CASE REPORT

Successful pneumonectomy for invasive pulmonary aspergillosis and advanced non-small cell-lung cancer

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SUMMARY

Aspergillus spp. is a pathogenic fungus in patients with malignancy, immunosuppression or respiratory diseases, and invasive pulmonary aspergillosis (IPA) caused by its infection is an aggressive and often lethal disorder. We report a case of non-small-cell lung cancer (NSCLC) where pneumonectomy concomitantly enabled radical cure of the underlying disease and IPA against which different antifungal drugs had been ineffective. In a patient with locally advanced NSCLC that progressed despite chemoradiation, radiation pneumonitis and subsequently cavitory disease developed following the administration of corticosteroids. Based upon the isolation of *Aspergillus spp.* from sputum, a diagnosis of IPA was made and since the latter was refractory to multiple antifungal drugs, pneumonectomy was undertaken which resulted in successful treatment of both NSCLC and IPA. Surgical intervention should be considered as a therapeutic option for IPA complicating NSCLC that is refractory to medical management.

BACKGROUND

Aspergillus spp., a ubiquitous fungus frequently found in water and humid soil, aggressively invades into the lung after its inhalation through the airway as pulmonary aspergillosis, and sometimes disseminates systemically.¹ It is highly pathogenic for patients with underlying respiratory diseases or immunosuppressive conditions such as malignancy and administration of corticosteroids or antitumour drugs.^{2–3} Among the various disease patterns of aspergillosis, invasive pulmonary aspergillosis (IPA) is characterised by its invasiveness into tissue and haemorrhagic infarction.⁴ Although IPA is initially treated with antifungal drugs, death rates remain high despite the effectiveness of voriconazole (VCZ).⁵ Furthermore, the underlying critical diseases might not only worsen prognosis, but they might also exclude the possibility of surgery as a therapeutic alternative, and in particular, extended surgery such as pneumonectomy has rarely been applied.^{6–7} To concomitantly overcome both IPA and underlying diseases is therefore challenging.

CASE PRESENTATION

A 60-year-old man with a 135 pack-year history of smoking was admitted to our hospital with haemoptysis. His chest CT showed a mass that had spread from the left hilus to the upper lung lobe, and invaded the left main pulmonary artery and left main bronchus, causing obstructive pneumonia

of the left upper lobe (figure 1). Clinical laboratory tests showed no abnormalities except high γ -glutamyl transpeptidase activity (231 IU/l, normal range 0.0–73.0 IU/l) and squamous cell carcinoma antigen (5.7 ng/ml, normal range 0.00–1.50 ng/ml). From the pulmonary function test (FEV₁ 2.36 l, FEV₁% 68.40%, %FEV₁ 80.7%), he had mild chronic obstructive pulmonary disease (COPD) relevant to stage I in the GOLD (global initiative for chronic obstructive lung disease) categories. Stage IIIA (cT4N1M0) pulmonary squamous cell carcinoma was diagnosed from the sputum cytological and imaging findings. The tumour broadly invaded into the left pulmonary artery, thereby

Figure 1 Chest CT images on admission (top and bottom) show a mass of the primary non-small-cell lung cancer lesion and an infiltrative shadow suggesting obstructive pneumonia at the left upper lung lobe.

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leading to the decision that immediate surgical resection cannot attain radical cure at that point. Then, the patient received curative concurrent chemoradiation with cisplatin 40 mg/m² on days 1 and 8 plus docetaxel 40 mg/m² on days 1 and 8 of a 28-day cycle for two cycles, in addition to thoracic irradiation (daily 2-Gy fractions to 60 Gy). However, this multidisciplinary treatment did not completely cure the non-small-cell lung cancer (NSCLC). He developed fever thereafter, and his chest CT showed an extensive infiltrative shadow and ground-glass opacity in accordance with the area being irradiated as well as the tumour which was reduced in size but persisted (figure 2). No causative pathogens were isolated from the sputum cultures, and all empirical antibiotic approaches were ineffective. Given the potential for radiation pneumonitis, hydrocortisone (300 mg/day) was started, which reduced the shadow. After 12 days of administration, a cavitary lesion appeared within the shadow and rapidly augmented (figure 3). *Aspergillus spp.* was isolated from the sputum culture and the serum *Aspergillus* antibody was positive, although the serum *Aspergillus* galactomannan antigen was negative and plasma (1→3)-β-D glucan was not detected. According to a diagnosis of IPA based on these results, monotherapy with VCZ was started. In reference to clinical practice guidelines of the Infectious Diseases Society of America and the previous reports, micafungin was added as salvage therapy since the lesion rapidly deteriorated after 3 days of VCZ monotherapy.^{8–10} However, both the antifungal drugs even

failed to prevent disease progression. The entire lesion was localised in the left lung and preoperative examinations containing a pulmonary function test and ventilation–perfusion scintigraphy showed an adequate pulmonary reserve for pneumonectomy because the right lung was intact, suggesting that pneumonectomy was feasible and tolerable. Together with the absence of alternatives for a complete cure and the request from the patient for surgical resection, we decided pneumonectomy for the patient as salvage therapy, and the patient provided written informed consent to undergo left pneumonectomy. The pathological findings from resected specimens confirmed radiation pneumonitis, squamous cell carcinoma and abscess containing numerous *Aspergillus spp.* supporting IPA (figure 4).

OUTCOME AND FOLLOW-UP

No postoperative complications arose and the patient has remained event free.

DISCUSSION

To our knowledge, this is the first description of a complete cure of concurrent IPA and underlying NSCLC by pneumonectomy. Curative surgical resection has limited application in IPA because of its early dissemination and the poor conditions of the hosts, and in particular, pneumonectomy, the extended surgery, has been very infrequently reported.⁶ Treatment with antifungal drugs is therefore the first choice for IPA, whereas its mortality of approximately 40–90% is unsatisfactory, and

Figure 2 Chest CT images show a reticular shadow consistent with the radiation field suggesting radiation pneumonitis (top) and the residual non-small-cell lung cancer mass after chemoradiation (bottom) at the left upper lung lobe.

Figure 3 Chest CT images show an extensive cavity within the infiltrative shadow of invasive pulmonary aspergillosis (top) and the residual non-small-cell lung cancer mass (bottom) at the upper lung lobe.

Figure 4 Gross (A) and microscopic (B–D) images of the specimens resected by pneumonectomy represent mixed tissue invasion by *Aspergillus* spp. (B, Grocott staining), squamous cell carcinoma (C, HE staining) and fibrotic changes caused by radiation pneumonitis (D, HE staining).

especially the death rates in patients with COPD and lung cancer are between 90% and 100%, indicating that IPA in this case is difficult for the treatment of the disease.^{11–14} In addition to such serious conditions, comorbid radiation pneumonitis to which corticosteroids were administered might have negatively affected the diagnosis and treatment of IPA in this case, as the previous report showed that corticosteroid therapy and chemotherapy were risk factors for IPA in patients with lung cancer.¹⁵ Pneumonectomy as an optional treatment after failure of standard treatment led to the simultaneous cure of IPA and NSCLC in the patient with these severe difficulties. Meanwhile, the onset of IPA in comorbid radiation pneumonitis might have resulted in delayed diagnosis, suggesting that the possibility of other comorbid diseases should have been considered more carefully.

In conclusion, although pneumonectomy is unlikely to be a therapeutic option for IPA, such an extended surgery might be warranted when no other treatments can completely cure the IPA and the underlying pathologies.

Learning points

- The onset of invasive pulmonary aspergillosis (IPA) should be noticed in immunocompromised patients with the underlying respiratory diseases.
- Comorbid diseases can make a rapid diagnosis of IPA difficult.
- Extended surgery such as pneumonectomy under an adequate pulmonary reserve might be warranted as a therapeutic option for IPA and serious comorbid diseases after failure of standard treatment.

Competing interests None.

Patient consent Obtained.

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