CLINICAL IMAGE

Colon mucormycosis with renal spread resistant to lipid complex amphotericin and isavuconazole treatment in a heart transplant recipient

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We report a case of a 67-year-old male patient who presented with colon mucormycosis after heart transplantation (HTx). His immunosuppression included prednisone, tacrolimus, and mycophenolate mofetil. Two weeks after HTx, the patient experienced abdominal distension and epigastric pain. Abdominal computed tomography demonstrated cecal wall thickening, presence of excessive peritoneal fluid, and signs of pancreatitis. Endoscopic examination revealed circumferential ulceration in the splenic flexure of the colon and in the cecum, covered with a large amount of green coating (FIGURE 1A). Microscopic examination of the intestinal wall biopsy specimens showed tissue necrosis and fungal hyphae, the morphology of which resembled *Aspergillus* (FIGURE 1B and 1C). The tissue culture was positive for *Rhizopus* sp.

According to the 8th European Conference of Infections in Leukemia guidelines,[1] the treatment of mucormycosis includes surgical resection of mucor foci as well as high doses of liposomal amphotericin B and isavuconazole as rescue treatment. Before bowel surgery, the patient was treated with high doses of lipid complex amphotericin B (Abelcet) due to a suspicion of pulmonary aspergillosis. On colectomy with end ileostomy, a dark, cloudy fluid was found in the peritoneal cavity (FIGURE 1D). Around the splenic flexure of the colon, an inflammatory tumor was found, which infiltrated the retroperitoneal space (FIGURE 1E). The cecum showed wall necrosis which caused perforation to the retroperitoneal space. Further necrotic foci were found in the adipose capsule of the left kidney (FIGURE 1F). Surgery included extensive excision of necrotic foci. A small amount of cloudy, black fluid was drained from the inside of blue translucent spots which were found at the base of the serous membrane of the small intestine (FIGURE 1G). Surgical specimens evidenced extensive gangrenous necrosis with focal suppuration, fungal colonies in the lumen and on the serous surface, as well as extensive necrosis of the peri-intestinal adipose tissue with suppuration containing fungal colonies in the peri-intestinal tissue and in the mesentery.

Following the surgery, the patient's condition improved; however, soon after he deteriorated. Repeat computed tomography of the abdomen revealed a cyst in the area of the left kidney, which was biopsied, drained, and cultured, yielding no growth of *Mucor* sp. Even though no *Rhizopus* sp. was found in the biopsy of the cyst, urine cultures were positive for this fungus. Isavuconazole was added to the ongoing lipid complex amphotericin therapy.[1] Despite intensive treatment, the patient's clinical condition further deteriorated, leading to death 3 months after HTx due to overwhelming fungal sepsis. Autopsy findings showed kidney cortex and medulla necrosis caused by fungal infection (FIGURE 1H). Fungal hyphae were found in the interstitial tissue of the left kidney, lumen of the renal tubules, perirenal adipose tissue, as well as on the wall and in the lumen of blood vessels, with their thrombosis.

Opportunistic fungal infections may occur in immunocompromised patients, with mortality in gastrointestinal zygomycosis exceeding 85% and in disseminated disease, 95%.[2] *Rhizopus* sp. are the predominant (67.5%) etiological fungi.[3] As mucor is an ubiquitous fungus, the route of

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Received: September 12, 2021.
Revision accepted: October 25, 2021.
Published online: December 1, 2021.
Pol Arch Intern Med. 2022; 132 (1): 16156
doi:10.20452/pamw.16156

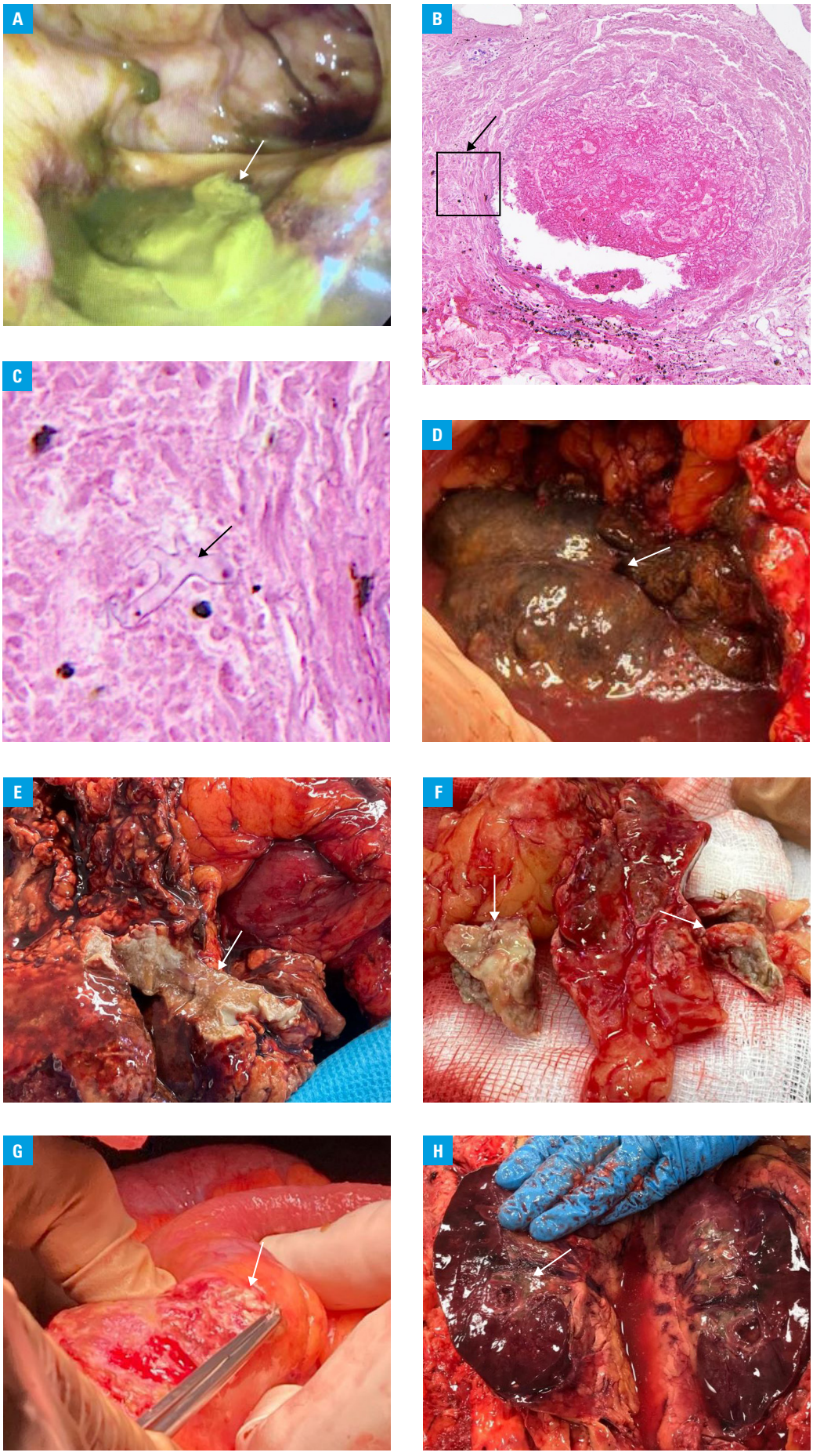

FIGURE 1 **A** – mucosa of the large intestine infiltrated by mucor (greenish area, arrow); **B**, **C** – microscopic examination of the intestinal wall biopsy specimens (hematoxylin and eosin staining) showing a clot occluding the arterial lumen surrounded by mucor--infiltrated perivascular tissue (**B**; arrow indicates the area presented on the next panel; magnification × 100) and magnificated mucor hyphae in the perivascular tissue (**C**; arrow; magnification × 400) **D** – necrotic cecum seen on laparotomy (arrow); **E** – resected retroperitoneal abscess (arrow); **F** – left kidney capsule with 2 mucor foci (arrows) on both sides; **G** – small intestine wall with mucor infiltration (arrow) of the serous membrane; **H** – autopsy examination showing typical mucor infiltration and organ damage with an abscess (arrow) in the left kidney and a fistula to the renal vein

infection is mostly via the lungs, but it can as well invade the body after ingestion. Early diagnosis and intervention, including surgical resection, debridement, and intensive antifungal treatment may be lifesaving. The progression is usually fast, the invasion of the vasculature typically causes necrosis and infarction of host tissues, as seen in the presented case. There is an unmet need to implement modern molecular microbial analytic techniques (eg, metagenomics, metabolomics) into daily clinical practice, particularly in patients referred for organ transplantation.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

HOW TO CITE Lango-Maziarz A, Kołaczkowska M, Siondalski P, et al. Colon mucormycosis with renal spread resistant to lipid complex amphotericin and isavuconazole treatment in a heart transplant recipient. Pol Arch Intern Med. 2022; 132: 16156. doi:10.20452/pamw.16156

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