Urokinase application for hemothorax in pulmonary mucormycosis

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Introduction

Pulmonary mucormycosis is an uncommon but often lethal opportunistic infection. It has a high mortality and morbidity rate. The occurrence of a hemothorax and the consecutive need of repetitive surgical interventions even increases the morbidity.

We present a case of pulmonary mucormycosis in a 20-year-old woman with acute B-lymphoblastic leukemia. Despite long term use of antifungal medication the infection persisted and could only be treated by surgery. Postoperative hemothorax was treated in combination with urokinase instillation into the chest cavity. Currently the patient is in remission and doing well.

The use of urokinase to minimize the use of repetitive surgery in hemothorax occurrence could be a new approach in the treatment of mucormycosis.

Patient Course

An 18-year-old woman with an acute B-lymphoblastic C220 negative, BCR-ABL1 negative leukemia. Treatment was started according to hyper-CVAD scheme but could not be completed due to a cerebrovascular insult with left side hemiparesis which was caused by a septic embolism in the context of generalized mucormycosis. The mucormycosis was treated with dual antifungal therapy (amphotericin B and posaconazole). MRI confirmed a regression of the cerebral mucor which allowed to reduce the treatment to only posaconazole due to the nephrotoxicity of amphotericine. Both the B-ALL and the mucormycosis continued to be in remission.

Two years later the patient admitted herself to the emergency room because of severe hemoptosis (repetitive amounts of 20 ml). A fungal infection was suspected and treatment with amphotericine B and posaconazole as well as amoxicillin was started. From hematology the patient was referred to our clinic. A CT scan revealed a bleeding spot in the right lower lobe with signs of mycotic infection (Figure 1).

Surgical Procedure

We performed an open decortication with partial resection of the lower and middle lobe of the right lung. To remove all of the infected tissue a part of the diaphragm also had to be removed. Additionally a VAC-sponge was placed in the thorax. The histological check-up confirmed the diagnosis of invasive mucormycosis.

Antifungal therapy with posaconazole and amphotericine was continued. Five days later a planned second look was performed with an additional change of the VAC-sponge. Eight days after the initial operation the sponge was changed again and a Goretex patch for partial replacement of the diaphragm has been placed and the chest has been definitively closed.

Subsequently the Patient was highly unstable with hemothorax and an emergency revision thoracotomy was performed and the now confirmed hematoma removed. Over the course of a week the x-rays showed progressive worsening, which led to the suspicion of a recurring hemothorax (Figure 2) and two consecutive surgical evacuations had to be performed.

Eight days later, to address the ongoing hemothorax problem we began conservative treatment with urokinase instillation into the right thoracic cavity for 10 days.

Follow-Up

A brain MRI has been performed to control the progress of the cerebral mucor manifestation. The MRI showed a partial remission of the mucor and no new brain lesions. The patients left side hemiparesis continued to improve treatment with ongoing physiotherapy. 47 days after the initial hospitalization in the clinic of thoracic surgery the patient was discharged into rehabilitation.

Currently, 10 months after the pulmonary resection, the patient is showing improvements in both labor parameters and clinical presentation (Figure 3). She is in remission in both leukemia and mucormycosis.

Comment

Mucormycosis

Mucormycosis is a dangerous and often lethal disease caused by fungi of the order mucorales. While in immunocompetent patients phagocytes kill the mucor by generating oxidative metabolites and cationic peptides defensins, immunocompromised patients are much more at risk. One of the defining characteristics of mucormycosis is vascular invasion, which can lead to thrombosis and necrosis. The fungus is likely to spread and is difficult to control surgically. If present in the chest cavity it can lead to recurring hemothorax. Though not as common as other opportunistic fungal infections such as aspergillosis or candidiasis it continues to be a problem in immunocompromised patients.

The mortality rate for mucormycosis infections ranges from 40% to over 90% in patients with stem cell transplantation and dissemination, despite of state of the art medical care.2,3

Treatment

Early diagnosis of the fungus is the key of successful treatment. If possible the underlying disease should be cured. Treatment for mucormycosis is a combination of antifungal medication and if possible surgical debridement of the infected tissue.

Hemothorax

To fight the potentially serious hemothorax in intensive care medicine the usual approach is to either perform a thoracotomy or video-assisted tube thoracoscopic (VATS) to drain the residual blood. In recent years the use of a tissue plasminogen activator (t-PA) such as urokinase, which liquefies the clotted hemothorax, has come up as a less invasive method for treatment.4

Conclusions

Our case shows the successful treatment of an immunocompromised patient with mucormycosis using the combination of surgical removal of the infected tissue and antibiotics. To minimize the need for repetitive surgery in recurrent hemothorax the use of urokinase is a treatment option. Due to the rare coincidence of surgically resected mucormycosis patients and recurrent hemothoraces a prospective analysis of the real benefit of urokinase instillation versus surgical evacuation will be difficult.

References


Images: A brain MRI has been performed to control the progress of the cerebral mucor manifestation. The MRI showed a partial remission of the mucor and no new brain lesions. The patient’s left side hemiparesis continued to improve treatment with ongoing physiotherapy. 47 days after the initial hospitalization in the clinic of thoracic surgery the patient was discharged into rehabilitation. Currently, 10 months after the pulmonary resection, the patient is showing improvements in both labor parameters and clinical presentation (Figure 3). She is in remission in both leukemia and mucormycosis.

Figure 1: CT scan revealed a bleeding spot in the right lower lobe with signs of mycotic infection.

Figure 2: A CT scan revealed a bleeding spot in the right lower lobe with signs of mycotic infection.

Figure 3: A CT scan revealed a bleeding spot in the right lower lobe with signs of mycotic infection.