CASE REPORT

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Caspofungin may effective for initial treatment of pulmonary aspergillosis

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ABSTRACT

Introduction: Invasive aspergillosis mostly involves lungs. Patients may present with fever, cough, hemoptysis and many other sign and symptoms. Underlying conditions that compromises pulmonary and immune responses to inhaled *Aspergillus* species serve as risk factors for pulmonary invasive aspergillosis. We are presenting a case of simple aspergilloma, successfully treated by caspofungin and surgery. **Case Report:** A 64-year-old male patient has rheumatoid arthritis for ten years. Since three months he had interstitial pulmonary disease secondary to rheumatoid arthritis and hemoptysis. We performed microbiologic and pathologic investigations of the bronchoalveolar lavage after computerized tomography for diagnosis of aspergillosis. Caspofungin was used for initial treatment of simple aspergilloma and also for follow-up treatment after apical wedge

resection. The patient was discharged from the hospital at eighth week on itraconazol antifungal therapy. **Conclusion:** Three classes of drugs are available for the treatment of aspergillosis: polyens, azoles and echinocandins. Echinocandins have activity against *Aspergillus* spp. But have a limited role because they have not been studied for initial treatment of invasive aspergillosis.

Keywords: Antifungal treatment, Aspergillosis, Caspofungin

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INTRODUCTION

Aspergillus spp. may cause a variety of pulmonary diseases, depending on immune status and the presence of underlying lung disease [1]. *Aspergillus* species are ubiquitous in nature and inhalation of infectious conidia is a frequent event. Tissue invasion is uncommon and occurs most frequently in the setting of immunosuppression associated with therapy for hematologic malignancies, hematopoietic cell transplantation or solid organ transplantation [2]. Most invasive infections are caused by members of *A. fumigatus* species complex. Caspofungin is an echinocandin class antifungal drug. Echinocandins target fungal cell glucan synthesis by competitively inhibiting the beta-1,3-D-glucan synthase enzyme complex in susceptible fungi. This enzyme complex is

composed of at least two components: catalytic subunits called Fks1p and Fks2p, and a GTP-binding protein, Rho1, which regulate the activity of glucan synthesis [3]. Echinocandins are widely used for the treatment of invasive candidiasis, especially in critically ill and neutropenic patients and less commonly in salvage regimens for invasive aspergillosis [4, 5]. Recent studies conclude that surgical resection should be considered for all patients with pulmonary aspergilloma who have acceptable pulmonary reserve. Echinocandin class of antifungal drugs have not been studied adequately as initial antifungal treatment of pulmonary aspergillosis. In this case we used caspofungin alone for initial treatment of pulmonary aspergilloma before and after surgery.

CASE REPORT

A 64-year-old male patient presented to us with hemoptysis for one week. He was a farmer by profession and had rheumatoid arthritis for ten years. He was taking prednisone 20 mg per day for last three months for interstitial pulmonary disease secondary to rheumatoid arthritis and azathioprine 100 mg per day for anti-CCP positivity for last one month. He had fifteen days of cough and productive sputum and was given amoxicillin-clavulonate 2 gm per day by his family practitioner. He was referred to our hospital with hemotysis of one week duration. The complete blood cell counts and blood biochemistry were within normal range except for high erythrocyte sedimentation rate (110 mm/1st hr) and high C reactive protein (13.7 mg/dL). Chest radiograph showed a suspicious mass in the right apical lobe. Bronchoscopy were done for investigating tuberculosis by acid fast staining of bronchoalveolar lavage (BAL). Computed tomography (CT) scan was performed because of suspicious mass on chest radiograph. There was a 5.8x5.1x8.6 cm right apical pleural based cavitary lesion with thick irregular wall. It was forming a small air crescent (Figure 1). Acid fast stain of BAL was negative. Routine staining of sputum and BAL showed hyphae with septa. Microbiologic culture showed *A. fumigatus*. We diagnosed the case as simple aspergilloma and began conventional amphotericin B treatment. Patient has allergic rash after amphotericin B infusion and on third day of hospitalisation he has abdominal pain. Despite his symptoms, hepatic transaminases were within normal range. Acute cholecystitis was diagnosed after general surgery consultation and abdominal ultrasonography showed sludge in the gallbladder. We decided on caspofungin treatment of intravenous loading dose (70 mg/day) followed by 50 mg/day infusion once daily. Patient was evaluated by chest surgery consultation and it was decided to wait for thoracic surgery consultation because of the abdominal complaints. Cholecystitis regressed in one week by medical treatment. Patient was operated at third week of antifungal treatment. Apical wedge resection was performed to remove the cavitary lesion and the fungus ball. Pathologic

examination of surgical specimen showed hyphae with septa, bronchial invasion and interstitial pulmonary disease (Figure 2). Antifungal treatment with caspofungin continued by intravenous route for five weeks after surgery. After eighth week of hospitalisation patient was discharged with itraconazole 200 mg twice daily peroral route. At 12 weeks, antifungal treatment was stopped. Patient's symptoms such as cough, hemoptysis and productive sputum were not seen after tenth week of treatment.

DISCUSSION

Three classes of antifungal drugs are available for the treatment of aspergillosis: polyens, azoles and echinocandins. Echinocandins have activity against *Aspergillus* spp, but have a limited role because they have not been studied for initial treatment of invasive aspergillosis. Echinocandins are used for treatment of

Figure 1: Air crescent formation with fungus ball in the lungs.

Figure 2: Histopathologic examination shows hyphae with septa, characteristics of aspergillosis (H&E, x 200).

invasive candidiasis especially in critically ill patients and less commonly for invasive aspergillosis especially as salvage treatment. The major advantages of echinocandins relative to other antifungal drugs are their fungicidal activity against *Candida* spp including fluzole resistant species combined with their relatively low potential for renal or hepatotoxicity [5]. Growth of *Aspergillus* species is inhibited even by very low concentrations in vitro with the effects predominantly observed at apical sub-apical branching where cell wall remodelling and beta glucan synthase are most active [6, 7]. Azoles are the first agents of choice for pre- and post-operative antifungal therapy. In our patient allergic rash occurred at the beginning of treatment with conventional amphotericin B. As amphotericin B-lipid complex was not available and due to patient's cholecystitic symptoms such as nausea and vomiting antifungal treatment option was switched to caspofungin. Caspofungin was used in standard dose of 70 mg on first day and subsequent dosing was 50 mg/day. In this case we preferred to use caspofungin as initial treatment especially because of the abdominal symptoms. After one week of treatment we made an interval reviewing of treatment for using caspofungin alone or in combination. We made a decision of using caspofungin alone because of improving clinical condition of the patient. Antifungal treatment after surgery of aspergillomas has been strongly recommended by most of the authors [8]. Antifungal treatment options after surgery depend on patient's clinical situation. Itraconazole and voriconazole are first line agents for oral antifungal treatment of aspergillosis [8]. Duration of antifungal therapy is not well defined in literature. Some authors have recommended lifelong therapy because of the relapses [9]. Others suggest that a four week course of therapy post-operatively is reasonable, if the aspergilloma was fully resected without spillage. If there is spillage, then a minimum of 12 weeks therapy is recommended in an attempt to prevent pleural aspergillosis [8]. In our case, we used itraconazole for seven weeks after caspofungin intravenous therapy.

Risks and benefits of medical and surgical therapy vary with the manifestations of the disease and patients pulmonary status. Surgery is the mainstay of treatment for symptomatic patients with simple aspergilloma to prevent or treat life-threatening hemoptysis [8]. Surgery of pleural based aspergilloma will be risky. Most of the surgeons prefer lobectomy or cavernectomy because of the pleural hemorrhagic complications. In our case we preferred pleural based wedge resection of cavitary lesion in order to preserve patient's vital capacity in the future.

CONCLUSION

Aspergilloma is a fungus ball composed of aspergillus hyphae, fibrin, mucus, and cellular debris found within a pulmonary cavity. In the treatment of aspergilloma, surgery and antifungal therapy must be

given together. Choice of antifungal agents is the main cause of successful treatment. Caspofungin shows satisfactory antifungal activity against aspergilloma before and after surgery despite inadequate data about its use.

Author Contributions

Alper Sener – Substantial contributions to conception and design, Acquisition of data, analysis and interpretation of data, Drafting the article, revising it critically for important intellectual content, and Final approval of the version to be published

Senol Kobak – Substantial contributions to conception and design, Acquisition of data, Revising it critically for important intellectual content, Final approval of the version to be published

Timucin Alar – Substantial contributions to conception and design, Acquisition of data, Revising it critically for important intellectual content, Final approval of the version to be published

Ugur Gonlugur – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Asli Muratli – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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REFERENCES

1. Zmeili OS, Soubani AO. Pulmonary aspergilosis: a clinical update. QJM 2007 June;100(6):317–34.
2. Segal BH. Aspergillosis. N Engl J Med 2009 Apr 30;360(18):1870–84.
3. Douglas CM. Fungal beta(1,3)-D-glucan synthesis. Med Mycol 2001;39 Suppl 1:55–66.
4. Pappas PG, Kauffman CA, Andes D, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;48(5):503–35.
5. McCormack PL, Perry CM. Caspofungin: a review of its use in the treatment of fungal infections. Drugs 2005;65(14):2049–68.

6. Beauvais A, Bruneau JM, Mol PC, Buitrago MJ, Legrand R, Latgé JP. Glucan synthase complex of *Aspergillus fumigatus*. *J Bacteriol* 2001;183(7):2273–9.
7. Bowman JC, Hicks PS, Kurtz MB, et al. The antifungal echinocandin caspofungin acetate kills growing cells of *Aspergillus fumigatus* in vitro. *Antimicrob Agents Chemother* 2002;46(9):3001–12.
8. Walsh TJ, Anaissie EJ, Denning DW, et al. Treatment of aspergillosis: clinical practice guidelines of the Infectious Diseases Society of America. *Clin Infect Dis* 2008;46(3):327–60.
9. Denning DW, Riniotis K, Dobrashian R, Sambatakou H. Chronic cavitary and fibrosing pulmonary and pleural aspergillosis: case series, proposed nomenclature change, and review. *Clin Infect Dis* 2003;37 Suppl 3:S265–80.

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