# A CASE OF PULMONARY ASPERGILLOSIS IN AN IMMUNOLOGICALLY INTACT 15-YEAR-OLD BOY

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## ABSTRACT

*Aspergillus* is a fungus which could cause a number of infectious and allergic diseases especially in immunocompromised patients.

We report a case of 15-year-old boy with a small post-pneumonic cavity formation in the 3rd segment of the right lung. After conventional intravenous antibiotic treatment the X-ray changes were still persisting. The boy was in good general condition, without intoxication syndrome, with intact immune status. Physical examination was normal except for mild rare cough. The diagnosis was confirmed by imaging, serological and microbiological tests. Oral itraconazole (200 mg daily) was administered for 6 months along with monthly monitoring of the liver function. CT scan controls were performed in the 2nd, 4th and 6th month. Complete resolution of the cavity was observed in the final CT scan. No operative treatment was necessary.

Although typical for immunocompromised patients, an immunologically intact child without other underlying diseases can also develop pulmonary aspergillosis. Small lesions respond well to conservative treatment without surgery.

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## INTRODUCTION

*Aspergillus* is a fungus which could cause a number of infectious and allergic diseases especially in immunocompromised patients. It is widespread in the environment and is often cultured from both outdoor (*i.e.* soil, plant debris) and indoor environment, including hospitals. A wide spectrum of pulmonary involvement is described in the literature (1).

The most common cause of pulmonary diseases is *Aspergillus fumigatus*, although *Aspergillus flavus* is a more common cause of allergic rhinosinusitis, postoperative aspergillosis and fungal keratitis. *Aspergillus terreus* is responsible for invasive pulmonary aspergillosis (IPA) in some institutions and unfortunately is amphotericin B-resistant. *Aspergillus niger* could be an occasional cause of IPA or *Aspergillus* bronchitis, but is also a coloniser of the airways (2, 3).

IPA is typical for individuals with severe immunodeficiency. Patients at increased risk are those with malignancy, organ transplantation or autoimmune disease, and patients in intensive care units (4-7).

Arendrup *et al* reported two cases of IPA that occurred within one day of gardening work involving tree bark chippings (5). They described severe interstitial pneumonia or miliary type picture with possible cavity formation. The authors discussed that the clinical presentation may be confused with extrinsic allergic alveolitis (EAA) (8).

The most common and best-recognised form of pulmonary involvement caused by *Aspergillus* species is aspergilloma which usually develops in a pre-existing cavity in the lung. It is composed of fungal hyphae, leukocytes, fibrin and mucus.

The most common isolate from such lesions is *A. fumigatis*, although others (*Zygomycetes* and *Fusarium*) are also described. A lot of pulmonary diseases manifesting as cavity formation could be complicated by aspergilloma, namely tuberculosis (most common), sarcoidosis, bronchiectasis, bronchial cysts and bullae, ankylosing spondylitis, neoplasm and pulmonary infection (9, 10). In a study including 544 patients with pulmonary cavities caused by tuberculosis, 11% had radiological data of aspergilloma (11, 12). It is hypothesised that the inadequate drainage of the cavity is the cause of *Aspergillus* growth.

The diagnosis of pulmonary aspergilloma is usually based on clinical picture and is confirmed by serological and microbiological methods (13). Chest X-ray could demonstrate a mass in a pre-existing cavity. The typical appearance of aspergilloma is an upper-lobe, mobile, intra-cavitary mass with an air crescent in the periphery.

Due to its high lung penetration, itraconazole is a viable option for conservative treatment in selected patients with aspergilloma (17). Long-term oral itraconazole therapy has been associated with radiological and clinical improvement in more than 50% of the cases. Occasionally a complete resolution of the cavity has been documented (14-16).

Surgery of the cavity is advised in patients with persisting X-ray changes and recurrent haemoptysis but may be associated with mortality rates of up to 7–23% (18-23).

## CASE PRESENTATION

We present a clinical case of 15-year-old boy with a vague cavity formation in the 3rd segment of the right lung after pneumonia treatment.

The child had no family history of pulmonary diseases or serious diseases in the past except drug allergy against sultamicillin. The boy lives in Sofia, in a flat, and is an active swimmer.

The onset of the illness was in July 2018 when pneumonia was diagnosed due to cough, fever, general fatigue and X-ray changes. The boy was treated for 7 days with an intravenous antibiotic (amikacin) in a hospital and after that, for 7 more days with an oral antibiotic (levofloxacin) at home. However, due to the persistence of the X-ray morphology he was admitted to the hospital for diagnostic work-up.

The boy was hospitalised in the Multiprofile Hospital for Active Treatment of Pulmonary Diseases „St. Sofia" in August 2018 in a good general condition, without intoxication syndrome. Physical examination was unremarkable except for a mild rare cough.

Laboratory blood tests were performed: full blood count and liver enzymes – normal; cellular and humoral immunity – without disorders; HIV status – negative.

The initial chest X-ray upon admission showed two-sided hilar congestion; soft, gentle infiltrate was observed with clear borders from the surrounding parenchyma and hyper-lightening at the centre associated with a shadow in the right lung hilus.

On the next day chest computed tomography (CT) scan was performed, showing formation of a lobular cavity with wall thickness of up to 2 mm located in the upper right lobe (3rd segment), and soft tissue formation adjacent to the ventral contour of the cavity. Perifocally in the same segment were found multiple micronodular lesions. CT morphology was highly suggestive of aspergilloma in the right upper pulmonary lobe. In differential diagnosis another mycotic infection and less likely tuberculosis should also be considered (Fig. 2.)

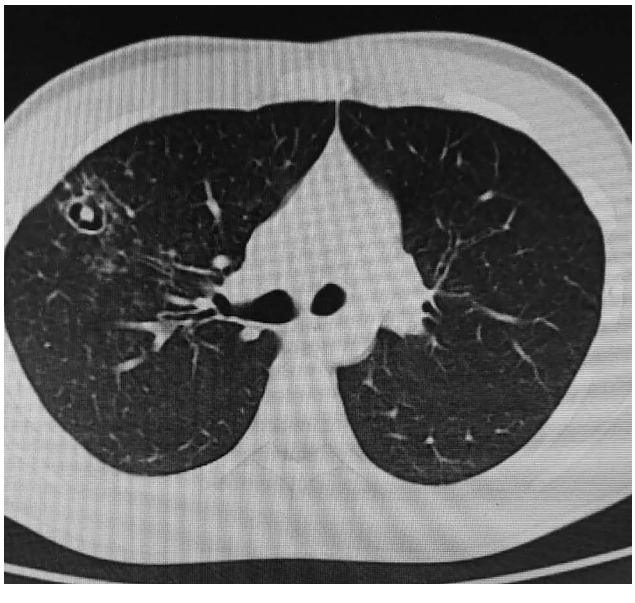

**Figure 2.** Initial CT findings.

Flexible fibrobronchoscopy was normal for the age, in the upper right lung there was an atypical division of the segmental bronchi. Bronchoalveolar lavage fluid (BAL) was collected for microbiology and cytology.

No bacterial growth was detected in BAL. Sputum and BAL microscopy, and culture results for tuberculosis were also negative.

Immunological tests for tuberculosis were also conducted. Tuberculin skin test (TST) was normal – 13 mm, according to Bulgarian reference values. Interferon Gamma Release Assays (IGRA) test was negative as well.

The diagnosis was confirmed with the isolation of *Aspergillus niger* from BAL submitted for fungal culture (Fig. 3). The serology test for *Aspergillus* was also positive.

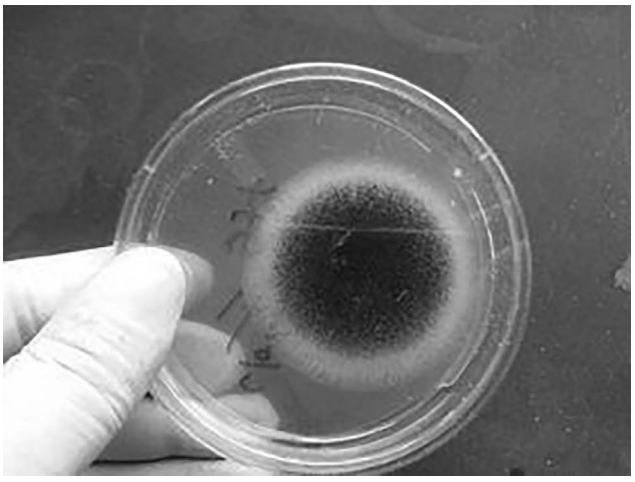

**Figure 3.** Culture confirmation.

Histopathology and BAL cytology showed epithelial cells, many macrophages, less neutrophils and eosinophils, spores and *Aspergillus* hyphae. The morphological diagnosis was aspergillosis (Fig. 4).

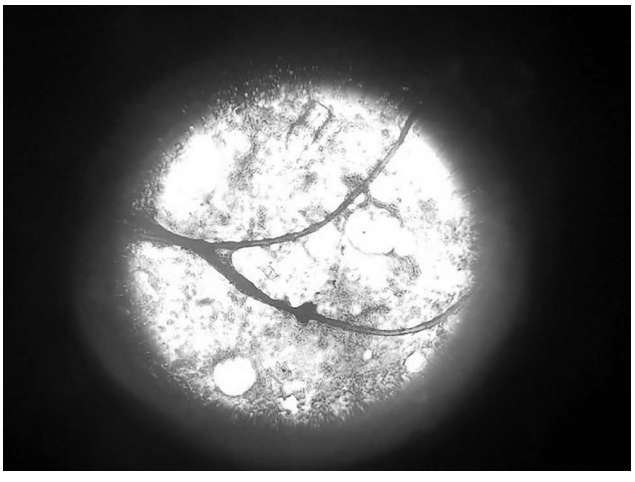

**Figure 4.** Microscopy confirmation.

After consultation with a paediatric thoracic surgeon an observational approach was chosen to assess the patient's condition.

In the differential diagnosis were considered also post-pneumonic cavity formation, pulmonary tuberculosis, pulmonary echinococcosis or other pulmonary parasitosis, and pulmonary mycosis.

Oral itraconazole (200 mg daily) was administered for six months along with monthly monitoring of liver enzymes. The child had no complaints during the treatment course.

CT controls were performed in the 2nd, 4th and 6th month (Fig. 5, 6 and 7, respectively). Complete resolution of the cavity was observed in the final CT. No operative treatment was necessary.

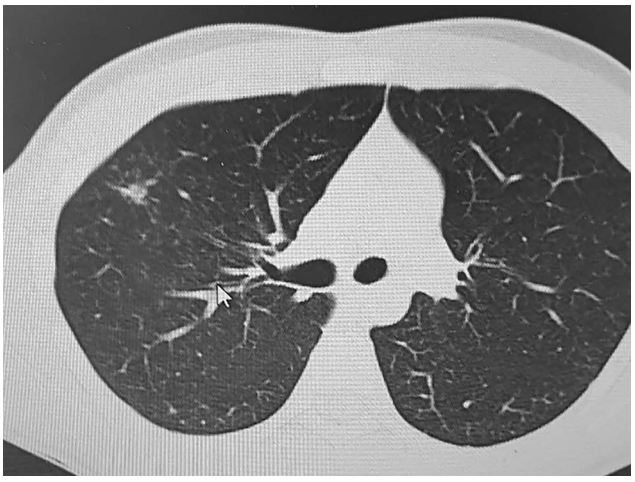

**Figure 5.** Control CT in the 2nd month of treatment – a small residual fibrotic focus is observed in the right upper lung at the cavity site.

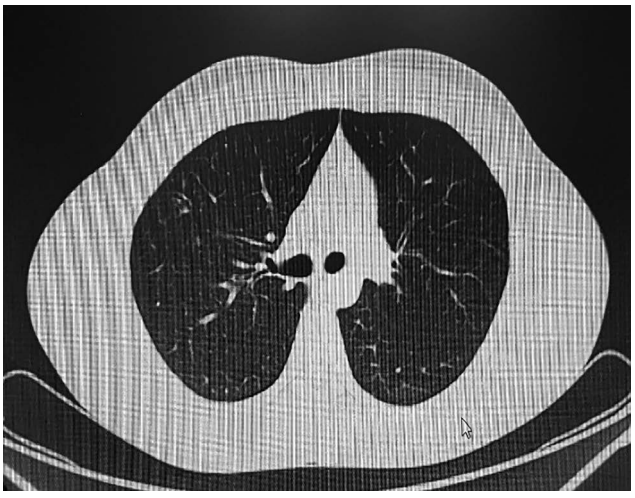

**Figure 6.** Control CT in the 4th month of treatment – a discrete fibrotic focus is observed in the right upper lung. There are no CT findings for focal and nodular lesions in the pulmonary parenchyma.

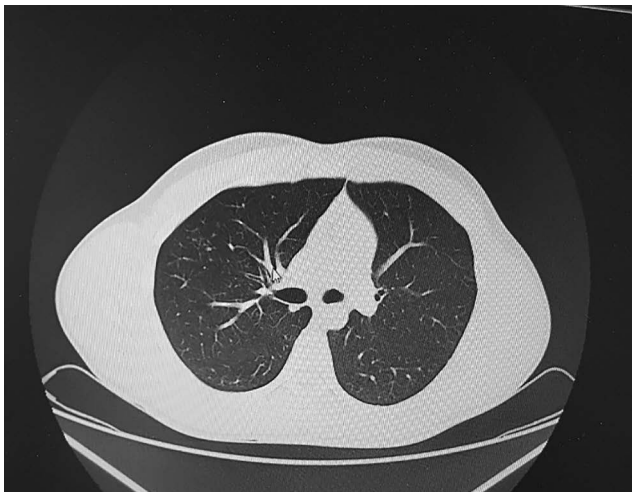

**Figure 7.** Control CT in the 6th month of treatment (final CT) – normal image of the lung and the mediastinal structures. There are no CT findings for focal and nodular lesions in the lung.

After the end of the antimycotic treatment *Aspergillus*-specific IgE were examined and the result was <0.1kU/l (normal <0.35).

## DISCUSSION

Chronic necrotising aspergillosis is usually found in patients with chronic pulmonary disease or light immunodeficiency. Aspergilloma is usually detected in patients with pre-existing lung cavities, and allergic bronchopulmonary aspergillosis is generally observed in patients with atopy, asthma or cystic fibrosis (24, 25).

Actually, our patient did not have immune deficiency or any kind of underlying disease, and was generally a healthy teenager before the *Aspergillus* infection.

Although typical for immunocompromised patients, an immunologically intact child without other diseases can also develop pulmonary aspergillosis (24, 29). Small lesions respond well to conservative treatment without surgery.

The various clinical presentations of *Aspergillus* infection and the development of one form of the disease into another depend mainly on the immune status of the patient. There is a variety of infection hypersensitivity states in allergic aspergillosis, saprophytic infection in pre-existing pulmonary diseases and invasive forms in immunocompromised patients (26-34).

More studies are needed to better characterise the type and pathogenesis of infectious, allergic and saprophytic *Aspergillus* diseases.

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