CLINICAL IMAGE

Fatal case of invasive fungal disease due to *Aspergillus* infection in a liver transplant recipient

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A 33-year-old woman 5 months after liver transplantation due to acute liver failure of unknown etiology was admitted to a department of neurology with slightly deteriorated general condition, presenting remitting fever episodes up to 38.5 °C with daily tension-like bilateral pulsating headache phenotype, nausea without vomiting, and phono- and photophobia lasting for 4 weeks. At this time, her immunosuppressive therapy included tacrolimus alone. On admission, magnetic resonance imaging (MRI) and computed tomography (CT) revealed subarachnoid hemorrhage, ischemic stroke in the left cerebellum hemisphere, and multiple hyperdense lesions in the left frontal lobe. Cerebrospinal fluid (CSF) analysis revealed high pleocytosis (>900 cells/μl, reference range [RR], ≤5/μl) with predominance of neutrophils and a high concentration of protein (>200 mg/dl, RR, 15–45 mg/dl). Multiplex-polymerase chain reaction (PCR) of the CSF for bacterial, viral, and cryptococcal infections did not detect any of the tested pathogens. Blood and CSF bacterial cultures as well as the serum galactomannan (GM) antigen test remained negative. After transferring the patient to our Transplantation Unit, broad-spectrum antimicrobial therapy was initiated with vancomycin, meropenem, and micafungin due to a high C-reactive protein (CRP) concentration (153.1 mg/l; RR, 0–5 mg/l) and a moderate rise in procalcitonin concentration (0.28 ng/ml; RR, 0–0.05 ng/ml). Five days after admission, the patient reported severe abdominal pain. An urgent CT scan revealed a splenic artery aneurysm (FIGURE 1A) with splenic hemorrhage (no pathological findings were detected in the lung parenchyma and nasal sinuses). Immediate splenectomy was performed with 1000 ml of blood-containing fluid evacuation. Histopathologic examination revealed unifocal fungal colony in the removed spleen. At the same time, a positive result for GM antigent test was obtained (first positive result in the patient's history) confirming invasive aspergillosis. Antifungal treatment with voriconazole was immediately introduced. Due to neurologic deterioration, repeated MRI scans were performed and revealed widespread cortical lesions with ischemic changes in both cerebral hemispheres and presence of mycotic aneurysms (FIGURE 1B). Concurrent visual disturbances in the right eye resulted in vitrectomy. Clinically, the presentation indicated intraocular inflammation of fungal etiology, and although this was not confirmed by PCR testing, intravitreal administration of voriconazole and amphotericin B was initiated. Despite the treatment, 2 weeks later sudden vomiting and deterioration in responsiveness occurred. A brain CT scan revealed a large heterogeneous acute hematoma (95 mm × 40 mm) in the left frontal lobe and basal ganglia on that side, with layers of sedimenting blood indicating active bleeding. Immediate hematoma evacuation and decompressive craniectomy were performed but the patient died after the surgery due to multilocational cerebral hemorrhage.

The presented case illustrates an example of disseminated fungal infection with mycotic aneurysms (MAs) of the brain and spleen vessels being a complication after solid-organ transplantation. Angioinvasive fungal diseases targeting the cerebral vasculature are characterized by a notably high mortality rate.[1] Histologically, MAs result from an infectious process causing arterial wall destruction, thereby classifying them as pseudoaneurysms.[2] Neuroaspergillosis can contribute to severe medical conditions, such as formation of

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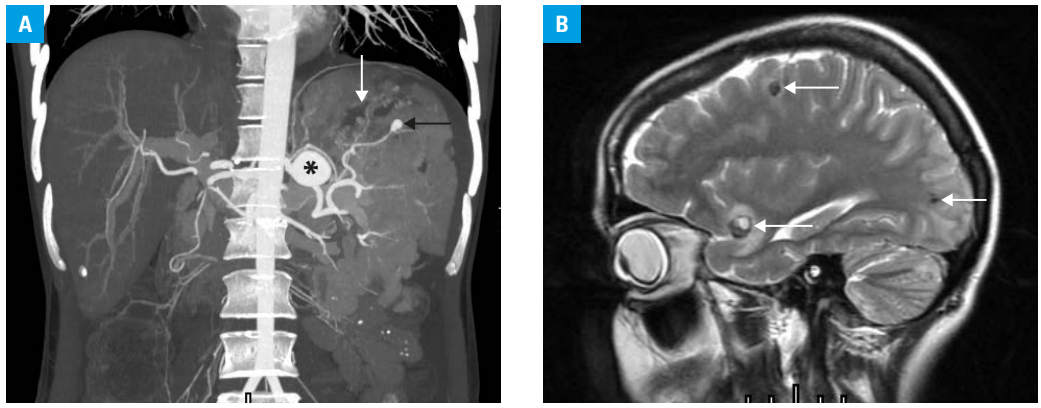

FIGURE 1 **A** – computed tomography scan of the abdominal cavity with contrast enhancement showing splenic artery aneurysm (asterisk), small mycotic aneurysm of a small branch of the splenic artery (black arrow), and irregular splenic hematoma (white arrow); **B** – magnetic resonance imaging of the brain (T2-weighted image) showing mycotic hematomas (arrows); due to their small size (early stage), the changes did not exhibit a typical profile of fungal granulomas, which are characteristic of larger lesions.

brain abscesses, cerebritis, meningitis, and cranial sinus thrombosis. Patients may experience a variety of symptoms, including persistent fever, intense headaches, significant lethargy, mental status changes, seizures, dizziness, or neurologic deficits.[3] In this case, identifying invasive aspergillosis was challenging despite clinical symptoms. The patient fulfilled host and clinical criteria for possible invasive fungal disease (IFD) due to post-transplant immunosuppression and focal lesions on imaging. However, a definitive diagnosis of proven IFD relied on identifying the fungus on spleen histopathology.[4] Identifying IFD is a complex task, demanding a team-based, multidisciplinary approach and requiring a detailed evaluation that combines histopathology, microbiology, and diagnostic imaging, all considered within the specific clinical scenario. Despite introduction of modern therapies, including new azole derivatives, pharmacotherapy of IFD remains a challenge.[5]

ARTICLE INFORMATION

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