中文題目：慢性肺麴菌病發生於放射線治療所引發之支氣管擴張症–案例報告

英文題目：The Development of Chronic Pulmonary Aspergillosis in Pre-existing Radiation-related Bronchiectasis：A Case Report

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Introduction

Pulmonary aspergillosis leads to diverse clinical manifestations, ranging from asymptomatic colonization to fatal invasive aspergillosis. The diagnosis of chronic pulmonary aspergillosis (CPA) is challenging because of indolent clinical course and non-specific symptoms. Pre-existing structural lung lesions are risk factors and may hint the diagnosis. Herein, we present a case of CPA developed in a previously formed bronchiectasis after radiation therapy.

Case report

This 86-year-old man had history of early stage nasopharyngeal carcinoma with complete remission after concurrent chemotherapy and radiotherapy 6 years ago. Mild fibrosis and bronchiectasis, which was thought to be radiation-related, developed in right upper lung apex thereafter without serial radiologic change for years. This time, he presented with progressive exertional dyspnea, generalized malaise, cough, and chest pain for more than 1 week. Auscultation of the chest revealed decreased breath sound in right lower lobe and bilateral slight rhonchi and the remainder of physical examination was essentially normal. The white-cell count was 22980 per microliter; 95% of the cells were neutrophils and the C-reactive protein level was 250 mg per liter. Chest X-ray [fig.1] revealed massive right pleural effusion and persistent opacity in right apex. Then, chest computed tomography (CT) [fig.2] show massive pleural effusion, favoring empyema and incidentally finding of cavitary lesion with "ball-in-hole" appearance in right lung apex. Tracing and comparing his serial chest CTs [fig.3], they revealed fibrosis with mild bronchiectasis in right apex after radiotherapy since 2017. Moreover, progressively expanding thick-walled cavity with intra-cavitary nodule was noticed in recent one year.

Initial survey including sputum bacterial culture and acid-fast stains were negative. Drainage from right pleural effusion showed pus-like material which grew *Streptococcus intermedius* later. For non-resolved right empyema and undetermined cause of right upper lung cavity, he underwent video-assist thoracic surgery (VATS) with right upper lung segmentectomy and decortication. The specimen in right upper lung revealed focal necrosis, acute and chronic inflammatory cell infiltration and stromal necrosis with aggregation of fungal hyphae [fig.4]. Tissue culture revealed *Aspergillus fumigatus*. In addition, the serum *Aspergillus fumigatus* and *Aspergillus niger* IgG revealed 44 mgA/Liter (reference range, < 40 mgA/Liter) and 47.2 mgA/Liter (reference range, < 40 mgA/Liter). The serum galactomannan antigen index was 0.075 (reference

range, < 0.5).

Under impression of chronic cavitary pulmonary aspergillosis, intravenous voriconazole were administered first, and then we shift to oral voriconazole after discharge. The course after discharge is uneventful .

Discussion

This case demonstrates the serial radiological findings of pathologically confirmed CPA. Initially, radiation pneumonitis with fibrosis and bronchiectasis in right lung apex was noticed for several years. However, the follow-up chest CTs reveal progressive cavitation and the characteristic "ball-in-hole" pattern of CPA in recent months.

However, a consistent appearance in thoracic imaging is only a hint, but it is not sufficient to diagnose CPA. Direct evidence of *Aspergillus* infection or an immunological response to *Aspergillus* spp. is crucial to differentiate CPA from aspergillus-colonized patient. In clinical practice, histopathological specimen obtained by invasive procedure is not always available. Hence, serological evidences are indispensable for diagnosis. The serum galactomannan antigen has high sensitivity and specificity in invasive pulmonary aspergillosis, but the sensitivity is low for diagnosing CPA [1]. Therefore, serum *Aspergillus* antibody, which has a sensitivity around 80 to 90 percentage is important to diagnose CPA [2]. In our case, we diagnosed CPA with radiological finding and serum *Aspergillus* IgG. Additionally, histopathological specimen and tissue culture report are also consistent with the diagnosis.

Antifungal therapy can lead to improvement of symptoms and radiological findings. The azoles, particularly itraconazole and voriconazole, are the mainstays of antifungal therapy for CPA. Anti-fungal therapy for at least 6 months is recommended and more long-term, even life-long, treatment duration may be necessary for some cases [3].

Conclusion

We reported a case of CPA developed from the bronchiectasis secondary to previous radiation therapy. Clinicians need to keep alert and list CPA in the differential diagnoses for a lesion developed in a pre-existing structural change of lung.

References

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