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Case Report

A Lung Granuloma Case Possibly Associated with a Working Environment: A Case Report

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ABSTRACT

Lung granulomas are uncommon in Thailand. The disease typically develops from an occupational environment and is mostly caused by infection. Herein is a case report of a female patient, aged 48, working as a nurse in an Accident and Emergency Department at a hospital. Eighteen years prior to admission the patient was diagnosed with myasthenia gravis and pulmonary tuberculosis. The chest X-ray and CT scans showed a solitary pulmonary nodule in the lower left lung. The patient received an open thoracotomy with a left lobectomy. Granulomatous and nonseptate hyphae were found in the pathology diagnosis. The patient was thus diagnosed as having a lung granuloma. The galactomannan antigen test was positive. The solitary pulmonary nodule—found from the use of a Polymerase Chain Reaction (PCR) test—was an *Aspergillus* spp. The fungus culture was collected from air samples. The air samples were collected by the impaction technique using a microbial air sampler. Three types of *Aspergillus* spp. were found as well as *Penicillium* spp. and *Monilia sitophila*. The *Aspergillus* spp. was a match for the patient's disease. The patient was diagnosed as having a lung granuloma possibly *Aspergillus* nodule which was caused by airborne *Aspergillus* spp. from the occupational environment.

1. Introduction

Lung granuloma is a form of lung lesion often found to be related to chronic inflammation mostly by an infection such as pulmonary tuberculosis or other fungal infection. Frequently, the fungi particularly *Aspergillus* spp. are the cause of the disease [1]. Considering pulmonary infections caused by the *Aspergillus* spp, the pulmonary infection can be classified into acute, subacute and chronic. The acute form is invasive pulmonary aspergillosis (IPA), which progresses very rapidly and invasively in immunocompromised patients. The chronic form is chronic pulmonary aspergillosis (CPA), which has different subtypes including (1) *Aspergillus* nodules, (2) aspergilloma, and (3) chronic cavitary pulmonary aspergillosis (CCPA) and chronic fibrosing pulmonary aspergillosis (CFPA). Simple aspergilloma and *Aspergillus* nodules are less severe forms of CPA [2,3]. CPA almost always affects patients with some form of underlying respiratory pathology, the most common predisposing factor for CPA is previously treated pulmonary tuberculosis [2,4]. Other associations include COPD, bronchiectasis, previously treated lung cancer, allergic bronchopulmonary aspergillosis (ABPA), and pneumothorax. Patients with CPA are usually middle-aged and present constitutional symptoms (i.e., weight loss, malaise, sweats, anorexia), chronic productive cough, breathlessness, chest discomfort and occasionally hemoptysis. Radiological findings include lung cavities with or without an aspergilloma, infiltrates, nodules, or pleural fibrosis. The aspergillus-specific IgG is diagnostic for *Aspergillus* in sputum culture or PCR, or biopsy/aspiration. Another more common pattern is slowly evolving, single or multiple lung cavities, usually with thick walls with or without a fungus ball (aspergilloma). This form is chronic cavitary pulmonary

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aspergillosis (CCPA). The pathology of CCPD does not include angioinvasion, but hyphae are confined to a pre-existing lung cavity with effects to pre-existing structural lung disease and minor immunological defects that take months to years to present. Aspergilloma, as a late manifestation of CPA, arise in pulmonary cavities and present as a rounded fungal ball of fungal hyphae, fibrin, mucus and cellular debris [2,3]. A simple aspergilloma is a solitary lesion stable over months with or without main symptoms while a complex aspergilloma is a serious complication that includes hemoptysis. *Aspergillus* nodules are unusually incidental findings on CT scan with similarities to a malignant lesion, such that diagnosis cannot be confirmed until after excision biopsy [2]. The *Aspergillus* nodule appears as a lung granuloma. The fungus enters the respiratory system in the form of spores. This disease is normally severe for patients with low immunity [3–5] such as those with cancer.

Aspergillus fumigatus is the most common species associated with all pulmonary syndromes. *Aspergillus flavus* is the more common cause of various forms of allergic rhinosinusitis, postoperative aspergillosis and fungal keratitis [3]. As for the occurrence of lung granulomas caused by fungi in the occupational environment, the types of fungi that can be detected in hospital buildings include *Aspergillus* spp. [6]. and *Candida* spp. [7]. The *Aspergillus* fumigatus and *Penicillium* sp. could be detected in buildings where the room temperature is between 4 oC and 30 oC and the relative humidity is between 11 % and 96 % [8]. In a study in Iran, the fungi detected in hospital air can cause invasive diseases among medical staff [5,6] albeit the occurrence is rare and usually in persons with compromised immunity.

There has been no information available regarding the occurrence of lung granulomas in Thailand. Only the estimated prevalence of CPA is relative high and accounted for 19,044 cases per year, approximately half of tuberculosis cases. For IPA, the estimation is that it presents in about 13.5% of leukemia patients, 3% of kidney transplant patients, and 4% of lung and liver transplant patients [9]. According to a report on *Aspergillus* spp. from work or work environments in Thailand, there has not been any research that assesses the possibility of lung granulomas being contracted in the occupational environment. There has, however, been one case of a patient in the nursing profession, which led to a study of the occupational environment in hospitals. Air samples were collected in the workplace and the isolation of fungi from the samples analysed. Based on the pathology of the patient and the information provided regarding the patient's residence—a two-story house—no origin of the airborne fungi was found. To her knowledge, the patient had never lived in a previously flooded building. It was thus hypothesized that the workplace was the source of airborne fungi. In Thailand, there has not been a report of a case of a patient with granulomas caused by contact with fungi in the occupational environment. Our aims were to (a) report the first case of a patient (b) underscore the possibility of contacting the fungi in the occupational environment, and (c) suggest future research on pulmonary diseases caused by the occupational environment.

2. Case report

We reported the case of a 48-year-old Thai female patient who had been working as a nurse in the neurological ward. She was diagnosed with myasthenia gravis disease in August 2017. Mestinon was the only treatment for her myasthenia gravis. In addition, no corticosteroids were listed in her prescription. The patient had been a nurse for 27 years. Her main responsibility had been to care for patients in the neurological ward where there was natural ventilation. Air conditioners were installed in the semi-closed building.

Fig. 1. Chest X-Ray image showing pulmonary nodule in the superior segment of LLL.

The patient had no history of an abnormal respiratory system, had no fever, and had not lost weight. The patient had, however, suffered from chronic allergies for 10 years, and the patient had been diagnosed with pulmonary tuberculosis 18 years earlier, for which she had received antituberculosis agents for 6 months. Based on an examination, it was found that the patient had ptosis and was diagnosed with myasthenia gravis, which was not considered a risk factor for a lung infection.

Chest X-rays showed a solitary pulmonary nodule in the lower left lung (Fig. 1). The doctor required further examination and her CT scans revealed a 2-cm solitary pulmonary nodule in the lower left lung. Calcium was found around the nodule (Fig. 2).

The patient underwent thoracic surgery in September 2017. After surgery, the patient continued working in the hospital. The result of the biopsy pathology showed the presence of granulomatous and nonseptate hyphae (Fig. 3) which could be an invasive fungus or fungal ball (commonly *Aspergillus* spp), colonizing the respiratory system.

The laboratory examination results follow: hemoglobin 10.0 g/dL, hematocrit 31.7%, white blood cell count 6.26 ×103/μL

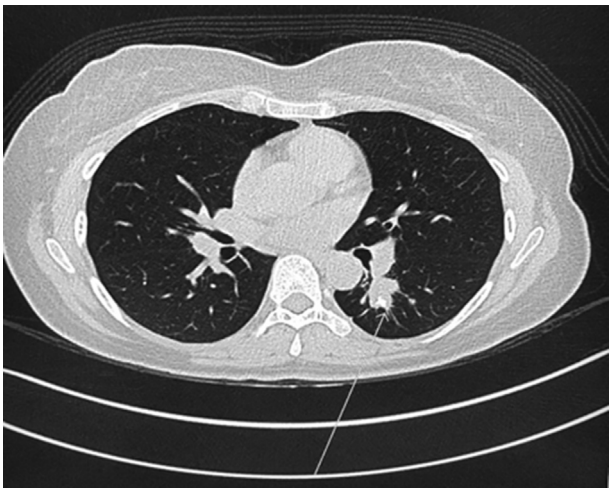

Fig. 2. Computed Chest X-Ray image A 2 cm speculated pulmonary nodule in the superior segment of LLL with eccentric calcifications.

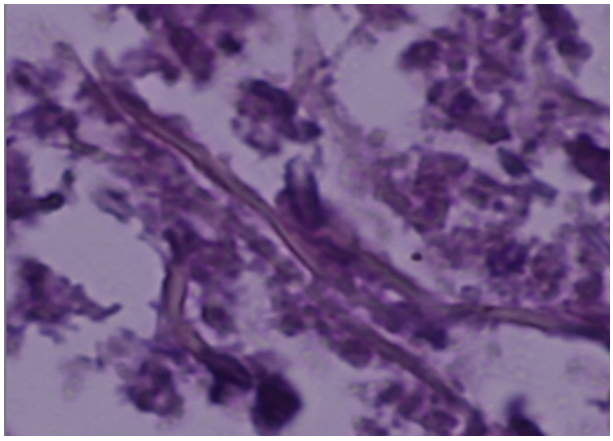

Fig. 3. PAS stain highlighting slender nonseptate hyphae: Section revealed fibrotic nodules with chronic inflammatory cell infiltrate, including macrophages. Some slender nonseptate hyphae are seen separately within necrotic tissue.

(neutrophils 65.5%, lymphocytes 21.3%, monocytes 11.5%, eosinophils 1.0%, basophils 0.7%), and platelets 344 × 10^3/μL. Surgical pathology results follow AFB – no acid-fast bacilli; Wright's stain – no fungus found; and modified AFB – no partially acid-fast branching filaments. Fungus culture result indicated no growth. Blood antigen test indicated: Cryptococcus antigen and Histoplasmosis antigen – negative; and *Aspergillus* galactomannan antigen – positive. PCR examination results from the pathological tissue indicated *Aspergillus* spp. was found.

A culture for biological hazards in the air of the workplace was performed. The air samples were collected using the impaction technique using a microbial air sampler (SAMPL'AIR™, bioMérieux Industry, Hazelwood, USA). The air intake rate was 50 L/min. The air samples were collected in 11 areas of the hospital building using the Sabouraud agar at a room temperature between 26.1 oC and 27.6 oC and relative humidity between 50.5% and 60.8%. The sample collectors were cleaned with 70% alcohol before and after each collection. The twelve samples were collected from the patient reception area (1) pantry room (2) administration room (3), nurse station (4), two strokes patient care areas (5,6), two strokes patient care areas (5,6), medical equipment rooms (7), two patients care areas (8,9), meeting room (10), indoor control sample (blank agar) (11), and outdoor sample (12). First, a 1-week isolated culture and a fresh smear were done to identify the organisms by microscopic method. From the air samples, five species of fungi were found—mostly *Aspergillus* spp. (viz., *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus fumigatus*, *Penicillium* spp. *Monilia sitophila*) (Table 1).

3. Discussion

The report of the patient showed that the patient had pulmonary tuberculosis and myasthenia gravis in the past. From the CT scan, nonseptate hyphae were found and cancer cells were not. According to the results of the culture from biopsies, no tuberculosis was found. It was thus assumed that the patient had lung granulomas and the diagnosis was confirmed by detecting other fungi species in the samples. No histoplasmosis or *Cryptococcus spp*. was found. The result of the galactomannan antigen was positive. Based on the PCR test, Aspergillus spp. was found, which is related to a history of pulmonary tuberculosis [10,11]. This might mean that lung granulomas were caused by *Aspergillus* spp. after the treatment of the TB. The prevalence of the disease is about 18 per 100,000 population, and 25% of patients are diagnosed with the disease by chest X-ray images [4]. It is likely that infection with *Aspergillus* spp. is from contact with the *Aspergillus* spp in-hospital or in-community. It has not, however, been confirmed which environmental factors contribute to the prevalence of the *Aspergillus* spp since the incubation period has not been clearly indicated albeit the occupational environment is a factor with known *Aspergillus* spp. infection [4,12].

As for the patient's professional background, the patient had been working as a nurse for 27 years. She worked at least 8 hours a day. In terms of the occupational environment, the ward floor has high humidity and the ward is a semi-closed building with air conditioners. The researcher collected air samples from 10 areas in the ward to identify the origin of the fungus. One sample of indoor control blank agar which does not collect indoor air then determines whether there was any mold growth. As an experimental control to confirm that there was no contamination from the storage equipment or culture agar, one outdoor control was performed. The fungi culture indicated *Aspergillus* spp. was found in the air samples in all 11 areas sampled; *Aspergillus fumigatus* was found in 9 of the 10 areas in the ward. The high room temperature and high relative humidity in Thailand heightened the chances of the patient contacting spores in the workplace (Table 1). The results have two known limitations. First, there was no corresponding examination of the patient's residence. Second, the patient was at high-risk due to a history of pulmonary tuberculosis and that the patient was susceptible to a fungal infection.

Table 1
Types of fungi identified from air samples in the patient ward

Air samples areas	Room temperature (°C)	Relative humidity (%)	Types of fungi identified from workplace air samples O = growth, × = no growth				
			A. niger	A. *flavus*	*A. fumigatus*	*Pencillium spp.*	*Monilia sitophila*
1.Patient reception area	27.2	58.0	O	×	×	×	O
2. Pantry room	27.2	57.4	O	O	O	O	O
3. Administration room	26.1	49.6	×	×	O	×	O
4. Nurse station	27.0	57.9	O	×	O	O	O
5. Stroke patient care areas	27.1	59.0	O	O	O	×	O
6. Stroke patient care areas	27.4	60.2	O	O	O	O	O
7. Equipment room	27.5	50.0	O	O	O	×	×
8. Patient care area	27.3	60.8	O	O	O	×	O
9. Patient care area	27.6	58.8	O	O	O	O	×
10. Meeting room	27.2	50.5	O	O	O	O	×
11. Indoor control (blank) sample	27.6	58.5	×	×	×	×	×
12. Outdoor sample	28.1	63.7	O	×	O	×	O

From the occupational point of view, the lung granulomas could be *Aspergillus* nodules for which the source of contact was the working environment. The ward was a semi-closed building and the patient contacted the *Aspergillus* spp. in the air at work. Since the patient did not show symptoms of the disease prior to the beginning of her nursing profession at the neurology ward and the patient worked in this specific environment for more than 20 years; it is likely that this patient had *Aspergillus* spp. infection after being exposed to the air at her workplace. Another factor that might influence the occurrence of *Aspergillus* nodule, in this case, was the previous diagnosis of pulmonary tuberculosis. Pulmonary tuberculosis and some other chronic diseases such as bronchiectasis, diabetes mellitus, and malignancy were reported to be the predisposing factors for *Aspergillus* nodules patients [12]. The current findings were consistent with previous reports of CPA in Thailand and elsewhere in which having a previous diagnosis of tuberculosis was associated with CPA [2–4,9].

The diagnosis was confirmed after examination of the surgical tissue biopsy and the PCR test, where *Aspergillus* spp. was found. Although the *Aspergillus* galactomannan antigen presented in this case, this test is not a conclusive test for aspergillosis. Similarly, Kang et al. reported on *Aspergillus* nodules for which there had been a positive *Aspergillus* galactomannan antigen in only 8 of 26 patients [12]. Likewise, Boch et al. reported low sensitivity (23%) vis-à-vis positive serum *Aspergillus* galactomannan antigen for detection of invasive pulmonary aspergillosis [13]. The patient in the current case study had supportive evidence of presenting *Aspergillus* nodules related to her working environment as she had previously been diagnosed with pulmonary tuberculosis. Although there had been no examination for in-air fungi in her working environment at the beginning of her work, the patient confirmed in-air fungi contamination in her working environment. The diagnosis of work-related lung granuloma was made based upon evidence of *Aspergillus* spp identified from in-air samples rather than from a concentration of fungi colonies using a quantitative method. During the cultivation of fungi, many fungi were identified, albeit the absolute concentration of airborne fungi (CFU/m^3) was not calculated. It is likely that the lung granulomas were caused by *Aspergillus* spp, possibly an *Aspergillus* nodule. As such, the *Aspergillus* nodule may have been due to airborne exposure at the workplace.

The caveat to diagnosing a work-related lung granuloma, in this case, is the lack of qualitative and quantitative measures of fungi exposure in the home environment. Furthermore, other coworkers in the same working environment had no documentation of any tuberculosis or *Aspergillus* infection. In addition, lacking any regular monitoring data of airborne fungi concentration in this ward also limit the ability to make a link between airborne concentrations and the onset of disease.

In conclusion, the patient was in the nursing profession and had previously been diagnosed with pulmonary tuberculosis and myasthenia gravis. The patient had been through a long duration of being exposed to in-air *Aspergillus* spp. in the workplace. The patient was thus highly likely to contract *Aspergillus* spp. causing a left lung granuloma and possibly an *Aspergillus* nodule.

Conflicts of interest

The authors declare no conflicts of interest.

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