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Pulmonary Aspergillosis: A Case Report of Invasive Aspergillosis Caused by *Aspergillus fumigatus*

Ravil HUSEYNOV[1], Samir JAVADOV[2],
Iskender KARALTI[3*], Bayram TAQIYEV[4]

Corresponding author: Iskender.karalti@gmail.com

[1,2]The department of Medical Microbiology and Immunology, Azerbaijan Medical University, Azerbaijan, Baku
[1]Orcid ID: 0000-0002-7381-5740/rav.huseyn@gmail.com
[2]Orcid ID: 0000-0001-8971-9895/scavadov@amu.edu.az
[3,4]Central Laboratory of Educational-Therapeutic Clinic, Azerbaijan Medical University, Azerbaijan, Baku
[3]Orcid ID: 0000-0002-5316-4776/Iskender.karalti@gmail.com
[4]Orcid ID:0000-0002-9910-0401/Dr.tagisoy@gmail.com

Abstract: *Aspergillus* – a genus consisting of mold species widely distributed in the environment. The spectrum of pulmonary diseases includes invasive aspergillosis (IA), chronic pulmonary aspergillosis (CPA) and allergic bronchopulmonary aspergillosis (ABPA).

We report a case of invasive aspergillosis caused by *Aspergillus fumigatus* in a 65-year-old patient admitted with complaints of shortness of breath, general weakness, and malaise. Diagnosis of "probable" aspergillosis was established based on microbiological and radiological investigations. During microbiological analysis *A.fumigatus* was isolated an identified based on cultural and morphological characteristics. Despite the medical treatment, the patient's complaints worsened. He refused artificial lung ventilation apparatus.

Probably, chronic obstructive pulmonary disease (COPD) together with late diagnosis and absence of appropriate treatment resulted in the development of IA and lethal outcome. CPA develops in immunocompetent patients, suffering from tuberculosis or other diseases accompanied by the formation of cavities in lungs. This case demonstrates the importance of reliable and timely diagnosis of aspergillosis in order to provide patients with adequate treatment.

Taking into account difficulty of obtaining of punctate for histopathological examination and absence of radiological signs physicians should give more attention to the probability of aspergillosis in patients with chronic disease in order to apply adequate therapy and reduce the number of lethal outcomes.

Key words. *Aspergillus fumigatus*, Invasive aspergillosis, CPA, COPD

Pulmoner Aspergilloz: *Aspergillus fumigatus* 'un Etken Olduğu Invaziv Aspergilloz Vakası

Öz: Aspergillus, küf türlerinden oluşan ve çevrede yaygın olarak bulunan bir mantar türüdür. Akciğer hastalıkları spektrumuna invaziv aspergilloz (İA), kronik pulmoner aspergilloz (KPA) ve alerjik bronkopulmoner aspergilloz (ABPA) gibi hastalıklar dahildir.

Nefes darlığı, genel halsizlik ve rahatsızlık yakınmaları ile başvuran 65 yaşındaki bir hastada Aspergillus fumigatus'un neden olduğu invaziv aspergilloz vakasını sunuyoruz. Mikrobiyolojik ve radyolojik araştırmalara dayanarak "olası" aspergilloz tanısı konuldu. Mikrobiyolojik incelemede A.fumigatus kültürel ve morfolojik özelliklerine göre tanımlandı. Tıbbi tedaviye rağmen hastanın durumu daha da kötüleşti. Hasta mekanik ventilasyon cihazını reddetti.

Muhtemelen, kronik obstrüktif akciğer hastalığında (KOAH) geç tanı ve uygun tedavinin olmaması İA gelişimine ve letal sonluğa neden olmuştur. KPA, akciğerlerde kavite oluşumu ile sonuçlanan tüberküloz veya diğer hastalıklara maruz kalan immünokompetan hastalarda gelişir. Bu olgu, hastalara yeterli tedaviyi sağlamak için aspergilloz tanısının güvenilir ve zamanında konulmasının önemini göstermektedir.

Histopatolojik inceleme için biyopsi alınmasının zorluğu ve radyolojik bulguların bulunmaması göz önünde bulundurularak, doktorlar yeterli tedaviyi uygulamak ve ölümcül sonuçların sayısını azaltmak için kronik hastalığı olan hastalarda aspergilloz olasılığına daha fazla dikkat etmelidir.

Anahtar kelimeler. *Aspergillus fumigatus*, İnvaziv aspergilloz, KPA, KOAH

Introduction

Aspergillus – a genus consisting of mold species widely distributed in the environment. Despite the fact that inhalation of mold spores is a frequent phenomenon only in a few cases it causes pulmonary infections. Clinical features, course, and prognosis mainly depend on organism's immune status. The role of genetic factors should be taken into account as well. The spectrum of pulmonary diseases includes invasive aspergillosis (IA), chronic pulmonary aspergillosis (CPA) and allergic bronchopulmonary aspergillosis (ABPA). IA occurs in solid organ and hematopoietic stem cell transplant (HSCT) recipients. Insufficiency of the immune system in these patients leads to the development of acute invasive diseases. CPA develops in immunocompetent patients with chronic pulmonary diseases. Tuberculosis is among the most frequent risk factors of CPA. Other risk factors are an atypic mycobacterial infection, sarcoidosis, chronic obstructive pulmonary diseases (COPD), bronchiectasis, lung cancer, ABPA, pneumothorax. The proportion of patients with previously treated tuberculosis varies between 15.3 and 93 %. In addition, during ABPA allergic response to conidia entered the organism causes fungal sensibilization (Kosmidis & Denning, 2015).

Case report

A 65-year-old man was hospitalized in the Department of Pulmonology and Allergology of Educational-Therapeutic Clinic of Azerbaijan Medical University with complaints of shortness of breath, general weakness, and malaise. According to the information given by relatives, he had been considering himself unhealthy for a long time and underwent stationary and ambulatory treatment in Scientific-Research Institute of Lung Diseases (Baku, Azerbaijan). The general condition of the patient was severe, conscience was clear. Objective examinations revealed pallor of the skin and mucous membranes, fever (38,8 ˚C). There were no visible deformations of joints and bone tissue. Lymphatic nodes were not enlarged. Heart rate– 146 bpm, blood pressure - 90/60 mmHg. Palpation of the heart area did not reveal any pathological pulsations and protuberances. The boundaries of relative cardiac dullness were widened. During auscultation cardiac sounds were normal, the accent of II tone was heard above aorta. Respiratory system: RR – 28 breaths per minute. On percussion dullness of lower lobes was observed. Blood oxygen saturation value vas low (SPO_2=52%). Gastrointestinal tract examination: the tongue was moist, swallowing action - painless. Stomach during palpation was soft, liver and spleen were palpable. Defecation was normal. Urogenital system: negative tapping symptom, painful urination. Computed tomography of thoracic organs showed diffuse emphysematous alterations caused bronchiectasis accompanied by cysts of different sizes, pleural thickening, and calcifications. Secondary reduction of the left lung upper lobe volume and hearth boundaries, calcified lymphatic nodes and atherosclerotic plaques of the aorta were observed. Bone structure examination revealed thoracal kyphosis, osteodegenerative alterations in cervical and thoracal vertebrae. Conclusion: massive destructive processes in left upper lobe accompanying diffuse emphysematous alterations in both lungs, characteristic for previous lung tuberculosis.

Microbiological investigation

Sputum sample sent to Clinic Microbiological Laboratory (The department of Microbiology and Immunology) of Azerbaijan Medical University was inoculated onto 5%-sheep blood, Eosin methylene blue (EMB) and Sabouraud Dextrose (supplemented with chloramphenicol) agars and incubated at 37ºC and 45ºC. After 2 days of incubation growth of white velvety colonies was observed. The colonies color changed to blue-green with age (Fig. 1). In order to avoid contamination

collection of sputum sample from the patient was repeated. For morphological identification, lactophenol cotton blue mount (LCBM) was used. Microscopic examination revealed septate hyphae, smooth walled conidiophores, and chains of conidia arising from a single row of phialides located on club-shaped vesicles. Echinulate conidia (2.5 to 3 micrometer) formed on the upper 2/3 of the vesicle is characteristic for *Aspergillus fumigatus* (Fig. 1).

The diagnosis of "probable" aspergillosis was established based on microbiological and radiological investigations (De Pauw et al., 2008) and voriconazole was administered. Despite the medical treatment, the patient's complaints of breath shortness, fatigue, weakness, malaise worsened. He refused artificial lung ventilation apparatus and died a day later.

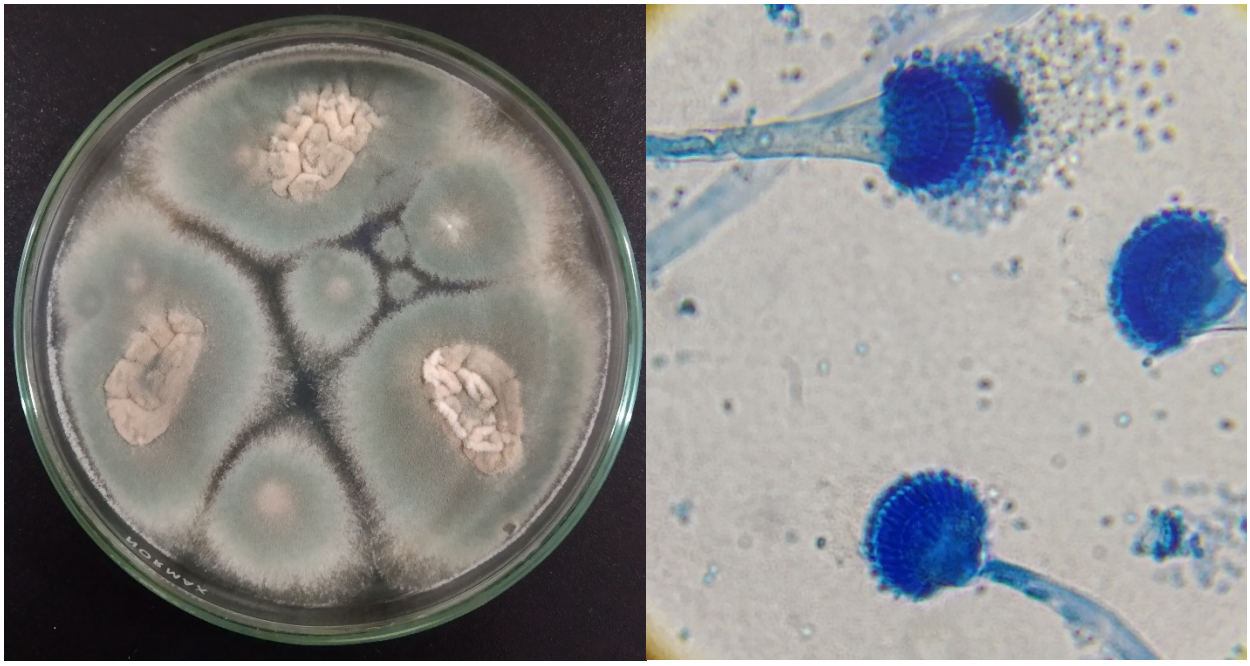

Figure 1. *A.fumigatus* colonies on SDA medium (left) and microscopy with lactophenol cotton blue stain (right).

Discussion

Pulmonary aspergillosis has many clinic variations including IA, chronic necrotizing aspergillosis (CNA), CPA and ABPA (Walsh et al., 2008). The most frequent causing agents are 4 species: *A. fumigatus*, *A. flavus*, *A. niger* and *A. terreus (Steinbach et al., 2012).* The main manifestations are shortness of breath, chronic sputum discharge, chest discomfort, fatigue, loss of weight. The complexity of diagnosis of aspergillosis is due to nonspecific symptoms and absence of classic risk factors. 3 levels of certainty exist regarding the diagnosis: "proven", "probable" and "possible" aspergillosis. The diagnosis of "proven" IA is based on histopathological examinations and positive culture from normally sterile organism site. "Probable" diagnosis is based on the presence of risk factors, clinical manifestations, radiological signs and microbiological examination (De Pauw et al., 2008).Clinical manifestation of aspergillosis depends on 2 factors: immune status of organism and presence of concomitant disease. IA develops in immunosupressive patients, ABPA – in atopic patients and patients with hyperreactive immune system, CPA – in immunocompetent patients (Maghrabi & Denning, 2017).This case demonstrates the importance of reliable and timely diagnosis of aspergillosis in order to provide patients with adequate treatment. According to Betancourt et al. (2015) the diagnosis of aspergillosis is accompanied with difficulties related to the absence of classic radiological signs and negative results of the microbiological analysis. Furthermore, the presence of tuberculosis can complicate the task. The comprehensive diagnosis was made by a histopathological diagnosis of material obtained after surgical manipulations (Betancourt, Garofoli, Sandhu, Boma, & Sy, 2015). In case of IA described by Naaraayan et al. (2015) the diagnosis of aspergillosis was made after

histopathological examination as well. The positive result of sputum cultivation was obtained only after a 13-rd day of patient's admission (Naaraayan, Kavian, Lederman, Basak, & Jesmajian, 2015). In the presented case differential diagnosis was made with tuberculosis. Probably, COPD together with late diagnosis and absence of appropriate treatment resulted in the development of IA and lethal outcome. CPA develops in immunocompetent patients, suffering from tuberculosis or other diseases accompanied by the formation of cavities in lungs (Thompson & Patterson, 2011). Radiologically it can be represented by aspergilloma, nodules or various thin-/thickwalled cavities. In the presented case, CT results confirmed the presence of diffuse emphysematous alterations in lungs favoring the development of CPA. Around 1.2 million people in the World have CPA as a consequence of tuberculosis (Denning, Pleuvry, & Cole, 2011). Isolation of pathogen from sputum can represent colonization, in particular in immunocompetent patients. Controversially, positive culture in immunosuppressed patients and recipient of HSCT and solid organs indicates a high probability of aspergillosis.

Conclusion

In the represented case based on anamnesis, clinical manifestations and radiological signs of aspergillosis was suspected and a microbiological investigation was performed. Taking into account difficulty of obtaining of punctate for histopathological examination and absence of radiological signs physicians should give more attention to the probability of aspergillosis in patients with chronic lung disease in order to apply adequate therapy and reduce the number of lethal outcomes.

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