Combined Medical and Surgical Management of Hepatic Mucormycosis in an Adult with Acute Myeloid Leukemia: Case Report and Review of the Literature

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Abstract Hepatic mucormycosis is a disease caused by a ubiquitous fungus which is especially important in patients with hematologic malignancies. We present a case of an adult patient with acute myeloid leukemia who developed the infection after undergoing chemotherapy. His successful management was an integrated approach of a minimally invasive surgical resection with anti-fungal therapy. We describe the management of this patient and a review of the literature.

Keywords Hepatic mucormycosis · Laparoscopic surgery · Hematologic malignancy

Introduction

Hepatic mucormycosis is a disease caused by a ubiquitous environmental filamentous fungus that is becoming increasingly important, especially in patients with hematologic malignancies [1, 2]. However, unlike most other invasive fungal infections that primarily affect immunocompromised patients (e.g., patients with cancer, transplant recipients, and patients with inherited immunodeficiencies), mucormycosis can also be seen in immunocompetent patients [3]. Ultimately it is a life-threatening fungal infection most commonly presenting as a rhino-sino-orbital (36%) or pulmonary (22%) infection [3]. We present a rare case of isolated hepatic mucormycosis in a patient with acute myeloid leukemia (AML).

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Case

A 39-year-old male initially presented with weight loss, chest pain, and dyspnea. His complete work-up including a bone marrow biopsy led to the diagnosis of AML with monocytic differentiation (CD14+, CD64+, CD117−). Cytogenetic studies were remarkable for normal karyotype with *MLL* (*KMT2A*) mutation. The patient was started on "7 + 3" induction therapy with cytarabine plus daunorubicin followed by 3 cycles of high-dose cytarabine (HiDAC) consolidation treatment. His disease relapsed less than a year later and he received 2 cycles of azacitidine and sorafenib but continued to have disease progression on bone marrow biopsy.

The patient subsequently underwent "CLAG" salvage chemotherapy with cladribine, cytarabine

and filgrastim. He was given posaconazole and levofloxacin prophylaxis and developed neutropenia (nadir WBC = 0.1 × 10^3/uL and ANC 0.0) and thrombocytopenia (nadir platelet count = 17,000/uL) 1 week after starting this therapy. Twelve days later, while still neutropenic, he developed a fever and right upper quadrant abdominal pain. Blood work revealed a transaminitis, (ALT = 521 U/L, AST = 495 U/L, and alkaline phosphatase = 134 U/L) with negative hepatitis A, B and C serologies. CT scans of both chest and sinuses were unremarkable, but a right upper quadrant ultrasound showed a right hepatic lobe mass. MRI demonstrated a 9.3-cm right inferior hepatic lobe mass with intrinsic T1 hyperintensity suggestive of hemorrhagic or proteinaceous contents and no central enhancement (Fig. 1), with no evidence of any other abdominal pathology. A core needle biopsy was obtained. Pathologic findings demonstrated angioinvasion by numerous broad aseptate fungal hyphae consistent with mucormycosis with surrounding hepatic infarction (Fig. 2). No material was available for fungal culture, but direct fungal sequencing from the pathology scrolls was positive for the Rhizopus species. Liposomal amphotericin B, 5 mg/kg, was initiated.

The patient was taken for laparoscopic-assisted partial hepatectomy of the segment VI abscess. The liver was mobilized, and ultrasound was used to verify the borders of the segment VI lesion. Given the patient's thrombocytopenia, we used a precoagulation technique directed at the uninvolved parenchymal margin of the liver which was used for the liver resection. Using the Neuwave© microwave ablation probe, the parenchyma was pretreated at 100 W for 30 s with sequential repositioning of the probe. The lesion was then resected using a Harmonic scalpel. After approximately 75% of the lesion was resected, manipulation of the lesion became rather challenging due to its size. We created a small right subcostal incision in order to complete the resection.

On repeat MRI obtained 1 week later (9 days after count recovery), there was evidence of progression of parenchymal infection within the liver (Fig. 3, left). The dose of the liposomal amphotericin B was increased to 7.5 mg/kg, and micafungin was added for synergistic effect. One week later, the lesions continued to enlarge on imaging surveillance and the patient was switched to isavuconazole salvage/palliative therapy, 372 mg daily, to be taken indefinitely. Unexpectedly, his symptoms and transaminitis resolved, and follow-up MRI 3 months after discharge revealed complete resolution of all hepatic lesions (Fig. 3, right).

Discussion

Mucormycosis was first reported in the literature in 1885. Between 1940 and 2003, there were 1049 reported cases of mucormycosis with an overall mortality of 54% [3]. Infection is most commonly found to be rhino-sino-orbital (36%), pulmonary (22%) and cutaneous (18%), with solid organ infection seen in only 4% of cases [3]. Hepatic involvement is

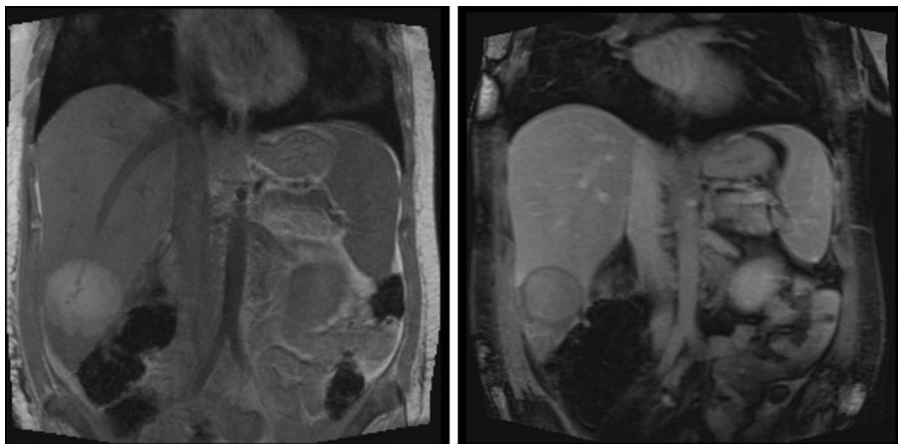

Fig. 1 T1 MRI image of the 6 × 7.7 × 9.3 cm mass in the right inferior hepatic lobe with intrinsic T1 hyperintensity suggestive of hemorrhagic/proteinaceous contents and no central enhancement

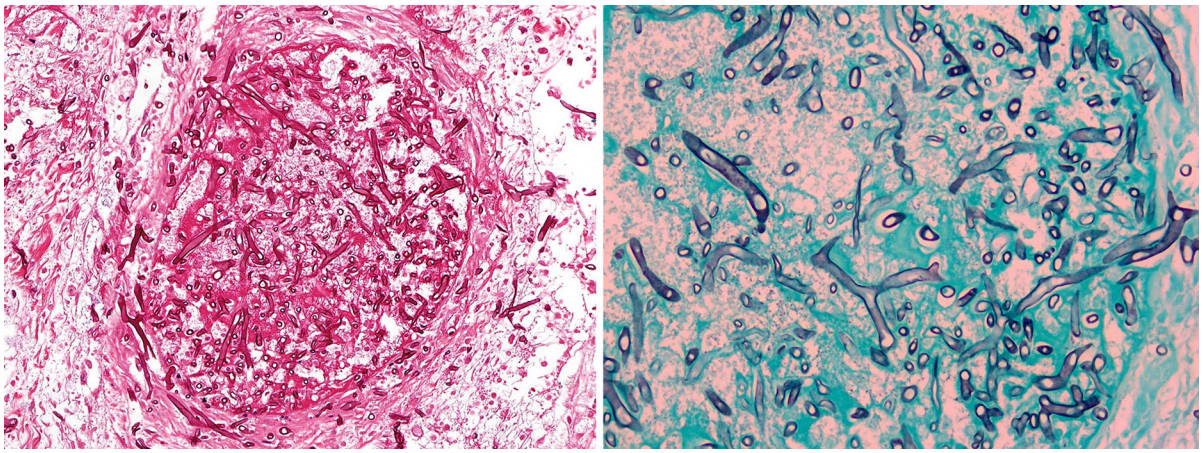

Fig. 2 Pathology images after biopsy of the segment VI hepatic lesion. Left, evidence of angioinvasion and fungal thrombi in the infarcted hepatic parenchyma (Hematoxylin and eosin stain, 100× magnification). Right, characteristic broad aseptate hyphae of mucormycosis (Grocott–Gomori methenamine silver stain, 400× magnification)

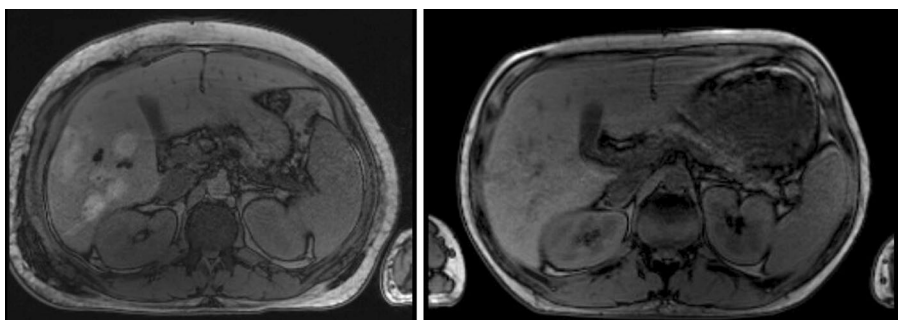

Fig. 3 Left, postoperative T1 MRI revealing postsurgical sequelae of partial hepatectomy with numerous ovoid lesions representing persistent mucormycosis surrounding the resection site. Right, resolution of hepatic mucormycosis after 3 months on isavuconazole

most commonly seen in combination with pulmonary or GI infection as part of disseminated disease, which is almost uniformly fatal [4]. Hepatic mucormycosis most commonly presents as a mass-like lesion with extensive liver infarction, but can also present as a Budd–Chiari syndrome or veno-occlusive disease [5, 6].

A review of the literature revealed 12 cases of isolated hepatic mucormycosis [1, 4, 7–16]. The mean age at presentation is 27 years old, with 4 of 12 (33%) patients under the age of 10 years. Six of 12 (50%) patients were male. Four of 12 (33%) patients were ostensibly immunocompetent; although of these four, one was suffering from a hepatitis A infection and one was a trauma patient who sustained gunshot-related hepatic injuries [10]. Of the immunocompromised patients, two suffered from AML (one with a history of bone marrow transplant), two suffered from acute lymphoblastic leukemia, two were liver transplant recipients, one was a kidney transplant recipient, and one suffered from myelodysplastic syndrome with a history of bone marrow transplant [4, 7, 8, 11]. Six of the 12 (50%) patients died, three of which had undergone hepatic resection (two of these died of sepsis) and one patient underwent percutaneous drainage and subsequently died after progression of the malignancy. The remaining two patients who died of their disease never received anti-fungal therapy. Of the six survivors, three underwent hepatic resection and two underwent percutaneous drainage. The sixth patient did not undergo any intervention based on the family wishes. Of note, the largest reported hepatic lesion was 5.3 cm [1]. All hepatic resections were performed via an open approach.

Our case has several unique features. Successful isavuconazole salvage therapy in mucormycosis has

only rarely been reported, and this case represents the first instance of successful therapy in hepatic mucormycosis. Surgically, this is the first case of laparoscopic-assisted partial hepatectomy for hepatic mucormycosis. The technique of parenchymal precoagulation with microwave ablation is also a first in the management of patients with this diagnosis and likely reduced his risk for significant peri-procedural bleeding in a patient with profound thrombocytopenia. The patient had a quick postoperative recovery with minimal pain due to smaller incisions and without postoperative bleeding or surgical site infectious complications. Lastly, the size of the lesion provided a technical challenge. At 9.3 cm, this lesion is much larger than previously reported lesions that were surgically resected.

Overall, isolated hepatic mucormycosis is a rare disease. A high index of suspicion is important for early diagnosis, in both immunocompromised and immunocompetent patients. An integrated medical and surgical approach can lead to positive outcomes, although mortality rates remain extremely high in these patients.

Authors' Contributions MS contributed to data collection, literature review and writing the manuscript; JN assisted with writing the manuscript; AA assisted with data collection; DVD assisted with writing and editing the manuscript; DAG was involved in study design, writing and editing the manuscript.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent For this type of study, formal consent is not required.

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