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Case report

Candida vascular complication in a liver transplant recipient due to yeast contamination of preservation solution

E. Levesque, G. Suet, J.C. Merle, P. Compagnon, R. Amathieu, C. Feray, F. Botterel, F. Foulet, D. Azoulay, G. Dhonneur. *Candida* vascular complication in a liver transplant recipient due to yeast contamination of preservation solution.
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Abstract: Infections remain a major cause of morbidity and mortality after liver transplantation. One possible cause of infection is preservation fluid contamination. Donor-derived pathogens, such as *Candida albicans*, have occasionally produced life-threatening complications in organ recipients, already described in renal transplantation. In the present case, we report the loss of a liver graft secondary to vascular complications because of *C. albicans* found in the preservation fluid. Our case report raises the question of implementing procedures, similar to those in renal transplantation, including early antifungal treatment and repeated radiological monitoring for the prevention and detection of vascular complications.

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Infectious complication represents a major cause of morbidity and mortality in patients with transplantation. The graft, and subsequently the preservation fluid (PF), can be contaminated with microorganisms from the donor or from exogenous origin during the recovery and handling of the graft.

Infectious agents, such as gram-positive and gram-negative bacteria, are present in 9.5–48% of PF in liver transplantation (LT) (1–3). Contamination with yeasts remains uncommon, with an incidence ranging from 0.4% to 4.1% (1, 4), with few data on the consequences. In renal transplantation, some cases of arteritis due to *Candida* species have been reported as a consequence of hematogenous spread of fungi to the arterial wall, leading to a destruction of vascular structures (5, 6). We report here the case of a patient who developed a mycotic aneurysm due to *Candida albicans*, which was isolated from the PF, and we discuss its medical management.

Case report

The donor was an 88-year-old man who died of a cerebrovascular accident and was hospitalized for 2 days before declaration of brain death. The donor had

received antibiotics (amoxicillin, clavulanic acid, and ofloxacin) 2 days before procurement for suspicion of pneumonia. Routine liver tests were normal (total bilirubin 6.1 μmol/L [normal values: 5–17 μmol/L], aspartate aminotransferase 25 IU/L [8–30 IU/L], alanine aminotransferase 9 IU/L [8–35 IU/L], international normalized ratio 1.09 [0.8–1.2]). Blood, urine, and tracheal cultures were sterile. No supplemental antibiotic was added to the PF (IGL-1 solution), according to our policy.

The recipient was a 64-year-old man with hepatocellular carcinoma secondary to non-alcoholic steato-hepatitis. LT was performed using the side-to-side cavo-caval technique with bilio-biliary anastomosis. The patient received a standard immunosuppressive protocol (including corticosteroids, tacrolimus, and mycophenolate mofetil). A prophylactic antibiotic treatment with piperacillin was administered during the operative daytime. On postoperative day (POD) 5, the PF culture was positive for *C. albicans* and *Morganella morganii*. The antimicrobial active agent (piperacillin: 16 g/day) was continued during 7 days, and antifungal therapy (fluconazole: 800 mg intravenous the first day, then 400 mg/day) was added on day 5. This treatment was stopped on POD 15. The cultures of kidney PF from the same donor were negative for fungal and bacterial contamination.

The early postoperative course was not complicated and the recipient had a good graft function. The routine computed tomography (CT) scan at POD 10 was considered normal without vascular anomaly.

On POD 15, acute cellular rejection was diagnosed by a histological examination of the liver. Corticosteroid boluses (500 mg per day during 3 days) were associated with an improvement of biological parameters.

On POD 22, the patient, hospitalized in the hepatology department, had fever and abdominal pain. The CT scan revealed a large peri-hepatic hematoma and the patient underwent an emergency surgical exploration. Hematoma culture grew *C. albicans*. Caspofungin treatment (70 mg, then 50 mg/day intravenously) initiated with a secondary confirmation that minimal inhibitory concentration was low (0.02 mg/L) for this yeast.

On POD 40, the patient presented in hemorrhagic shock, with complete disruption of arterial anastomosis on the CT scan (Fig. 1). Intraoperative exploration showed complete disruption of the arterial anastomosis with a mycotic aneurysm of the hepatic artery. The hepatic artery was ligated. Intra-peritoneal cultures and explant hepatic artery grew *C. albicans.* The caspofungin treatment was stopped and antifungal therapy (with fluconazole 800 mg/day and liposomal amphotericin B 250 mg/day) was initiated. On POD 70, the patient died from refractory septic shock due to peritonitis and gut ischemia with multiple organ failure.

Discussion

Transmission of pathogens, such as fungi, via PF, is a potential cause of infection among transplant recipients. It may be dramatic, leading to graft loss and even death due to mycotic arteritis and/or aneurysm (5–8) resulting in arterial wall rupture and/or anastomotic leakage.

In LT, 0.4–4.1% of PF is contaminated by yeasts (1, 4, 9). This fungal contamination is commonly a result of exogenous contamination and can occur at different phases of the transplantation process: (i) contamination of PF by the graft, especially from a polytrauma donor, or (ii) during liver recovery, as a result of digestive tract perforation, particularly during multiorgan procurement.

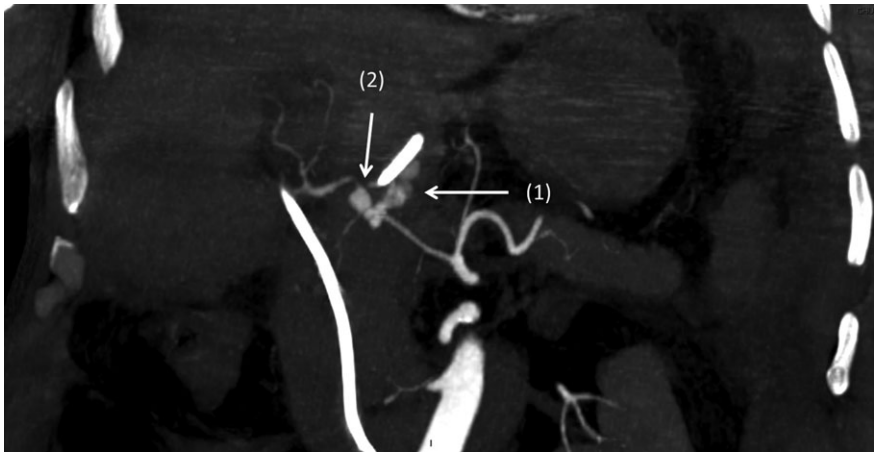

Fig. 1. Computed tomography scan at postoperative day 40: complete disruption of arterial anastomosis with leak of contrast product (1) and with presence of a mycotic aneurysm of the hepatic artery (2), right next to the anastomosis.

In contrast to kidney transplantation, to our knowledge, little is known about the consequences of yeast contamination of PF in LT. These infections appear to be associated with an unfavorable outcome in liver transplant recipients. In a large study evaluating the microbiological contamination of PF, Janny et al. (1) found 2 patients with PF positive for yeasts. In the 2 cases, the patients died in the intensive care unit with peritonitis and multiorgan failure. Similar serious complications in recipient patients have been observed by other authors and have been associated with lethal outcome (2, 3, 10). In our case, the lethal complication was a vascular arteritis due to *C. albicans* leading to liver graft loss. Hematoma and intra-peritoneal cultures grew *C. albicans*, and the artery explant showed the presence of a mycotic aneurysm. Typically, our case describes vascular *Candida* infection leading to anastomotic leak and/or vessel rupture as previously described (10), as a result of the ability of *Candida*, and especially *C. albicans*, to penetrate into endothelial cells leading to destruction of vascular structures (11).

The management of such contamination should be evaluated in a large cohort. Identification of risk to recipients would include (i) cases of digestive tract rupture during the procurement, and (ii) donors who have received broad-spectrum antibiotics (7). In such patients, a preventive fluconazole treatment would be proposed, as early initiation of antifungal therapy appears essential to limit the arterial invasion. The choice of fluconazole as the first-line antifungal treatment for infections caused by azole-susceptible *Candida*, and liposomal amphotericin B or echinocandin for infection due to azole-resistant *Candida*, is validated (12, 13). Moreover, an early detection of any endovascular ongoing silent pathological process should be developed and standardized. Systematic monitoring of the hepatic artery using CT scans is proposed for early identification of hepatic artery aneurysm.

In conclusion, in our specialized liver transplant intensive care unit, we now try to identify patients at risk of fungal contamination of PF and at risk of fungus-induced vasculitis, and we perform close monitoring of the hepatic artery by CT scan. Systematic evaluation should allow us to better estimate the incidence of this vascular complication in LT.

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