Cardiology in the Young

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Left atrial thrombosis with invasive pulmonary aspergillosis in children with immunodeficiency

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Brief Report

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Abstract

Invasive aspergillosis is a major cause of infectious disease in immunocompromised patients; however, cardiac involvement in pulmonary aspergillosis is not well-known. Two paediatric patients undergoing chemotherapy were diagnosed with cardiac aspergilloma, accompanied by pulmonary aspergillosis. In both patients, antibiotic and antifungal treatments were initiated immediately after the pneumonia was diagnosed; however, both died of multiple cerebral thromboembolisms.

Case 1

An 11-year-old boy diagnosed with B-lymphoblastic laeukemia and continuing chemotherapy visited the emergency room with neutropenic fever. His initial blood pressure was 114/82 mmHg, pulse was 160 beats/min, respiratory rate was 24 breaths/min, and body temperature was 37.7 °C. Complete blood count revealed white blood cell count, 320/μl; haemoglobin level, 10.2 g/dL; platelet count, 4,000/μl; absolute neutrophil count, 6/μl. Although no abnormalities were found on initial chest radiography (Fig 1a), broad-spectrum antibiotic, piperacillin/tazobactam, was administered. On hospital day 3, pulmonary consolidation in the right lower lobe was found on chest radiography and chest computed tomography (CT) (Figs 1b and 2d), and piperacillin/tazobactam was changed to teicoplanin. Caspofungin was administered as fungal pneumonia could not be excluded. However, on hospital day 4, pneumonia worsened on chest radiography (Fig 1c) and sudden dysarthria and mental change occurred. Brain magnetic resonance imaging (MRI) showed multifocal diffusion-restrained lesions with intralesional haemorrhage in both the cerebral hemisphere and left cerebellum (Fig 1e and 1f). He was subsequently transferred to the paediatric intensive care unit (PICU), and endotracheal intubation was performed. To decrease intracranial pressure, mannitol and dexamethasone were administered, and inotropes were started to control hypotension. On hospital day 7, the patient experienced sudden cardiac arrest, and cardiopulmonary resuscitation was performed three times. Subsequently, echocardiography revealed a large thrombus in the left atrium, which obstructed the right lower pulmonary vein (Fig 1g). The left ventricular ejection fraction decreased to 26%, and the hypotension persisted. The dose of inotropes was increased but septic shock and cardiogenic shock aggravated. The patient's parents did not want further treatment and signed a "do not resuscitate" order; the patient died.

Case 2

A 6-year-old boy who had been undergoing chemotherapy and radiation therapy for an atypical teratoid rhabdoid tumour was hospitalised at another hospital because of neutropenic fever. Empirical therapy with cefepime and vancomycin was initiated. Because there were consolidation on right middle lobe on chest radiography and a positive result for the aspergillus antigen test, caspofungin was administered. However, the lung consolidation did not improve, and the patient was transferred to our hospital. His initial blood pressure was 117/81 mmHg, pulse was 120 beats/min, respiratory rate was 28 breaths/min, and body temperature was 38.7°C. Laboratory tests revealed white blood cell count, 2460/μl; haemoglobin level, 9.6 g/dL; platelet count, 68,000/μl; and C-reactive protein level, 22.63 mg/dL. His symptoms included fever, cough, and blood-tinged sputum production. Initial chest radiography in our hospital revealed pulmonary consolidation in the right middle and lower lobes (Fig 2a). After admission, cefepime and voriconazole were administered; however, the patient suddenly became drowsy on hospital day 2. Brain MRI showed multifocal diffusion-restricted lesions in the bilateral cerebrum and cerebellum following which the patient was transferred to the PICU. Echocardiography revealed multiple thromboses in the left atrium and ventricle (Fig 2c and 2d), and cardiac CT revealed a

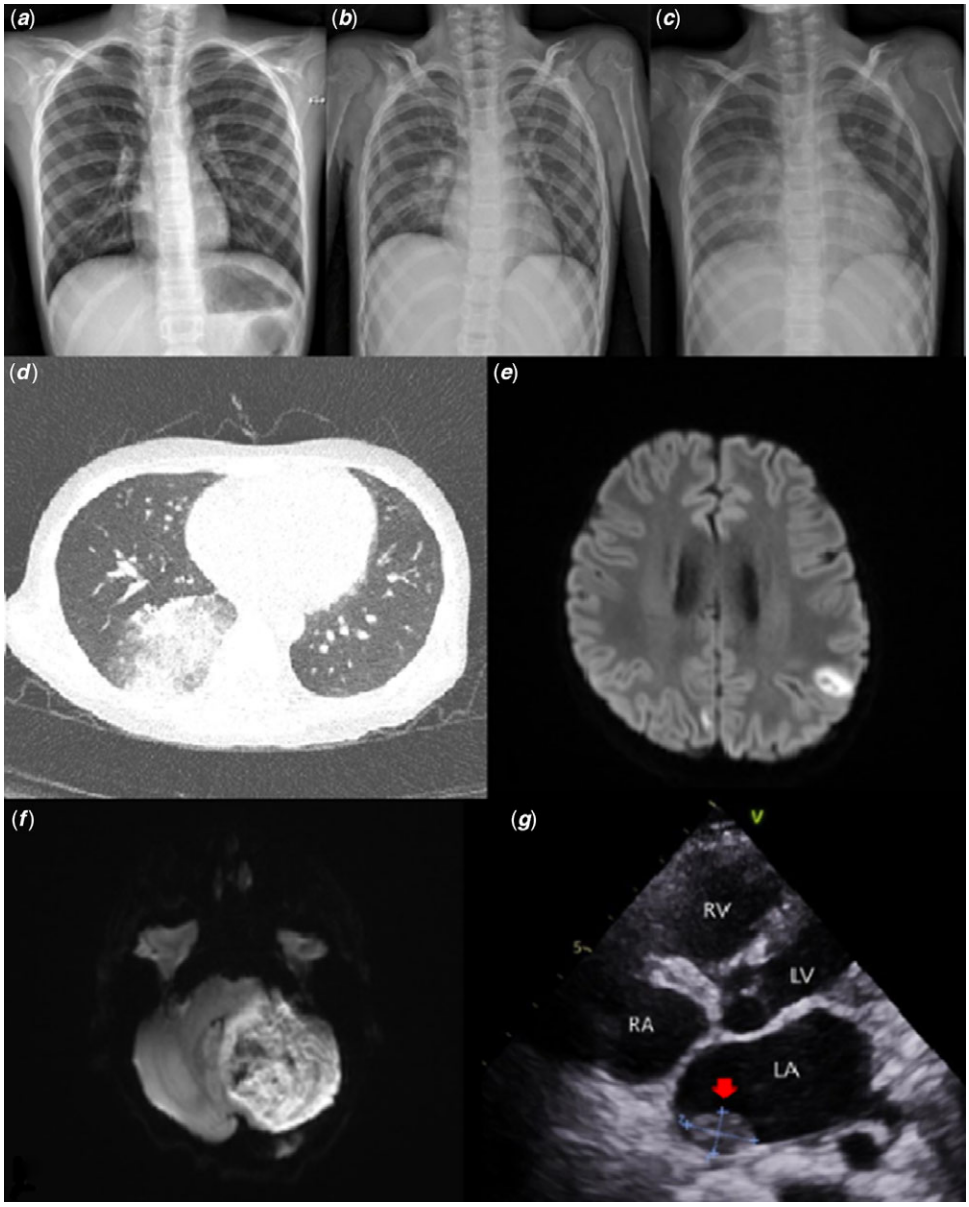

Figure 1. Imaging studies of case 1. (***a***) On the day of admission, no active lung lesion was found on the chest radiography. (***b***) On hospital day 3, pulmonary consolidation in the right lower lobe lung was found on the chest radiography. (***c***) Treatment with antibiotics and the antifungal agent started, but pneumonia worsened on hospital day 4. (***d***) On the chest CT scan, lobar pneumonia was found in the right lower lobe of the lung. (***e*** and ***f***) On the brain MRI scan, multifocal diffusion restricted lesions with intralesional haemorrhage at both the cerebral hemisphere and left cerebellum were found. (***g***) On echocardiography, a large thrombus with a size of 20 × 11.3 mm was identified in the left atrium.

left atrial thrombus involving the right middle pulmonary vein (Fig 2e). An open cardiac thrombectomy was performed to prevent further embolic event on hospital day 3, and the patient was extubated on hospital day 12. Post-operative chest radiography revealed improved pulmonary consolidation (Fig 2b), and the cardiac CT showed a completely removed left atrial thrombus (Fig 2f). Unfortunately, the patient had sudden increased muscular rigidity and tachypnoea on hospital day 13, and the brain CT showed acute intracranial haemorrhage of the frontoparietal lobe and an acute intraventricular haemorrhage of the right lateral ventricle. Although an emergency craniotomy and haematoma evacuation were performed, brain haemorrhage occurred repeatedly. The patient did not recover consciousness until hospital day 69. The patient's parents did not want further treatment; therefore, the physician's orders for life-sustaining treatment were prepared. Pathological examination of the thrombus revealed fungal hyphae with multiple necrosis and inflammatory cells, suggestive of invasive aspergillosis (supplementary figure).

Discussion

Invasive aspergillosis is a major cause of infectious diseases in immunocompromised paediatric patients. It is still a disease with high incidence and mortality despite improvements in various prevention and treatment methods.[1,2] Rapid initiation of antifungal treatment and control of predisposition are important.[1,2] Invasive aspergillosis rarely invades the heart, and in cases where the heart is invaded, it has been reported as a form of

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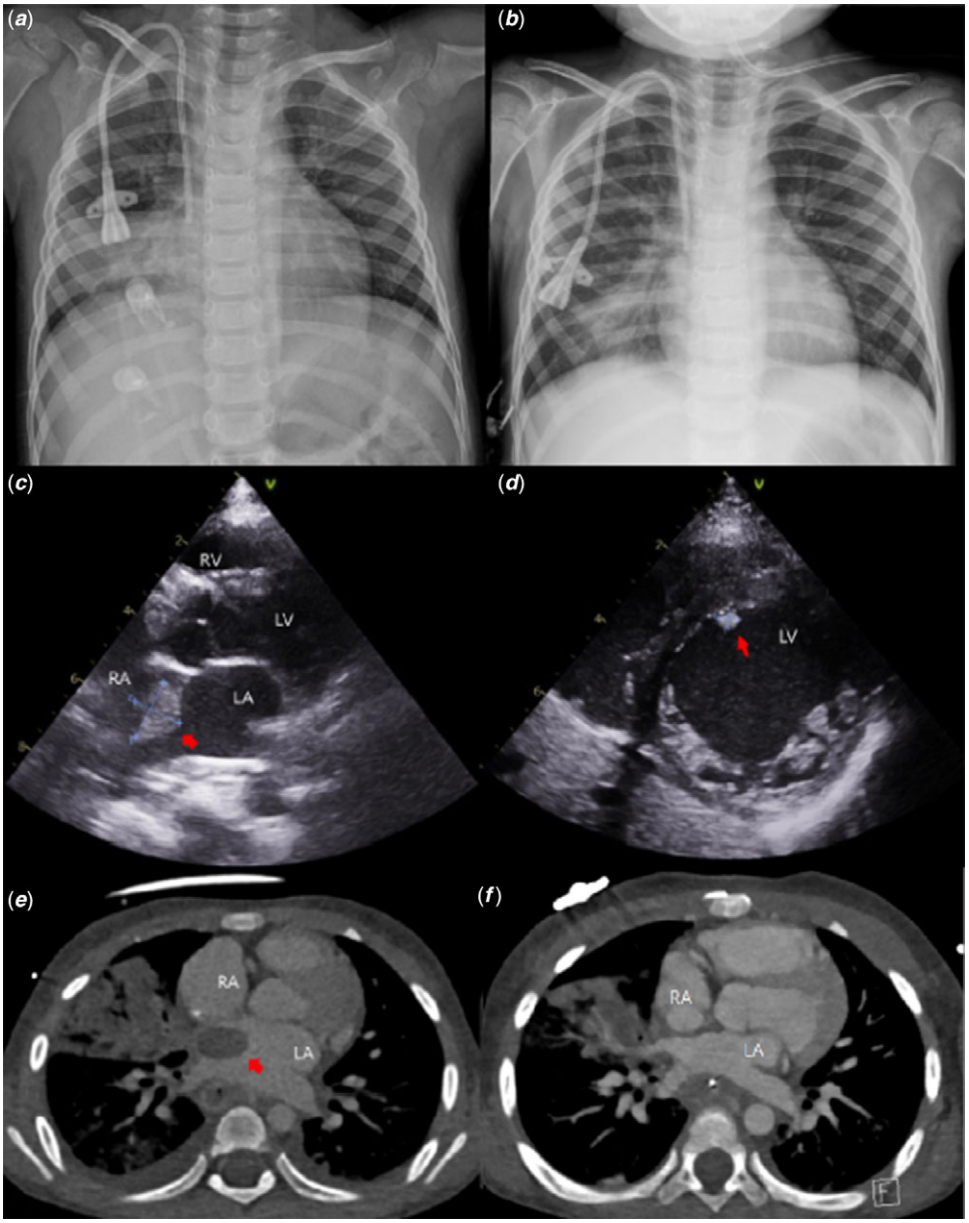

Figure 2. Imaging studies of case 2. (***a***) On the day of admission, right middle and lower lobar consolidations were shown. (***b***) On the 12 days after thrombectomy, right middle lobar consolidation improved. (***c***) Echocardiography showed a large thrombus (14.4 × 11.4 mm) in the left atrium and (***d***) another small thrombus (4.4 × 3.2 mm) in the left ventricular apex. (***e***) Cardiac CT revealed a 2.5-cm sized filling defect at the left atrium, obstructing the right middle pulmonary vein associated with lobar airspace consolidation of the right middle lobe. (***f***) After surgical thrombectomy, there was no residual intracardiac thrombus, but there was residual lobar airspace consolidation of the right lower lobe on cardiac CT.

endocarditis.[3,4] Left atrial thrombosis, accompanied by aspergillus pneumonia, is a rare complication and has only been reported in one immunocompromised adult patient.[5]

Two paediatric patients who were undergoing chemotherapy in the Hematology-Oncology Department of our hospital died after a diagnosis of the left atrial thrombosis associated with lobar pneumonia. In both patients, a sudden decline in consciousness occurred, and imaging studies revealed embolic cerebral infarction caused by left atrial thrombosis. The second case was pathologically confirmed to be aspergillosis that invaded the heart. Rather than being in the form of infectious endocarditis in the heart valve, aspergilloma occurred at the drain site of an affected pulmonary vein. Although the pathology was not confirmed in the first case, it was considered to be the same invasive aspergillosis because the clinical course was the same as in the second case. The first patient died of multiple cerebral infarctions and associated septic shock due to a late diagnosis of left atrial aspergilloma. The second patient underwent thrombectomy immediately after the diagnosis of left atrial thrombosis; however, he died of a post-infarction haemorrhage after open cardiac surgery.

If lobar pneumonia progresses rapidly in immunocompromised patients, early cardiac imaging studies, such as echocardiography or cardiac CT angiography, are required to detect cardiovascular invasion of aspergillosis. It is difficult to determine whether open cardiac thrombectomy is feasible in patients with multiple thromboembolic lesions in the brain. The European Society of Cardiology guidelines for infective endocarditis recommend urgent surgery if the infection is caused by fungus

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or if there is aortic or mitral valve endocarditis with persistent vegetation >10 mm after one or more embolic episodes despite appropriate antibiotic therapy.[6] However, since there is no recommendation on the safe time for cardiac surgery in patients with cerebral embolic infarction due to left atrial vegetation, a multidisciplinary approach is needed to treat this complex condition.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S104795112200302X

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