

## Cavitary Opacity following Lung Transplantation

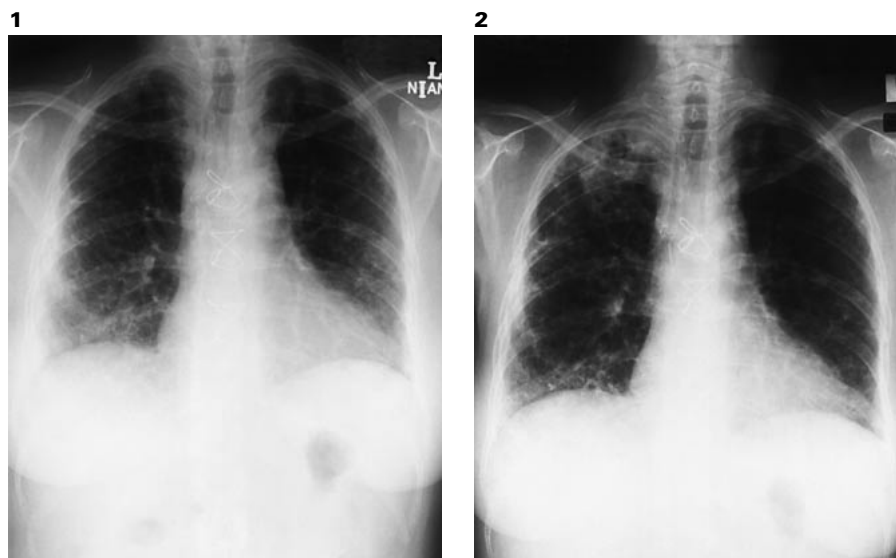
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A 43-year-old female underwent heart-lung transplantation for primary pulmonary hypertension. Initial immunosuppression consisted of cyclosporine A, mycophenolic mofetil and prednisone. Re-operation had to be performed for pleural bleeding due to extensive adhesions. The early postoperative course was further complicated by renal failure. However, the patient recovered and transbronchial biopsy (TBB) on postoperative day 30 showed no signs of rejection or infection. In the 2nd month after transplantation, she developed CMV pneumonitis requiring treatment with intravenous ganciclovir, which was complicated by central line infection with methicillin-resistant *Staphylococcus aureus*. Treatment

consisted of vancomycin and 4 weeks later no bacteria were grown from bronchoalveolar lavage (BAL) and TBB showed resolving CMV pneumonitis. Mycophenolic mofetil was replaced by azathioprine because of leucopenia.

Six months after transplantation the patient showed a drop in FEV<sub>1</sub> and eosinophilia. Steroid pulses were given for suspected rejection and symptoms improved. Four weeks later TBB revealed bronchiolitis obliterans organising pneumonia but no typical signs of rejection (A<sub>1</sub>B<sub>0</sub>). Another steroid pulse was given followed by clinical improvement. Nine months after transplantation TBB showed diffuse alveolar damage and no evidence of bacterial or viral infection (A<sub>0</sub>B<sub>0</sub>). Empiric therapy with ganci-



**Fig. 1.** Chest X-ray 1 year after heart-lung transplantation for primary pulmonary hypertension in a 43-year-old patient. There are some residual lesions following bronchiolitis obliterans organising pneumonia and bacterial empyema.

**Fig. 2.** Development of a cavitary lesion in the right upper lobe 14 months after transplantation.

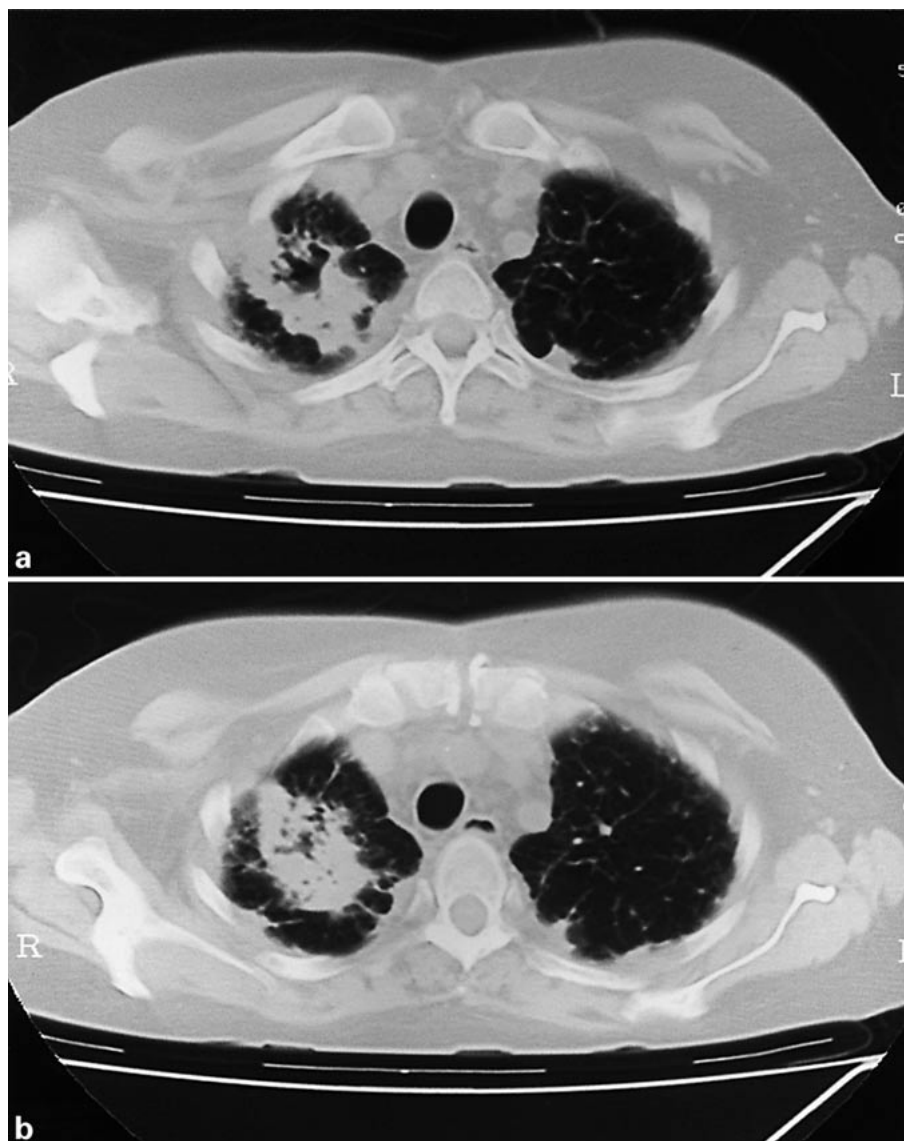
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**Fig. 3. a, b** Confirmation of the cavitary lesion on chest CT scan.

clovir, antibiotics and steroids was given and basic immunosuppression was switched from cyclosporine to tacrolimus. Because of persistent nodular changes on chest X-ray, open lung biopsy was performed 3 weeks later confirming bronchiolitis obliterans organising pneumonia but no infection. The patient developed postoperative methicillin-resistant *S. aureus* empyema, successfully treated with drainage and vancomycin. The chest X-ray 1 year after transplantation showed some apical pleural thickening and fibrotic changes but no consolidation as shown in figure 1. The clinical course was further complicated by the development of the bronchiolitis obliterans syndrome.

Fourteen months after lung transplantation the patient suffered from cough, shortness of breath, night sweats and fever. The chest X-ray revealed an infiltrate in the right upper lobe. Bronchoscopy with BAL and TBB was performed. Histology showed neither infection nor rejection ( $A_0B_1$ ) but pseudomonas and *Aspergillus niger* grew from BAL fluid. Antibiotic treatment was given and fluconazole added for concomitant esophageal candidiasis. The infiltrate progressed within 3 weeks to cavitation (fig. 2, 3a, b). The leucocyte count in the peripheral blood was slightly elevated.

*What Is Your Diagnosis?*

*What Is Your Next Diagnostic Step?*

## Diagnosis: Pulmonary Nocardiosis with Secondary Brain Abscess

As a next diagnostic step CT-guided fine needle aspiration with a 22-gauge needle was performed. Three needle passes were made and material obtained for cytological and various microbiological examinations. There were no malignant cells found and no bacteria or fungi grown. However, *Nocardia asteroides* grew from sputum collected after needle aspiration. Treatment with intravenous imipenem and amikacin was given for 3 weeks according to the sensitivity profile of the microorganism followed by oral minocycline. The opacity markedly improved within 4 weeks of treatment and the chest X-ray 10 weeks after initiation of treatment showed only residual lesions (fig. 4). Immunosuppression with tacrolimus, azathioprine and prednisolone was continued. After 6 months the patient complained of fever, fatigue, weight loss, nausea and a change in personality was noticed. CT scan showed a brain abscess located in the frontal lobe (fig. 5). Drainage was performed recovering 55 ml of pus containing *N. asteroides* and intravenous treatment with imipenem and amikacin was recommenced.

Pulmonary infiltrates are frequent following lung transplantation. In the early stage reperfusion injury, bacterial infection and rejection are the most common pulmonary complications [1]. In the later course opportunistic infections and transplant-associated malignancies have to be considered [2, 3]. Cytomegalovirus pneumonia

is a frequent cause of infiltrates whereas *Pneumocystis carinii* pneumonia became rare when prophylaxis with trimethoprim/sulphamethoxazole is given [4, 5]. The patient described above developed a cavitory opacity in the upper lobe 1 year after heart-lung transplantation following intensified immunosuppression because of recurrent rejection. The primary differential diagnosis included bacterial abscess, lung infarction, tuberculosis, aspergillosis and pulmonary malignancy. Aspiration pneumonia and anaerobic lung abscess were considered but no bacteria could be cultured from the BAL specimen. Aspiration to the upper lobe is unusual except in unconscious patients. There were also no laboratory signs of severe bacterial infection rendering bacterial septicemia with abscess formation unlikely. There were no clinical signs of venous thrombosis and a large embolic infarction in the upper lobe without further lesions is rare. Cavitory tuberculous lesions are typical in the upper lobe and transmission of *Mycobacterium tuberculosis* via transplanted lungs has been described, but BAL was negative for acid fast bacilli [6]. Atypical mycobacteriosis is not rare in lung transplant recipients, as recently reported [7]. However, none of the cases described developed a cavity. Invasive pulmonary aspergillosis can be associated with cavitory lesions [8]. However, the diagnostic yield of BAL to detect aspergillosis after lung transplantation is high in contrast to the



**Fig. 4.** Resolution of pulmonary nocardiosis on chest X-ray following intravenous and subsequent oral antibiotic treatment.

**Fig. 5.** CT scan of the brain showing development of a nocardia abscess more than 6 months after occurrence of pulmonary nocardiosis.



diagnostic yield of BAL in neutropenic patients [9, 10]. Therefore, aspergillus should have been detected in BAL, which was repeatedly performed in our patient. The incidence of non-small cell lung carcinoma is not increased in solid organ transplant recipients except in patients following heart transplantation [3]. The development of a large cavitary lesion within only 2 months made the diagnosis of a primary lung carcinoma very unlikely. However, transplant-associated lymphomas often develop following lung transplantation and can rapidly progress, especially if the immunosuppression is intensified [11, 12]. Following negative results of BAL and no conclusive diagnosis by CT-guided needle aspiration a surgical approach to obtain a definitive diagnosis was considered. Fortunately, sputum culture after needle aspiration revealed *N. asteroides* and adequate treatment could be initiated. A CT scan of the brain detected no lesions at that time. However, 6 months later the patient suffered from a brain abscess despite ongoing treatment with minocycline. Pulmonary nocardiosis is a rare but well-known complication following solid organ transplantation [13–16] and after bone marrow transplantation [17]. Primary pulmonary infections occur in the majority of patients. The onset is usually months up to years after transplantation. Patients can present with consolidation, nodules or cavities on chest X-ray and CT scan [18]. Pleural effusions are frequently present.

Brain abscess formation is a typical complication of nocardiosis [19]. Our patient developed a brain abscess 6 months after treatment for pulmonary nocardiosis was started. A 3-week course of intravenous amikacin and imipenem had been given followed by ongoing therapy with oral minocycline. The microorganism had been shown to be tetracycline sensitive. However, the patient was also heavily immunosuppressed because of bronchiolitis obliterans syndrome grade III. The late occurrence of a brain abscess might either reflect a too short initial course of intravenous treatment, a change in sensitivity to antibiotics or non-compliance. After neurosurgical intervention with drainage and treatment with intravenous imipenem/amikacin the patient's condition has improved.

### Comment

Sputum culture following non-conclusive needle aspiration has been helpful in this case to establish the diagnosis of pulmonary nocardiosis.

### Key Words

Transplantation · Nocardia · Pulmonary infiltrate

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