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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Incidental finding of pulmonary tumorlet in a case of surgically treated bronchiectatic cavity superimposed by aspergilloma

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SUMMARY

Introduction Intracavitary aspergilloma is the consequence of a saprophytic infection of the lung with cavitary disease. Pulmonary tumorlet are nodular proliferations of the neuroendocrine cells less than 5 mm in diameter. Both aspergilloma in the bronchiectatic cavity of the lung and pulmonary tumorlet has rare been seen.

Case outline We present a 71-year-old woman with a medical history of recurrent pneumonia complicated with cough and hemoptysis. Computed tomography (CT) scan of the chest showed pulmonary soft tissue mass in the right lower lobe of the lung 42 × 50 mm in diameter. Direct microscopy of the specimens of bronchioalveolar lavage showed spores of *Aspergillus*. Galactoman Ag test was also positive. Right lower lobectomy and mediastinal lymph node sampling was performed via thoracotomy. Pathohistological findings showed aspergilloma with the presence of pulmonary tumourlet and diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) in the lymphovascular spaces. Five years follow up showed no abnormalities on the CT scan, and the patient remained alive without medical problems.

Conclusion The concomitant occurrence of bronchiectasis, aspergilloma, and precancerous lesions such as pulmonary tumourlet and DIPNECH is rare and further increases the risk of developing malignant tumors as well as recurrent infections. Therefore, surgical treatment can prevent the development of premalignant lesions and the occurrence of recurrent infections accompanied by dyspnea and hemoptysis as the main symptoms. The question of the connection between pulmonary tumourlet and chronic inflammatory lung diseases is raised. We hope that future researches will provide answers to this question.

Keywords: bronchyectasis; aspergilloma; pulmonary tumourlet; DIPNECH

INTRODUCTION

Aspergillus is a genus of mold which includes about 200 species, including *Aspergillus fumigaus*, *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus terreus* and *Aspergillus nidulans*, which are most common human pathogens [1]. Spreading of the disease depends of the patients immunological and respiratory systems. *Aspergillus* causes infectious as well as allergic diseases [2]. Chronic pulmonary aspergillosis (CPA) is often seen in patients with lung diseases that cause structural damage to lung parenchyma, and have the whole spectrum of progressive disease manifestations caused by *Aspergillus* species [3]. Chronic cavitary pulmonary aspergillosis is a slow destructive type of CPA [4]. Aspergillosis is most often seen in patients with common chronic lung disease or in immunocompromised patients. *Aspergillus* species, a saprophytic fungus, can colonize pulmonary cavities caused by tuberculosis, sarcoidosis, echinococcosis and bronchiectasis [5]. Also, it is well known to complicate malignant diseases [6]. Fungus ball, intracavitary mycetoma, aspergilloma, is the consequence of a saprophytic infection of the lung with cavitary disease. Cough and hemoptysis are the most common symptom [7]. Furthermore, pulmonary tumourlet, defined as nodular proliferations of neuroendocrine cells less than 5 mm in diameter, are a rare pathology [8]. In most cases they are detected incidentally, the most common in bronchiectatic cavity or in areas of lung destruction that are removed surgically. The coexistence of a pulmonary neuroendocrine tumourlet and aspergilloma has rarely been seen [9].

The aim of this case report was to present a rare case of surgically treated pulmonary bronchiectatic cavity superimposed with aspergilloma and an incidental finding of pulmonary tumourlet.

CASE REPORT

A 71-year-old woman with a medical history of recurrent episodes of pneumonia followed by hemoptysis and cough, with expectoration of

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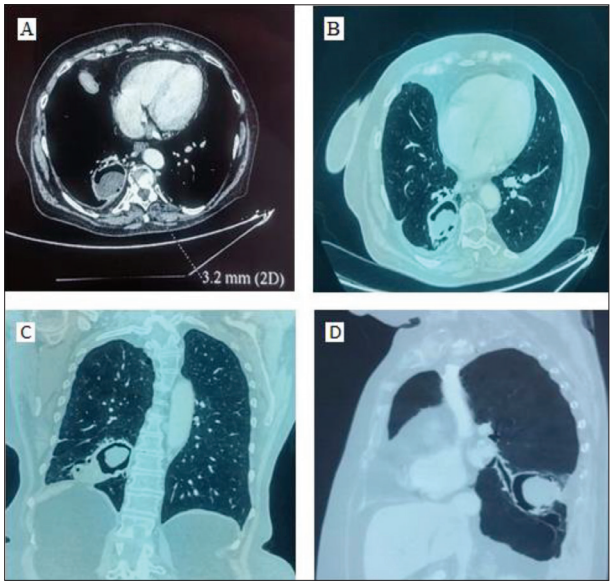

Figure 1. The aspergilloma in the intrapulmonary cavity; A – soft tissue window, axial section; B – lung parenchymal window, axial section; C – lung parenchyma window, coronal section; D – lung parenchyma window, sagittal section

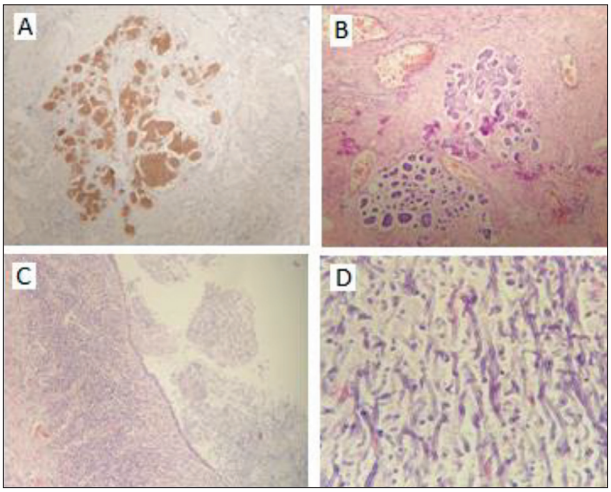

Figure 2. A – hematoxylin-eosin staining of bonchiectatic wall filled with fungus ball, mass consisted of fungal hyphae and necrotic fragments; bronchial wall is infiltrated by inflammatory cells, consisted mainly from lymphocytes, plasma cells and eosinophil leukocytes, lined by metaplastic squamous epithelial cells; magnification 100 ×; B – branching elongated hyphae of *Aspergillus*; periodic-acid-Schiff stain; magnification 400 ×; C – diffuse idiopathic pulmonary neuroendocrine cell hyperplasia; magnification 200 ×; D – neuroendocrine marker CD 56 expression in neuroendocrine cell hyperplasia; magnification 200 ×

brown-yellow sputum, was admitted to our department. The patient had a medical history of smoking, chronic obstructive pulmonary disease, arterial hypertension and mastectomy due to breast cancer. The results of spirometry, diffusion of carbon monoxide (CO) and laboratory were normal. Chest computed tomography (CT) scan is the golden standard for diagnosing of the lung diseases. It showed pulmonary soft tissue mass in the right lower lobe of the lung, oval cavitation approximately 42 × 50 mm in diameter, presence of "air in the form of a crescent sign," and the communication with subsegmental branches of the apicobasal segmental bronchus. Chronic pneumonitis and traction bronchiectasis, with no pathologic enlargement of the lymph nodes was also seen (Figure 1). Direct microscopy of the specimens of bronchoalveolar lavage identified spores of *Aspergillus*. Galactoman Ag test was positive. The patient was initially treated with antimicrobic therapy for two weeks before surgery. Right lower lobectomy and mediastinal lymph node sampling was performed via thoracotomy.

Pathological examination of the specimen showed intrapulmonary cavity in the right lower lobe, 45 mm in diameter. Intracavitary material was brown, necrotic, compatible with aspergilloma. Aspergilloma composed of numerous hyphae of *Aspergillus* was seen on the sections of the lung parenchyma along the bronchial wall. Hyphae were visualized by immunohistochemical methods periodic acid-Schiff and Grocott. Signs of vascular invasion by tumour cells, round, bright cytoplasm, in predominantly organoid arrangement, were observed in the vascular spaces. Group of uniform tumor cells were detected in a microscopic focus and measured less than 5 mm. Immunohistochemical staining for CD56, TTF-1, synaptophysin and cytokeratin were positive, while napsin A, CD34, p40, LCA were negative. Ki67 level was 2–3% in these cells. Lymph nodes specimens showed no metastatic tumor cells. The specimen contained a several areas of pulmonary tumorlet and diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH). Final pathohistological findings corresponded to aspergilloma with the presence of pulmonary tumorlet and DIPNECH in the lymphovascular spaces (Figure 2).

Five-year follow up showed no abnormalities on the chest CT scan, and the patient was without medical problems.

We confirm that we have read the journal's position on issues involving ethical publication and affirm that this work is consistent with those guidelines. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

DISSCUSION

Aspergilloma occurs as a consequence of saprophytic infection of the previously formed cavity of the lung parenchyma. Cough and hemoptysis are the most common symptoms. After the formation of aspergilloma, the effect of antimicrobial drugs is drastically reduced. In such situations, surgical treatment may be the only choice [7]. Pulmonary tumorlet, which represents nodular proliferations of neuroendocrine cells, are rare and do not exceed 5 mm in diameter [8]. These proliferations occur most often as a consequence of Kulchitsky cells hyperplasia in various lung diseases. They often occur in several places. Hyperplastic foci of these cells larger than 5 mm in diameter represents carcinoid tumors [8, 10, 11, 12]. They are most often detected on surgical material after lung

resections due to diseases that cause destruction of the lung parenchyma. There are several subgroups of neuroendocrine tumors with common characteristics: pulmonary tumorlet, DIPNECH, carcinoid tumors [10]. Concomitant occurrence of neuroendocrine tumors and aspergilloma is rare [9]. They are most often asymptomatic and occur in other lung diseases characterized by destruction of the lung parenchyma and the presence of a chronic inflammatory process. Cellular atypia and cell necrosis are rare, while mitotic activity is usually absent [11]. Recently published studies consider pulmonary tumorlet and DIPNECH precancerous lesions. However, proliferation to carcinoid tumors is rare [12, 13]. Nodal metastases are very rare and usually occurs in hilar lymph nodes [14].

It most often appears between the ages of 60 and 70, and it is four times more likely in men than in women (1:4). Dyspnea is the most common symptom. Small nodules up to 5 mm in diameter on a chest CT scan in patients with dyspnea without clear causes may raise the suspicion of the presence of pulmonary tumorlet and DIPNECH. Positron emission tomography/computed tomography in those cases is not the best diagnostic choice due to their size [8]. There are still no clear guidelines for monitoring and selecting the treatment for pulmonary tumorlet and DIPNECH. Also, prevention measures for their occurrence have not been determined yet. However, risk groups should be advised to quit smoking, practice physical activity, avoid exposure to certain physical and chemical substances such as asbestos, arsenic, tar, chromium, nickel, etc. Avoiding alcohol consumption is also advised [9]. Octreotide, 18F-DOPA amino acid analogs, inhaled corticosteroids, and beta agonists were part of the studies examining their effect in the treatment of neuroendocrine tumors and precancerous lesions such as pulmonary tumorlet and DIPNECH [8, 13]. Chronic inflammatory lung diseases, granulomatous lung diseases and bronchiectasis are the most common lung diseases in which pulmonary tumorlet occurs [10]. In our case, the presence of pulmonary tumorlet and aspergilloma in the bronchiectatic cavity were identified at the same time.

The question of the connection between pulmonary tumorlet and chronic inflammatory lung diseases is raised. The presence of bronchiectasis, aspergilloma, and precancerous lesions, such as pulmonary tumorlet and DIPNECH further increase the risk of developing malignant tumors as well as recurrent infections. So far, no consensus has been reached on the timing and type of surgery in patients with aspergilloma. Despite no comparative studies of antifungal therapy in patients preparing for surgery, voriconazole remains the first option, as it has been related to reduced mortality [15–19]. The presence of chronic inflammation and the negative effect of the infection on the remaining part of the lung parenchyma further complicate recovery after surgery. Therefore, surgical treatment can prevent the development of premalignant lesions and the occurrence of recurrent infections accompanied by dyspnea and hemoptysis as the main symptoms. We hope that the future researches will provide answers to those questions.

Conflict of interest: None declared.

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Узгредни налаз плућних туморлета у случају хируршки лечене бронхиектатичне шупљине насељене аспергиломом

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САЖЕТАК

Увод Интракавитарни аспергилом је последица сапрофитне инфекције плућа са кавитарном болешћу. Плућни туморлети су нодуларне пролиферације неуроендокриних ћелија пречника мањег од 5 *mm*. Ретки су случајеви истовременог откривања аспергилома у бронхоектатичној шупљини плућа и плућних туморлета.

Приказ болесника У раду је приказан случај болеснице старосне доби 71 годину, са понављаним упалама плућа које су праћене кашљем и хемоптизијама. Компјутеризована томографија грудног коша показала је мекоткивну масу пречника 42 × 50 *mm* у доњем десном плућном режњу. Узорци бронхоалвеоларне лаваже су показали споре аспергилуса (директна микроскопија). Тест *Galactoman Ag* је такође био позитиван. Урађени су десна доња лобектомија и узорковање медијастиналних лимфних чворова приступом кроз торакотомију. Патохистолошки налаз је показао бронхоектатичну шупљину у плућима са аспергилом и присуством плућних туморлета у лимфоваскуларним просторима. После пет година праћења компјутеризована томографија грудног коша није показала абнормалности и болесница је била без здравствених тегоба.

Закључак Истовремена појава бронхиектазије, аспергилома као и преканцерозних лезија као што су плућни туморлети и дифузна идиопатска хиперплазија неуроендокриних ћелија плућа (*DIPNECH*) ретка је и додатно повећава ризик од развоја малигних тумора и рекурентних инфекција. Хируршким лечењем може се спречити развој малигних тумора и појава рекурентних инфекција праћених диспнејом и хемоптизијама као главним симптомима. Поставља се питање повезаности преканцерозних лезија плућа и хроничних инфламаторних болести. Надамо се да ће будућа истраживања дати одговоре на ово питање.

Кључне речи: бронхиектазије; аспергилом; плућни туморлети; *DIPNECH*