Kirurško zdravljenje imunokompromitiranega bolnika z invazivno glivično okužbo

Surgical treatment in severely immunocompromised patient with invasive fungal infection

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Izvleček

Namen: *V prispevku želimo prikazati primer uspešnega kirurškega zdravljenja hudo imunsko oslabelega bolnika z invazivno glivično okužbo.*

Prikaz primera: *Na Oddelek za torakalno kirurgijo je bil zaradi nenadnega težkega dihanja sprejet 58-letni bolnik, sicer 30 let kadilec. RTG PC je govoril v prid obsežnega pnevmotoraksa. Šlo je za bolnika z znanim T-celičnim limfomom, B-limfomom tipa MALT, kronično obstruktivno pljučno boleznijo ter stanjem po kemoterapiji in radioterapiji. V času hospitalizacije se je bolnikovo stanje začelo slabšati. Odkrili smo spremembe na pljučih, ki so v kombinaciji z laboratorijskimi izvidi govorile v prid glivični okužbi. Po odvzemu kužnin se je izkazalo, da gre za glivično okužbo z Aspergillus fumigatus. Po predhodni konzultaciji z drugimi specialisti smo opravili kirurški poseg. Opravljena je bila »video assisted toracoscopic surgery«, nato pa torakoto-*

Abstract

Purpose: *We present a case report of successful surgical treatment of a 58-year-old severely immunocompromised male patient with invasive fungal infection.*

Case presentation: *A 58-year-old male with a smoking history of 30 years was admitted to hospital because of sudden shortness of breath. Radiographic imaging showed an extensive pneumothorax. The patient had a history of T-cell lymphoma, B-cell MALT lymphoma, and chronic obstructive pulmonary disease. He had also previously undergone chemotherapy. During hospitalization, his health state started to deteriorate. On the basis of imaging and microbiological culture results, he was diagnosed to have a fungal infection with Aspergillus fumigatus. After careful preoperative care, preparations, and several consultations, we performed video-assisted thoracic surgery. Because*

mija z ekscizijo apeksa desnih pljuč (tumorja in bule) s hemostazo po poškodbi interkostalne arterije. Končno diagnozo smo postavili na podlagi mikrobioloških in histopatoloških izvidov. Uvedena je bila primerna antimikotična terapija z vorikonazolom. Po kontrolnem CT-ju, ki ni pokazal novih sprememb ali progresa bolezni, smo bolnika v hemodinamsko stabilnem stanju z novo terapijo odpustili v domačo oskrbo.

Zaključek: *Kljub slabim napovednim dejavnikom je bil operativni poseg učinkovit in bolnikovo stanje se je zelo izboljšalo.*

of poor visibility, inaccessibility, and rupture of an intercostal artery, we performed thoracotomy with excision of the right lung apex. Histopathology and microbiology results confirmed the initial diagnosis. Postoperatively, a 1-year treatment regimen with voriconazole was introduced. The follow-up CT scan showed no signs of fungal infection progression. The patient was given further instructions and discharged from the hospital in a cardiorespiratory compensated state.

Conclusion: *Despite poor prognostic factors, the surgical procedure was successful and the patient's health state considerably improved.*

INTRODUCTION

Aspergillosis despite being a rare disease is becoming increasingly frequent and is leading to high morbidity and mortality (1–4). To date, more than 250 species of Aspergillus have been detected (2). It is reported that more than 40 of these species are harmful to humans (5). Clinical manifestations of aspergillosis are largely determined by the host immune response to Aspergillus spp. The spectrum of the disease ranges from noninvasive forms, causing allergy, local saprophytic lung disease, and finally to invasive systemic Aspergillus dissemination (6–9). With the advancement in technology and medication, the overall survival of patients with aspergillosis is increasing. However, these patients still require a multimodal approach from the start, especially those who are immunocompromised (9).

Figure 1. *Chest X-ray at admission revealing a large right sided pneumothorax.*

CASE PRESENTATION

A 58-year-old male with a smoking history of 30 years was admitted to hospital due to sudden shortness of breath and lower chest pain. At admission, a chest X-ray (CXR) was performed. It showed signs of an extensive right-sided spontaneous pneumothorax (SPTH), as illustrated in Figure 1. The patient was transferred to the Department of Thoracic Surgery, and a thoracic catheter was inserted. After an immediate improvement of the patient's state, his history taking revealed that he had T-cell lymphoma, B-cell MALT lymphoma, and chronic obstructive pulmonary disease and had undergone chemoradiotherapy. Because of exhausted therapy regimens and a refractory disease state, he had been on symptomatic care for more than 3 years. Nevertheless, the patient reported general wellbeing and a good functional status (WHO 1).

After a few days, because the patient exhibited persistent air leakage and fever, we performed a CT scan (Figure 2) and obtained blood cultures. The CT scan revealed a small anterobasal accumulation

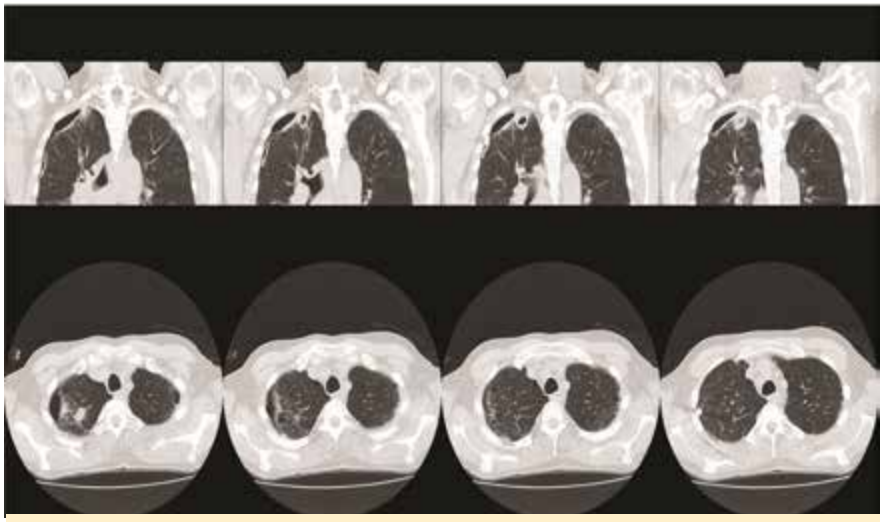

Figure 2. *CT scan revealing bilateral apical sub-pleural bullae, paraseptal emphysema and a cavitary nodular lesion in the right apical region.*

of air, apical sub-pleural bullae on both sides, and a 2-cm diameter cavitary nodular lesion in the right apex. No pathological infiltrates or any visible pleural effusion was observed. On the basis of the result of the previous 1-year-old CT study, which did not show any pathological changes, we hypothesized that the cavitary nodular lesion must have developed between the years 2016 and 2017.

The atypical apical changes in the right upper portion of the lung, overall deterioration of the patient's health state, and persistent air leakage prompted us to decide for surgical intervention. Because of the complexity of the situation, we consulted an infectious disease specialist, hematologist, pulmonologist, and anesthesiologist. We prescribed one ampule of pegfilgrastim subcutaneous and a 3-day empirical therapy with meropenem 1 g/8 h intravenous (iv) and fluconazole 400 mg/day iv. The consensus was that if the spirometry results were normal and the leucocyte count increased (at least above 2.0 × 109/L), the surgical procedure could be performed.

On the 13th day of admission, the leucocyte count reached the abovementioned threshold. First, video-assisted thoracic surgery was performed. Because of poor visibility, inaccessibility, and rupture of an intercostal artery, we performed thoracotomy with an excision of the right lung apex (tumorectomy with bullectomy). The collected samples (fluid and tissue) were subjected to microbiological, cytopathological, and histopathological analysis, which are some of the most important diagnostic procedures for diagnosing lung pathology (10).

The patient was admitted to the perioperative intensive care unit for further monitoring and for stabilization of vital functions. His vital signs gradually stabilized, and on the second day, he was re-transferred to our department. After a few days, histopathology and cytology results confirmed the diagnosis of an Aspergillus infection. After further consultation with the infectious disease specialist, a treatment regimen with voriconazole 200/12 h was introduced, and another CT scan was performed. Because of fever, we extended the therapy with meropenem for another 5 days. In the subsequent days of his hospitalization stay, there was an increase in liver enzymes due to the introduction of voriconazole. After an additional CT scan, we scheduled a pulmonologist check-up and a follow-up CT scan at 3 months after discharge. Voriconazole therapy was to be maintained for 1 year with regular laboratory check-ups at the clinic of his primary doctor. The patient was discharged from the hospital in a cardiorespiratory compensated state and feeling well.

DISCUSSION

Aspergillosis is a potentially fatal complication in immunocompromised patients with poor general condition (11). Surgical procedure may result in death, with a general perioperative mortality rate ranging from 14% to 32% (11). Differences in the reported mortality rate can be attributed to the extent of disease and the patients' overall functional state, which is frequently poor. In our case, the patient was not only suffering from SPTH, but he had also started to bleed during the operation and furthermore had several underlying diseases with an

accompanying neutropenia. It is known that patients who are myelosuppressed because of chemotherapy or hematologic malignancy are at an increased risk of infection. Postoperative fever is common, and if it develops in the setting of neutropenia, aggressive diagnostic and therapeutic interventions are required (11). Hence, it was decided that the patient had to show at least an increase in his blood cell count to above 2.0 × 109/L before we initiate surgery. Previous studies have reported the timing and outcomes of abdominal surgery in neutropenic patients. Jolissaint et al. concluded that a low absolute neutrophil count, especially one that is lower than 0.5 × 109/L or even 0.35 × 109/L, is a better threshold for defining "severe" disease in the surgical population (12). Kosan et al. also argued that patients with severe neutropenia should show an increase in neutrophil count before thoracic surgery is performed (11). On the other hand, a recent study by Grant et al. concluded that in cancer patients undergoing chemotherapy, leukopenia is not associated with morbidity or mortality and should not influence operative planning in either elective or emergent setting (13).

Despite poor prognosis, the patient survived. We attribute this to sufficient peripheral neutrophil count, careful preoperative care, surgical technique, and intensive perioperative physical therapy. Nevertheless, 2 months after his discharge, the patient's health state worsened, and he finally succumbed to the multitude of his underlying illnesses.

The authors are aware that patients with hematological malignancies are rarely adequate candidates for complex surgical procedures because of the associated complications in this setting (bleeding), secondary infections, and nonhealing wounds. However, according to international guidelines, in addition to antifungal therapy, surgical management may be appropriate in certain cases. For example, in cases where there is a large degree of necrosis that limits antifungal activity and/or there is an imminent threat to the great vessels or uncontrolled bleeding, pericardial involvement, pulmonary lesions contiguous with the heart, or invasion of the pleural space and/or chest wall (6). This decision depends on several factors, including the extent and location of the lesion, the degree of resection required, comorbidities, performance status, the ability of the patient to tolerate surgery, and the underlying disease (6). There have also been reports of good outcomes with an acceptable morbidity in such settings (14,15). Depending on the localization, different surgical approaches are available. Some other procedures are emergent debridement in cutaneous lesions and rhinosinusitis as well as valve replacements in cases of endocarditis (6).

Another important consideration in preoperative care and preparation for cardiothoracic surgery is respiratory management. Postoperative pulmonary complications present an important issue after major surgery. Pulmonary function tests and cardiopulmonary exercise tests can enable to determine whether patients can tolerate lung resection. The spirometry test results (FEV1/ppoFEV1) have been shown to be useful indicators of postoperative respiratory complications following thoracic surgery (16). In our case, the patient performed sufficiently and was therefore deemed acceptable for surgery.

CONCLUSION

The present case and other previous cases illustrate that despite aspergillosis being a rare disease, it is becoming increasingly frequent. This is especially true in immunocompromised patients who require a multimodal approach from the start. Adherence to such treatment may help to reduce morbidity and mortality due to pulmonary aspergillosis.

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