

REPORT

Pleural lavage of amphotericin B for treatment of empyema caused by *Candida albicans* infections: A case report

Zhang Qian¹, Zhuo Yeye¹, Chen Pan² and Chen Jie²

¹Department of Pharmacy, The First Affiliated Hospital of Shantou University Medical College, Shantou, Guangdong, China

²Department of Pharmacy, The First Affiliated Hospital, Sun yat-sen University, Guangzhou, Guangdong, China

Abstract: Chest fungal infection is a rarely seen lethal disease with rapid progression. Sufficient residence time of antifungal agent with therapeutic concentration in the chest is an essential point during anti-infection therapy, which is hard to achieve via conventional systemic drug delivery. We here by describe a case of successful treatment of fungal Chest infection via local pleural lavage. A 59 years old male was hospitalized due to chest pain. X-ray of chest and bacterial culture of thoracic drainage fluid and blood indicated severe chest infection of *Candida albicans*. The patient was initially administered intravenously with amphotericin B (25mg/day). However, the symptoms were not significantly improved after 5 days of treatment. Then one-hour pleural lavage of 5mg amphotericin B in volume of 50ml 5% glucose solution was added once daily. On day 12, bacterial cultures showed negative, and chest X-ray exhibited apparent decrease of shadow area, also other examinations such as body temperature and white blood cell count suggested significant improvement of infection. The therapeutic strategy of amphotericin B was maintained until two consecutive bacterial cultures were negative, then was switched back to intravenous drip alone for another one month found. No significant adverse effects were observed during the treatment. In conclusion, this case demonstrates a new local pleural lavage method of amphotericin B for chest fungal infection, which may provide a reference for the treatment of such cases.

Keywords: Amphotericin B, *Candida albicans* infections, pleural lavage.

INTRODUCTION

Empyema is a form of infection cause by pathogenic bacteria which intrude into pleural cavity. Most empyema is secondary to pulmonary infection. It is also accompanied by empyema and mediastinal abscess, rib or sternum osteomyelitis, sepsis and other complications, which seriously impact patients' recovery. Compared with bacterial infection, empyema caused by a fungal infection is rarely seen in clinical practice, its fast progresses and difficult therapy bring more harm, primarily because regular intravenous administration is difficult for achieving therapeutic concentrations. We report a case of empyema caused by *Candida albicans*, we treated the patient by pleural lavaging with amphotericin B and achieved a pronounced response.

Case report

A 59-year-old Asian man was admitted for treatment of stethalgia on the eighth day after radical surgery for esophageal carcinoma. Radiography showed major pleural effusion in the left chest and an indwelling chest tube drained a large amount of yellow-green chest liquid. The patient had no significant improvement and presented phlegm, sputum, weakness, chest tightness, shortness of breath, fatigue and other symptoms after administration of

imipenem/ cilastatin at 0.5g/q8h. He was transferred to ICU due to his chest disease, that required intubation and ventilation by a respirator. The patient had a history of smoking more than 35 years at an average of 40 cigarettes/day.

The patient was kept on Miconazole 150 mg/qd after transfer to the ICU. Three days later, his peripheral white blood cell (WBC) count was follow $15.05 \times 10^9/L$ with 92.6% neutrophils and 9.44ng/ml PCT. Bacterial culture of sputum demonstrated a low level of fungus and the pleural fluid drainage and blood cultures showed *Candida albicans*. The bedside chest radiograph (fig. 1) showed: 1. the appearance of hydropneumothorax and atelectasis on the left chest, which was compressed about 70%; 2. Lung exudative lesions considered to be inflammation. These results suggested that the infection state was not improved, so we changed miconazole to amphotericin B (5mg on day 1 and increased 5mg daily until 25mg as maintenance dose). On day 5, the chest tube drainage was thick and seemed like jelly, with plenty of pus in stoma attachment through electronic endoscopy. The drainage reduced further on the next day, but culture still showed a large number of *Candida albicans* cells.

According to the instructions for amphotericin B injection, the concentration of amphotericin B in hydrothorax is usually less than half the blood

*Corresponding author: e-mail: chenjiezs@163.com

concentration over the same period, suggesting that the patient with pyothorax had a lower amount of antibacterial drugs diffuse into the pleural fluid because of some acidic substances produced by his thickened pleura surface. In addition, the concentration of amphotericin B was felt further insufficient in the locality because of pleural drainage, which decreased the retention of amphotericin B in chest. Therefore, the patient held on amphotericin B injection failed to achieve the effective therapeutic target. In consideration of this, we used a daily lavage protocol on day 7 whereby 5 mg amphotericin B was dissolved in 50 ml of 5% glucose solution, injected it into the chest, and then drained the solution after one hour. The clinical procedure was well tolerated and the patient's fluid properties significantly improved, leading to a pale yellow clear liquid and smooth drainage on the 3rd day of medication. Associated infection index declined, and the chest radiography also significantly was improved (fig. 2). The drainage of chest fluid culture was negative for *Candida albicans* on day 12, and the patient was successfully extubated offline and continued treatment for general surgery. Pleural lavaging with amphotericin B was continued daily until consecutive cultures were negative twice (on day 15 and 18). Then intravenous amphotericin B continued to administer for 1 month until the patient improved and hence was discharged. No significant adverse effects were observed, and the patient's serologic and biochemical parameters were throughout the treatment.

DISCUSSION

In early 1970s, researchers had already cured fungal empyema by pleural lavage with amphotericin B. Colp used thoracic duct topical lavage with amphotericin B for treatment of empyema infected with *Aspergillus* (Charlotte *et al.*, 1975). In this century, there have been

several cases of fungal empyema where researchers used pleural lavage with antifungal agents to achieve good outcome. Amphotericin B has played an irreplaceable role in fungal infection because of its broad spectrum antibacterial agents and a strong antifungal effect. Utley *et al.* (1993) reported two cases of *Aspergillus empyema*, caused by infection of a bronchial fistula after pneumonectomy and postoperative thoracoplasty, where they lavage the chest surgery area with an antifungal agent while injecting systemic antifungal agents. After 21 days, the patient had improved and was discharged with a negative pleural effusion culture. Uruga *et al.* (2009) reported the case of patient with *Candida albicans glabrata* empyema which was second found in Japan, to pleural lavaged with amphotericin B and injected with micafungin, the pleural effusion reduced and became into negative after 27 days treatment. Bonatti *et al.* (2010) reported the use of voriconazole and caspofungin for injection, combined with pleural lavage with amphotericin B, in the treatment of four *Aspergillus empyema* patients. Guazzelli *et al.* (2012) reviewed 391 cases diagnosed with pulmonary aspergillosis, four of them were treated by open drainage of the cavity content and intrapleural instillation of amphotericin B. Pleural lavage with amphotericin B for treatment of *Aspergillus* was considered a permanent supplementary support. In summary, pleural lavage with amphotericin B for the treatment of empyema caused by fungus is effective and feasible.

In 1975, investigators started with amphotericin B at a dose of 5 mg, dissolved in 35 ml of 5% glucose solution, and gradually increased the dose to 25 mg. A daily chest lavage was performed for one hour, followed by draining. The reason why we used 35 ml of solvent was because of the position of the chest tube in the patient, suffering from tuberculosis and already had thickened pleura that was

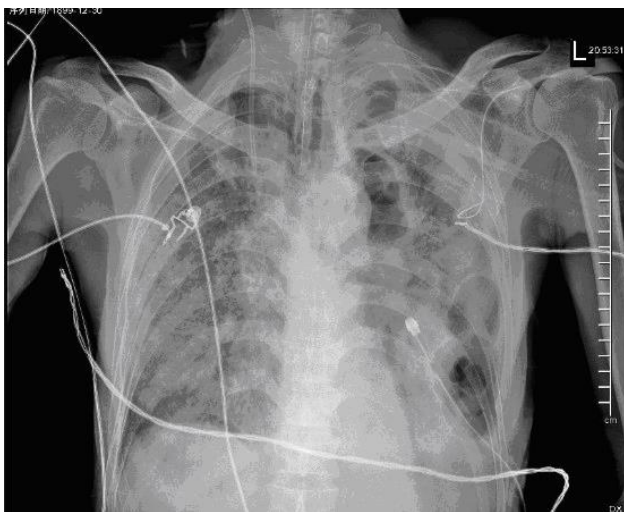


Fig. 1: Empyema before chest cavity lavage with amphotericin B

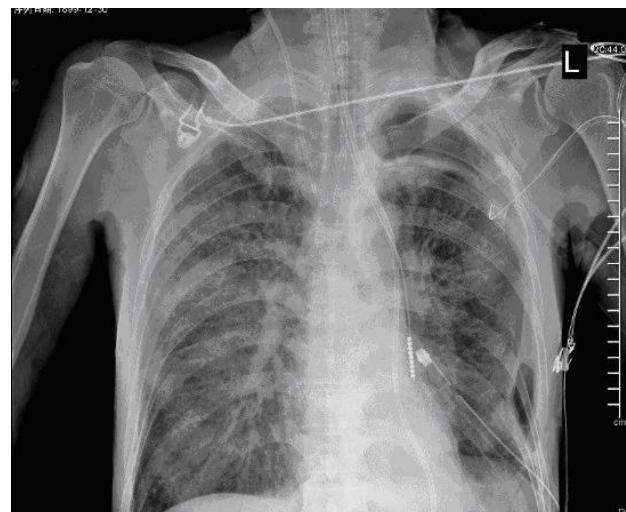


Fig. 2: Empyema after chest cavity lavage with amphotericin B

fibrotic. So the right pneumothorax could not accommodate more fluid, and a change of position might induce coughing in the patient. With this volume and dose, the chest tube fitted well and the patient displayed no adverse effects, indicating that this method, involving amphotericin B to lavage the pleura, is feasible. In 2013, Xu *et al.* (2009) cured a patient suffering from *Aspergillus empyema* by pleural lavage of amphotericin B, they put 5-25 mg of amphotericin B into 500 ml of 5% glucose, then poured the solution slowly into enterocoelia. They pointed out that the administration of amphotericin B needed to be slow in order to prevent the fluid which flew migrate from the fistula into lungs might cause breathing difficulties in patient who got bronchial fistula. From the studies above, we could determine that a dose of 5-25mg amphotericin B could be tolerated by the patient, enabling us to start at a pleural dose of amphotericin B at 5mg, and increasing to 25mg if necessary, in a 5% glucose solution of 50ml.

It was necessary to notice adverse effects of amphotericin B which might involve renal toxicity, liver toxicity, hematologic toxicity, cardiovascular system and nervous system toxicity. Therefore, we gave promethazine to patient to prevent adverse effects, before injecting amphotericin B, and rechecked the serology and biochemical parameters. Our patient could have acquired chest pain (Uruga *et al.*, 2009) or chemical pleurisy because of local stimulation during the time we administered amphotericin B in thoracic cavity, so we closely monitored the patient's tolerance, and regularly reviewed the chest. Fortunately, the patient did not experience any uncomfortable situation or adverse effects during the entire course of treatment.

CONCLUSIONS

An infrequent case presented a fungal pus pneumothorax. It was considered to manage a topical dose of amphotericin B because of the poor results of intravenous injection. Although, topical application of amphotericin B is rarely performed in China, and also lacks a definitive guide and strong support from evidence-based medicine. Therefore, we performed extensive research before using this method of treatment, and closely monitored for tolerability and adverse reactions in the patient. Finally, we succeeded in treating the patient, who was ultimately discharged. This case was designed to provide new usage of amphotericin B for fungal pus pneumothorax, and to provide a reference for the treatment of such similar cases.

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