia (potassium 3.4 and 2 mmol/L), and elevated values of acidum uricum (793 μmol/L), urea (6.6 and 7.9 mmol/L) and creatinine (234 and 216 μmol/L), too. Creatinine clearance was extremely low (23 ml/min). Inflammatory markers (C-reactive protein and leukocytes count) were within normal range. The number of neutrophils was normal 3,2 G/L (normal 2-6,8). The detection of lymphocyte subpopulations was not available in our laboratory at that time.

**Figure 1.** Chest X-ray showing round shadows with illumination in both lung apexes, more prominent in the right one

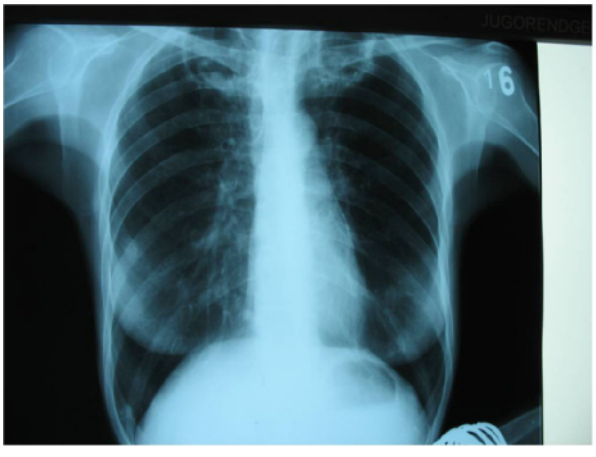
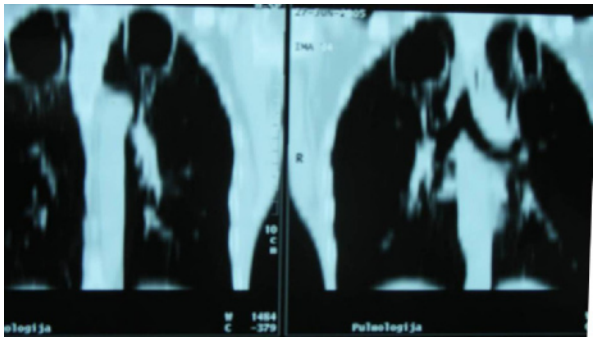


**Figure 2.** Computed tomography of the lungs pointed to cavernous changes in the thick walls that filled both apexes



Antinuclear antibodies (ANA) and anti-neutrophil cytoplasmic antibodies (ANCA) were negative; IgA, IgG, IgM, complement components C3 values were normal (Turbidimetric method); and HIV was negative. Hormone levels (T3, T4, TSH, cortisol) were within normal limits.

A chest X-ray showed round shadows with illumination in both lung apexes, prominent in the right one, 4 cm in diameter (Figure 1). Computed tomography (CT) of the lungs pointed to cavernous changes in the thick walls, which filled both apexes (Figure 2). Based on the imaging studies and clinical characteristics of the disease, and despite the negative sputum smears for acid-fast bacilli, the patient was placed on anti-tuberculosis therapy (AT) for presumptive diagnosis of pulmonary tuberculosis. Polymerase chain reaction (PCR) testing is not a part of routine diagnostic procedures in our country.

Fiberoptic bronchoscopy and transbronchial biopsy (TBB) were performed; however, the histopathology results did not reveal the etiology of the cavity. Considering the deterioration in the patient's general condition, fiberoptic bronchoscopy was performed two more times. In the meantime, there were several samples of sputum that had a negative Lowenstein culture. Finally, the histopathology results of the obtained TBB in the right upper lobe pointed to chronic necrotizing pneumonia with aspergillus hyphae; some of them were calcified.

The precipitation reaction between the patient's serum and antigen A. fumigatus remained negative. Total IgE values were normal (97 IU-l). Furthermore, specific IgE values to A. fumigatus were within normal limits (<0.10). The value of anti-Aspergillus IgM antibodies was 91 U/ml (positive > 70) and anti-Aspergillus IgG antibodies was 79 u/ml (positive >70). The galactomannan test is not available in our country. Abdominal echosonography showed reduced renal parenchyma, loose pyelon build, uneven echoes on the side of parenchyma. No abnormalities were detected in other abdominal organs. Treatment commenced with liposomal amphotericin B (20 days), according to creatinine clearance, and was then continued with voriconazole (oral 200mg+100mg, 50 days).

It was suspected that the patient had an eating disorder, given her low body weight (BMI = 12.3) and vomiting after food intake. After the psychiatric consultation, the established diagnoses were anorexic syndrome and anorexia nervosa. An additional interview with the patient's family revealed that her psychic disorders

started eight years before, after a divorce and loss of job; however, she did not receive any treatment at that time. Food intake control was advised. After the treatment with voriconazole, the patient became afebrile, her general condition started to improve slowly, as did the signs of azotemia. She was released from hospital and advised to continue with psychiatric therapy. Six months later, she had gained 4 kilos, her general condition was good, there were no signs of renal failure and the changes on her lungs were stationary.

## 3. Discussion

Aspergillus is a ubiquitous pathogen. It can be found as a saprophyte in the upper airways and rarely causes infections in immunocompetent patients [9,10]. We present a case of necrotizing pulmonary aspergillosis with a chronic course, which is rare and difficult to diagnose. Contributing factors to diagnosis were the existence of elevated temperature, cough, the lack of reaction to antibiotics and AT treatment, and bilateral cavities in the lungs. The initial diagnostic attempts had been relatively vague, despite the invasive methods that were performed (three fiberoptic bronchoscopies), until aspergillus fungi were found in one of the TBB tests. This helped us exclude other reasons that could have led to pulmonary cavities (tuberculosis and Wegener's granulomatosis).

The treatment of this patient with antifungals [7,9] was a real challenge, given that the above-mentioned drugs are nephrotoxic, and the patient had renal insufficiency. Because of extremely low creatinine clearance, the recommended dosages for this clearance were applied along with adequate rehydration, potassium compensation and multivitamin therapy. After receiving this treatment for a month, the patient's general condition improved considerably. She was afebrile and feeling well. Her levels of urea and creatinine were restored to normal (115 and 6.1, respectively). She was discharged from hospital and advised to continue with psychiatric therapy. The reason for the occurrence of this rare disease in our patient must have been an incredibly low food intake that in turn caused extensive weight loss and immune system breakdown [11,12]. Even though a precise cause-and-effect relationship between anorexia nervosa, immunodeficiency and pulmonary aspergillosis has not yet been clarified, we presume that the long-term malnutrition of our patient led to the failure of the host defense mechanisms. This failure then resulted in the invasive pulmonary aspergillosis and the infection that is solely associated with immunocompromised conditions. The data on the role of anorexia nervosa and eating disorders in the occurrence of immunodeficiency have given rise to controversy. According to some authors, these disorders are not associated with increased risk of infection [13]. On the other hand, a number of cases with decline of innate and cell-mediated immunity have been described in patients with anorexia [11,12]. The normal function of the immune system, especially the innate ones, as well as the normal function of Th1 cells, is essential to defend from aspergillus infection. One of the deficits that accompanies anorexia nervosa is skin anergy, which can explain the negative cutaneous test to aspergillus [14].

Our patient displayed many of the above-mentioned symptoms. It is possible that the long-term poor renal perfusion caused the prerenal azotemia and subsequent high levels of creatinine and low creatinine clearance. In the available literature, there are only a few case reports on the association of anorexia nervosa and pulmonary aspergillosis [15]. Bilateral cavitary changes in the lungs on chest x-ray and the poor general condition of immunocompromised patients are most often associated with pulmonary tuberculosis. Negative sputum smears for acid-fast bacilli must raise suspicion of other rare pulmonary diseases, including pulmonary aspergillosis [16]. Unfortunately, anorexic disorders are not infrequent. They mostly occur in younger women, and this is a rare example of the connection between the two conditions. Both diseases require persistence on the part of not only the physician, but also the patients and their families. The treatment of the anorexic syndrome is a long-term process.

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