Combination antifungal therapy for invasive pulmonary aspergillosis

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DESCRIPTION

A 58-year-old man with a history of AIDS and recurrent non-Hodgkin's lymphoma had 1-week complaint of fever, productive cough and chest pain 2 weeks after chemotherapy. He was on anti-retroviral triple therapy and antibiotics, but with no response. Physical examination was significant for tachypnea and bilateral crepitations. Chest x-ray showed right middle lobe hazy infiltrates and scattered small nodular lesions (figure 1). Laboratory data showed white cell count of $16.2 \times 10^9/l$ with neutropenia, and CD4 count of 70 cells/ μl . Bronchoscopy was performed (see video 1) and showed discrete, white coloured ulcerations of the airways. The transbronchial biopsy showed well-defined septate hyphae, dichotomously branching at an acute angle (figure 2). The overall outcome in patients with invasive pulmonary aspergillosis (IPA) is poor; however, our patient was treated with intravenous liposomal amphotericin B and voriconazole for 6 weeks, and recovered fully from his symptoms and radiological findings. He was started later on the recommended chemotherapy for lymphoma disease after introducing oral posaconazole as antifungal prophylaxis.

Clinicians are urgently seeking new strategies to remedy the poor outcome of IPA, for which the optimal therapy is unknown. Currently, voriconazole monotherapy is evidently better than polyene, but continues to be associated with unacceptably high mortality. Although some animal models and limited clinical reports suggest that combination

Video 1 Bronchoscopy showing the aspergillosis lesions of the airways.

antifungal therapy might offer improved outcome, the efficacy of combination therapy for IPA has not been conclusively established in controlled trials.¹

Figure 1 Chest radiograph showing right middle lobe hazy infiltrates and scattered small nodular lesions (arrows).

Figure 2 Septate hyphae consistent with Aspergillus infection by transbronchial biopsy (arrow).

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Potential advantages of combination antifungal therapy include a wider spectrum and potency of drug activity, more rapid antifungal effect, synergy, lowered dosing of toxic drugs and a reduced risk of antifungal resistance.¹

The most frequently used antifungal combination in clinical practice is that of triazole and echinocandin, most commonly voriconazole and caspofungin. The two drugs have a synergistic interaction, simultaneously inhibiting 1,3- β -D-glucan synthesis in the fungal cell wall and ergosterol synthesis in the fungal cell membrane.¹

The combination of azoles and polyene antifungal were not frequently used for fear of antagonism, although there is a lack of clinical evidence to support this concern.² Animal model studies recently showed the combination of ambisome and voriconazole to be more effective than individual drug monotherapy.³ Askari *et al*⁴ tested the effectiveness and safety of this combination, and reported on its safety and effectiveness. A similar combination was also successfully used in case reports of endocarditis and invasive aspergillosis in leukaemic patient.⁵ More rigorous trials to test the efficacy of this combination in treating invasive aspergillosis are needed.

Learning points

- Combination antifungal therapy can be an appropriate choice for the treatment of invasive pulmonary aspergillosis (IPA).
- The combination of lipid formulated amphotericin and azoles are safe and potentially effective for the treatment of IPA.

Competing interests None.

Patient consent Obtained.

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