Yonsei Medical Journal
Vol. 29, No. 1, 1988

Pleural Aspergillosis

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Pleural aspergillosis is an uncommon disease; only 29 cases have reported in the literature since 1958. We reported a patient with a pleural aspergillosis complicated a preexisting chronic empyema. Treatment consisted of pleuropneumonectomy, creation of an pleurocutaneous window followed by an intrapleural instillation of nystatin.

Key Words: Pleura. aspergillosis. empyema. intrapleural. nystatin.

Since Cleland described pleural aspergillosis in 1847, twenty nine cases of pleural aspergillosis have been reported. The etiologic factors for these aspergillosis were preexisting pulmonary tuberculosis, bronchopleural fistula, pleural drainage, and lung resection. Surgical removal of aspergillus-infected pleura is the treatment of choice in managing this disease.

Herein we reported a case of pleural aspergillosis with a mixed infection of Staphylococcus species which was managed by pleurectomy and intra-pleural antifungal agent application.

CASE REPORT

The patient was a 65-year-old man who contracted tuberculosis pleurisy in 1941 and pulmonary tuberculosis in 1956. From 1956 to 1957 isoniazid and streptomycin were given on a therapeutic basis. The patient remained well, with only occasional slight cough and sputum production, until September of 1986 when hemoptysis recurred. On admission to the hospital, chest X-ray films showed collapse consolidation with bronchiectatic changes in the left upper portion of the chest, and longstanding empyema with calcification in the posterolateral aspect of left chest (Fig. 1). Computed tomography revealed that a large empyema space on the lateral portion of left pleural cavity with calcifications, and a collapse consolidation with replacement of multicystic shadows (Fig. 2). Bronchoscopic examination showed a slightly elevated endobronchial lesion at the left lower basal segment. Biopsy finding of the endobronchial lesion was chronic nonspecific inflammation. Three specimens of sputum were negative for Mycobacterium tuberculosis and malignancy. Needle aspiration biopsy was performed in the left posterolateral portion of the chest and dark bloody material was obtained which was negative for bacteria, Mycobacterium tuberculosis and malignancy. The patient was discharged after conservative management for hemoptysis.

One month later after the first admission, he was readmitted because of a hemoptysis for one day. Thoracic surgical consultation was obtained, and underwater tube drainage was begun. All cultures of pleural fluid were negative for fungus and Mycobacterium tuberculosis, bacteria and malignancy. Pleural biopsy material showed marked fibrous thickening of pleura. Follow up chest computed tomography showed persisting empyema on the left chest with calcified rim. During the next three weeks, the pleural fluid drained 500-600cc daily, and was felt to be a candidate for pleuropneumonectomy. On the 80th. hospital day, the pleuropneumonectomy was performed. The biopsy materials of pleura and lung

Received October 23, 1987
Accepted December 3, 1987

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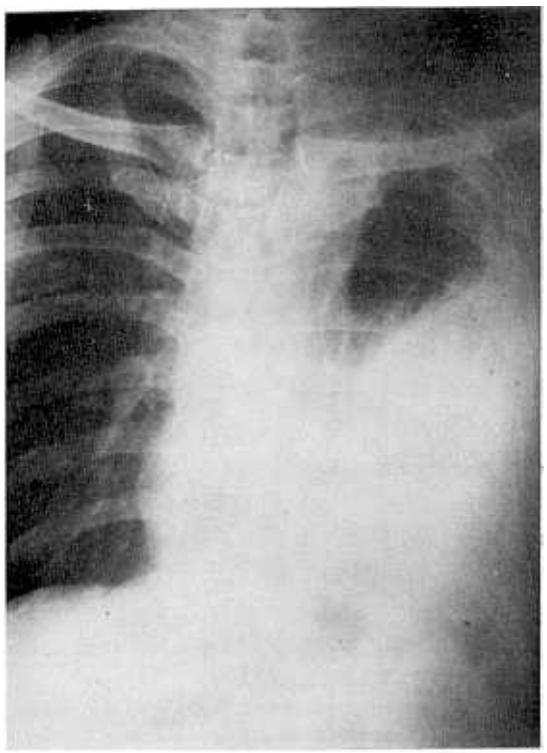

Fig. 1. A posteroanterior chest film showing chronic empyema and pleural thickening (on admission).

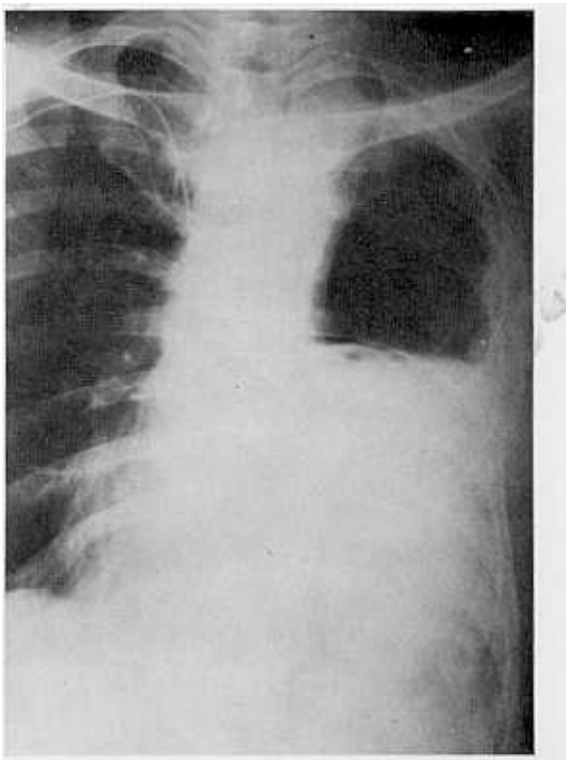

Fig. 3. A posteroanterior chest film after pneumonectomy showing fluid level.

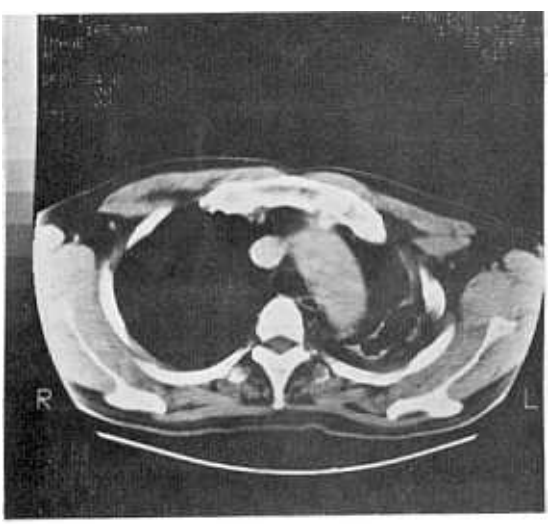

Fig. 2. Chest CT scan reveals a large empyema space noted on the lateral position of left pleural cavity with calcifications along its pleural rim.

were still negative for malignancy and fungsu. Large amount of blood and pleural fluid drained after pneumonectomy (Fig. 3), and the patient still was left with empyema negative for Aspergillus fumigatus and a bronchopleural fistula. Tube drainage seemed undesirable, so it was decided to create an open pleurocutaneous window formation to facilitate longterm drainage of the left-sided empyema. The bloody drainage from window was about 400cc daily, and the transfusion of 2-3 pints was needed daily.

Pleural biopsy at this time showed aspergillosis with focal mesothelial cell proliferation (Fig. 4). A culture study from intrathoracic cavity were positive for Pseudomonas aeruginosa. When the nature of the infecting organism became known, it was decided to treat the patient with local irrigations of nystatin. We began nystatin installation of 25 ml containing 100,000 units/ml once a day. In spite of regular cauterizations of the pleura and nystating installation, the patient died of respiratory insufficiency secondary to hemorrhage.

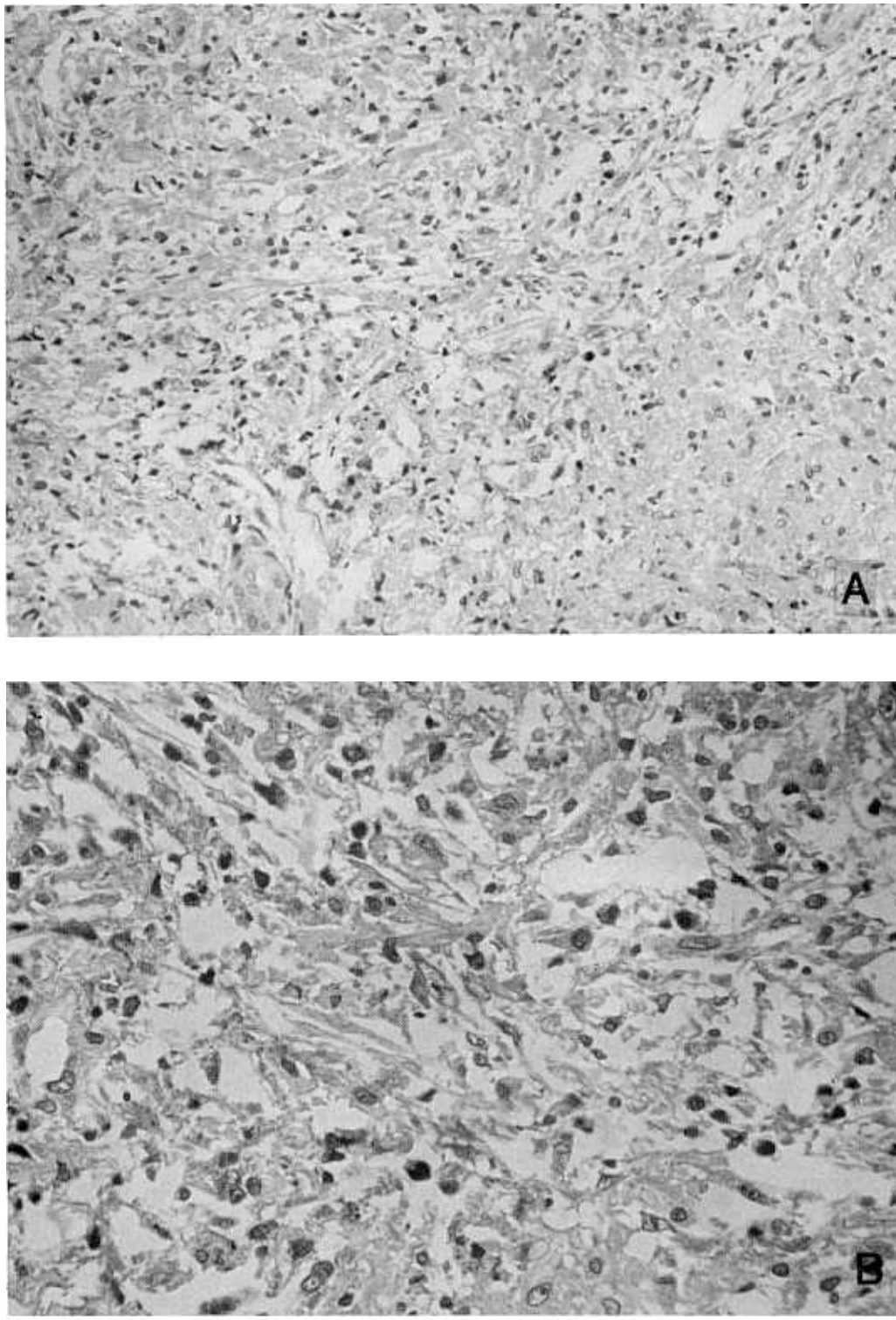

Fig. 4. Magnified section through pleura showing superficial nature of aspergillosis infection, A × 400, B × 1,000.

DISCUSSION

Aspergillus species was first described by Micheli in 1797. Cleland first described pleural aspergillosis in 1847, and 29 cases of pleural aspergillosis have been reported since 1958. Although pleural thickening is an early mainfestation of pulmonary aspergillosis, pleural aspergillosis is not associated with pulmonary aspergillosis. Tardieu *et al.* (1964) reported only one case which was associated with primary pulmonary aspergillosis. Thus pleural aspergillosis has little to do with allergic bronchopulmonary aspergillosis or aspergillosis bronchopneumoina.

Herring and Pecora (1976) analyzed etiologic factors after reviewing 25 cases since 1958; preexisting pulmonary tuberculosis, 87%; bronchopleural fistula, 74%; pleural drainage, 56%; and lung resection, 17%. This patient had longstanding pleural thickening and empyema after exposure to Tuberculosis mycobacterium, which was the most striking predisposition to pleural aspergillosis.

The routes by which aspergillosis reaches the pleura are through bronchopleural and pleurocutaneous communications. Malignant disease, corticosteroids, and exposure to cytotoxic agents have been incriminated in the development of aspergillosis, but were seen infrequently in these cases of pleural involvement. Less frequently, pleural aspergillosis appears to arise from a rupture of an aspergilloma or a pulmonary cavity complicating tuberculosis or sarcoidosis into the pleural space. Pleural aspergillosis occurs mostly in pleural empyema with a bronchopleural fistula or pleurocutaneous fistula due to an aerobic environment with necrotic exudates (Parry *et al.* 1982). Bronchopleural fistulas are usually due to underlying cavitary lung disease or pneumonectomy. In our patient, it was difficult to determine radiologically whether the fungus ball was in a lung cavity or in the pleural space. But likewise in the other cases reported, aspergillus infection of the pleura seemed to be a result of pleural empyema rather than of a rupture of a lung cavity into the pleura.

The diagnosis of pleural aspergillosis is established by the demonstration of the organism in pleural discharge or pleural biopsy. However, the microbiology in up to 50% of reported case is polymicrobial and includes Staphylococcus aureus, beta hemolytic Streptococci, and Mycobacterium tuberculosis, Klebsiella, and Pseudomonas in addition to Aspergillus (Krakowka *et al.* 1970). In these instances, although aspergillus may also produce an invasive infection of the pleura, the presence of Aspergillus could have been incidental and not caused the major clinical manifestations. This is not surprising, since these individuals had significant underlying bronchopulmonary disease and were colonized with a variety of lower respiratory tract microorganisms. In our patient, a mixed infection of Pseudomonas aeruginosa and Aspergillus was found with a locally invasive form of infection in which extensive necrosis and fibrosis of the lung, pleura, and chest wall were found probably caused by aspergillus. Also antibodies may be demonstrated by serological test.

Various recommendations have been made regarding treatment. In the case of a mixed culture like our patient, treatment should be directed towards drainage and debridement of the pleural space and underlying lung disease control because the role of aspergillus remain unclear. Antifungal agent should be reserved for those patients, who do not result in improvement with conventional treatment, who are in an immunodeficiency state or who display evidence of tissue invasion by aspergillus. However, surgical removal of aspergillus-infected pleura must be considered the cornerstone of therapy because the route of aspergillus pleural infection is through a bronchopleural or a pleurocutaneous communication (Colp and Cook 1975). If evidence of pleural or pulmonary invasion is present, nystatin or amphotericin B have been added both parenterally and by intrapleural infusion, but several months is often required to sterilize the pleura (Meredith *et al.* 1978; Costello and Rose 1985).

In reviewing the 24 cases of pleural aspergillosis since 1958 (Herring and Pecora 1976; Parry *et al.* 1982; Krakowka *et al.* 1970; Colp and Cook 1975), 19 patients were treated and cured while 5 patients died. Nine patients were given an intrapleural antifungal agent infusion and enjoyed a 67% cure rate. Intrapleural infusions of amphotericin B were more effective in sterilizing the pleura than nystatin, but the role of amphotericin B is not clear at this time (Table 1). In contrast to medical therapy, 13 patients under-

Table 1. Prognosis after infusion of intrapleural antifungal agent

Agent	Patients cured	Patients expired	Total
Nystatin	2	3	5
Amphotericin-B	3	0	3
Both	1	0	1
Total	6 (67%)	3 (33%)	9 (100%)

Table 2. Prognosis after operative management

Type of operation	Patients cured	Patients expired	Total
Repair of bronchopleural fist	1	0	1
Pneumonectomy	1	1	2
Pleurectomy	1	0	1
Pleurectomy + thoracoplasty	4	0	4
Pleurectomy + pneumonectomy	2	0	2
Mycetoma extraction + thoracoplasty	3	0	3
Total	12 (92%)	1 (8%)	13 (100%)

Acknowledgement

We are indebted to Mrs. Craig for reviewing the manuscript.

went resection of the pleural and adjacent pulmonary disease. All of the patients except one were completely cured. One patient died of respiratory insufficiency secondary to acute pneumonia and pulmonary hemorrhage after a pneumonectomy (Table 2). In spite of the fact that our patient died of pulmonary hemorrhage like the above case after undergoing a pleuropneumonectomy and intrapleural nystatin infusion, surgical removal is the treatment of choice in managing pleural aspergillosis.

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