Pulmonary Resection With Chest Wall Removal And Reconstruction For Invasive Pulmonary Mucormycosis During Antileukemia Chemotherapy

A 54-year-old woman undergoing chemotherapy for acute myeloid leukemia developed invasive pulmonary mucormycosis in the right upper lobe at the neutropenic nadir. Amphotericin B therapy became ineffective after an abscess formed in the affected lung, and insufficient infection control compelled us to interrupt chemotherapy. The lesion was suspected of invading the anterior chest wall. After right upper lobectomy combined with the anterior chest wall resection, the chest wall defect was reconstructed using autologous free rib grafts. Successful control of the fungal infection by resection enabled us to restart chemotherapy with concomitant use of Amphotericin B. In selected cases of leukemia-associated pulmonary mucormycosis refractory to Amphotericin B therapy, aggressive surgical intervention may facilitate antileukemia chemotherapy and prolong survival. (Jpn J Thorac Cardiovasc Surg 2003; 51: 163–166)

Key words: pulmonary mucormycosis, acute myeloid leukemia, chest wall reconstruction, autologous rib graft

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Pulmonary mucormycosis is a rare but severe fungal infection mainly occurring in immunocompromised patients. Surgical treatment is seldom indicated because most patients with this disease are in poor general condition. We report a case of pulmonary mucormycosis with chest wall invasion during antileukemia chemotherapy. The case was refractory to Amphotericin B therapy and benefited from surgery.

Case

A 54-year-old woman admitted to our hematology department for general fatigue and night sweats on September 6, 2000, was found on admission to have no abnormal shadow on chest X-ray and was diagnosed with acute promyelocytic leukemia (FAB M3). Remission-induction therapy was started immediately with cytarabine (Ara-C) and idarubicin hydrochloride (IDR), bringing about complete remission. She then underwent her first consolidation therapy with Ara-C and mitoxantrone hydrochloride (MIT) from October 12 and a second consolidation therapy with Ara-C and daunorubicin hydrochloride (DNR) from November 15. From day 11 since the last chemotherapy, she had a persistent low-grade fever and reported right anterior chest pain on December 4, when chest X-ray and computed tomography (CT) showed a localized infiltrative shadow in the right upper lobe (S^3). Serum C-reactive protein increased to 14.9 mg/dl, the white blood cell (WBC) count dropped to 100/mm^3 with 0% neutrophils, and serum beta-D glucan increased slightly to 22 pg/ml. Despite amphotericin B and G-CSF therapy, the fever continued and C-reactive protein remained high. Chest X-ray and CT showed slight resolution of the lung infiltration with an inner low-density area at-

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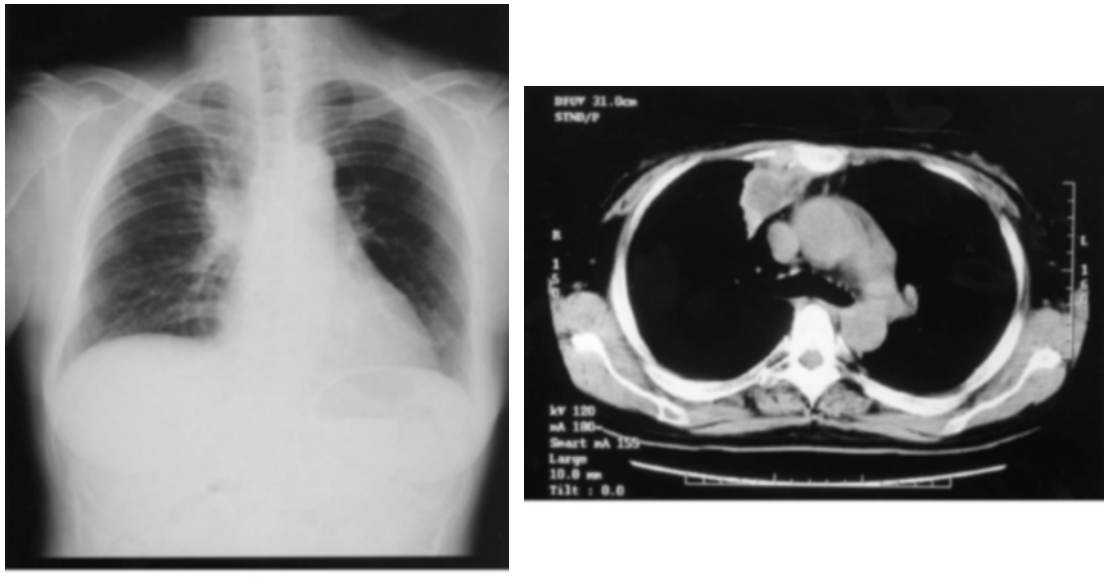

A B

Fig. 1. Preoperative chest findings.
A: X-ray shows a localized infiltrative shadow in the hilar region.
B: CT shows triangular consolidation with an inner low-density area close to the anterior chest wall.

tached firmly to the anterior chest wall (Fig. 1). Serum beta-D glucan increased to 58.4 pg/ml. Transbronchial biopsy showed nonseptate hyphae with irregular thickness and right-angled branching, compatible with mucormycosis. Because of the active invasive fungal infection with the abscess, hematologists could no longer continue chemotherapy and requested that we remove the lung into which amphotericin B could scarcely penetrate to finish the remaining 2 courses of consolidation chemotherapy as soon as possible. We decided to remove the pulmonary lesion after hematological conditions— WBC count: 2,800/mm^3 with 59% neutrophils; platelet count: $13.2 \times 10^4/mm^3$; and her general condition— improved.

On February 8, we operated with the patient supine under general anesthesia. Thoracoscopic examination showed that the lesion mainly occupied the S^3b segment of the right upper lobe, which had hyperemic visceral pleura and firmly adhered to the anterior chest wall. After right antero-lateral thoracotomy through the fifth intercostal space, we palpated the lesion invading the chest wall. Through median sternotomy, we resected the right upper lobe and chest wall en bloc, including part of the sternum, and the second to third ribs. To reconstruct the skeletal chest wall defect, we used autologous right sixth free rib grafts, taking 2 pieces of bone 5 cm long from the sixth rib and grafting them to the second and third rib defects (Fig. 2).

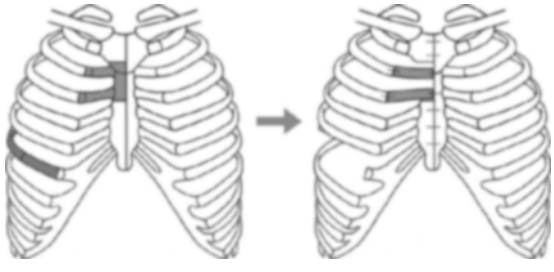

Fig. 2. Skeletal chest wall resection and reconstruction.

For fixation, we inserted absorbable poly-L-lactide costal coaptation pins (NEOFIX®) into the cut end of the grafted bones and the sternum and ligated them with absorbable sutures (1-Coated VICRYL®).

Macroscopic examination showed gangrenous changes in the center of the lesion (Fig. 3). Histopathological examination of the resected lung showed nonseptate hyphae with right-angled branching in a xanthogranulomatous inflammatory lesion with abscesses (Fig. 4), the infection infiltrating to the rib marrow and causing osteomyelitis. These pathological findings definitively confirmed pulmonary mucormycosis.

The postoperative clinical course was uneventful, and the woman underwent the remaining 2 courses of con-

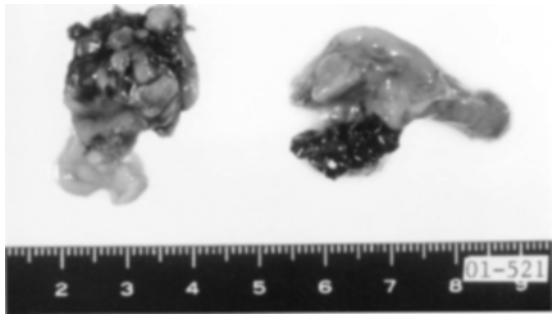

Fig. 3. Macroscopic appearance of removed gangrenous tissue contents of the lung abscess in the right upper lobe.

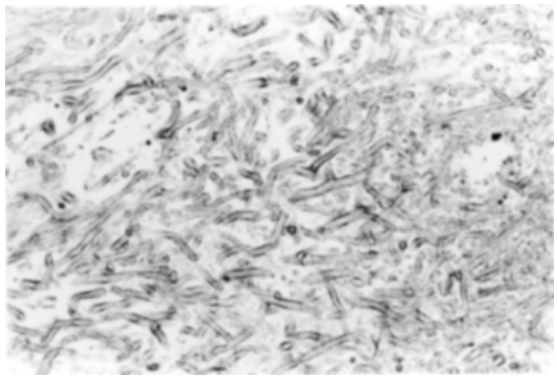

Fig. 4. Microscopic findings show broad irregular thickness and nonseptate hyphae with right-angled branching (HE staining).

solidation chemotherapy with concomitant prophylactic use of Amphotericin B. She was discharged on August 2, 2001. Now, 14 months after surgery, she is doing well without relapse of leukemia or mucormycosis or instability in the reconstructed chest wall (Fig. 5).

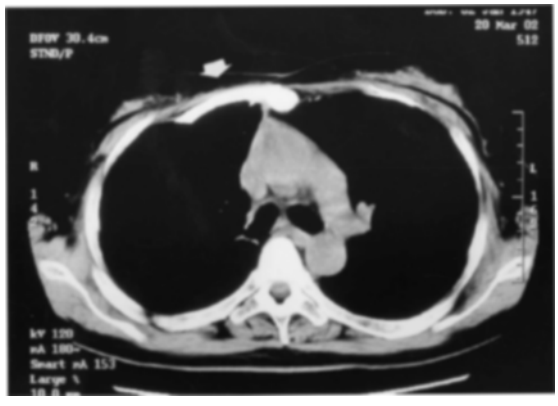

Fig. 5. Chest CT 14 months after surgery. Arrow: reconstructed autologous free rib graft.

Discussion

Pulmonary mucormycosis is a rare but severe opportunistic fungal infection in immunocompromised patients. It is mainly associated with hematological malignancy, diabetes mellitus, renal insufficiency, or organ transplantation, and usually occurs in severely neutropenic patients. The reported frequency of pulmonary mucormycosis in acute leukemia is 1.6%.[1] Pulmonary mucormycosis is classified into isolated pulmonary and disseminated disease. Disseminated disease is defined as involvement of 2 or more noncontiguous organs and often involves a rapidly fatal course.[2]

Amphotericin B is the therapeutic mainstay in the management of pulmonary mucormycosis. In treatment and outcome for isolated pulmonary mucormycosis in immunocompromised patients, early surgical intervention provides a significant survival advantage over medical treatment alone.[2-4] In our case, amphotericin B therapy was initially effective in reducing and localizing the lesion. An abscess refractory to amphotericin B formed in the lesion, however, interrupting scheduled chemotherapy for leukemia, making our patient a surgical candidate. Tedder et al.[2] reported that mortality in surgically treated patients was 9.4%, while that in those treated with medication alone was 50%. Lee et al.[4] reported 27% mortality for surgical and 55% mortality for medical treatment.

In the treatment of invasive pulmonary aspergillosis (IPA), which is more frequent in immunocompromised patients, aggressive surgical management has been recommended and is associated with acceptable surgery-related mortality and morbidity in several surgical series.[5-8] Surgical intervention, in principle, has been indicated in cases where the lesion appeared to be localized in 1 lung and patients were able to withstand surgery.

Given the life-threatening complications common with IPA, including fungal sepsis, respiratory insufficiency, and massive hemoptysis resulting from unsatisfactory medical treatment, indications for surgery in pulmonary mucormycosis are presumably similar to those in IPA.

Surgical procedures require the removal of infected lung tissue and, occasionally, combined removal of adherent structures. In reports of 36 surgically treated cases, lobectomy was conducted in 61%, pneumonectomy in 11%, and wedge resection in 8%.[2]

In our case, because we suspected the lesion involved

the chest wall, en bloc resection of the right upper lobe and anterior chest wall, including part of the sternum, and the second and third ribs with their cartilaginous portions, was necessary. Since the sternum was partially resected along with the 2 anterior ribs, the chest wall had to be reconstructed to restore stability. Nowadays, prosthetic materials such as polypropylene mesh and polytetrafluoroethylene (PTFE) are generally used in chest wall reconstruction with satisfactory results,[9] but they were considered to be inappropriate in our case due to intraoperative manipulation of infected lesions and postoperative infection. The patient was already immunocompromised at surgery and the risk of infection would increase in subsequent chemotherapy. Deschamps et al. reported that the frequency of wound infections in prosthetic chest wall reconstruction was 4.6% (9/197).[9] We used autologous free rib grafts with periosteum to reconstruct chest wall defects. Autologous free rib grafts are frequently used in reconstruction in head and neck surgery, orthopedics, and otology, but their use is relatively rare in chest wall reconstruction. Tunçözgür et al.[10] concluded that autologous rib grafts were effective and sufficient both in avoiding infection and rejection and in achieving stability. They confirmed that grafts with periosteum have advantages over deperiosteal grafts in the development of osteocytes and osteoblasts.

Conclusion

In selected cases, aggressive medical and surgical intervention combined to treat invasive pulmonary mucormycosis improves outcome and improves chances of survival. In our case, simultaneous chest wall resection was required and autologous free rib grafts for reconstructing the chest wall were useful and adequate.

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