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CASE REPORT

Appendiceal Perforation and Abdominal Wall Infection Caused by Invasive Mucormycosis in a Child with Acute Leukemia

Chuanxin Li[1,*], Yonghan Luo[2,3,*], Yanchun Wang[2], Qiang Bai[1]

[1]Department of General Surgery, Kunming Children's Hospital, Yunnan, People's Republic of China; [2]Second Department of Infectious Diseases, Kunming Children's Hospital, Yunnan, People's Republic of China; [3]School of Life Sciences and Technology, Kunming University of Science and Technology, Yunnan, People's Republic of China

*These authors contributed equally to this work

Correspondence: Qiang Bai, Department of Pediatric Surgery, Kunming Children's Hospital, Kunming, Yunnan, People's Republic of China, 650000, Email bqetyy@163.com

Abstract: Gastrointestinal mucormycosis is one of the most difficult forms of the disease to diagnose due to its lack of specific clinical features. It is extremely rare to observe gastrointestinal mucormycosis in pediatric acute leukemia patients undergoing chemotherapy. In this report, we describe a case of a child with acute leukemia who developed invasive mucormycosis, leading to appendiceal perforation and abdominal wall infection. Initially, surgical intervention was delayed due to concerns over exacerbating bone marrow suppression, which ultimately resulted in the progression of the intra-abdominal infection. However, after thorough debridement of the abdominal wall infection and treatment with liposomal amphotericin B, the patient gradually recovered. This case highlights the importance of early and complete debridement of abdominal wall infections and intra-abdominal abscesses to prevent the further spread of mucormycosis, shorten the course of the disease, and improve outcomes.

Keywords: appendiceal perforation, abdominal wall infection, invasive mucormycosis, children, acute leukemia

Background

Mucormycosis is caused by Mucoraceae, which are ubiquitous in organic matter exposed to air, such as fruits, vegetables, soil, fertilizers, and decaying plants and animals.[1] Although they can be isolated from the nasal cavity, stool, and sputum of healthy individuals, they have low pathogenicity and rarely cause disease in humans. Even among patients with severe immunodeficiency or organ transplants, mucormycosis is still uncommon. Mucormycosis ranks third among invasive fungal infections, following aspergillosis and candidiasis, with an incidence rate of 8.1%–13.0% and a mortality rate as high as 70%–96%.[2,3]

Mucormycosis tends to invade immunocompromised individuals, including those with congenital immunodeficiencies or patients with acute leukemia undergoing chemotherapy.[4] Bone marrow suppression and prolonged neutropenia significantly increase susceptibility. Additionally, the prolonged use of corticosteroids or broad-spectrum antibiotics can impair immune responses, further predisposing individuals to mucormycosis.[5] Moreover, severe metabolic acidosis, such as diabetic ketoacidosis, creates a favorable environment for fungal growth.

Mucormycosis can be classified based on the site of infection into pulmonary, rhinocerebral, gastrointestinal, cutaneous, disseminated, and other forms.[6] Gastrointestinal mucormycosis often presents with nonspecific symptoms such as abdominal pain, hematemesis, and melena, and may lead to necrotizing gastritis or intestinal ulcers in severe cases. Due to the lack of specific clinical manifestations, gastrointestinal mucormycosis is one of the most difficult forms to diagnose and is often only discovered during surgery or autopsy. Although mucormycosis has been reported in children with leukemia,[7–9] gastrointestinal mucormycosis is extremely rare during chemotherapy in children. This is the

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first report of appendiceal perforation and abdominal wall infection caused by invasive mucormycosis in a child with acute leukemia, providing a reference for clinical diagnosis and treatment in similar cases.

Case Presentation

A 3.5-year-old girl presented with pallor for one week and fever and cough for two days. She was diagnosed with acute lymphoblastic leukemia following blood tests and bone marrow biopsy. During chemotherapy, she developed paroxysmal abdominal pain. Physical examination revealed a soft abdomen with tenderness around the umbilicus, but no muscular tension or rebound tenderness. Abdominal ultrasonography suggested appendicitis. Due to bone marrow suppression, meropenem was administered for anti-inflammatory treatment without surgery. Three days later, the patient experienced persistent abdominal pain with a fever reaching 39.1°C. Physical examination revealed abdominal distension and significant tenderness in the lower right abdomen, accompanied by muscle tension and rebound tenderness. Repeat ultrasonography showed perforated appendicitis, and an emergency laparoscopic exploration was performed.

During surgery, adhesions between the intestines, omentum, and right peritoneum were noted, with the formation of a yellowish-white abscess (approximately 20 mL). The appendix was located in the pelvis, and the midsection and tip were necrotic with perforation. Further exploration revealed abscess formation between the right paracolic gutter, right liver lobe, and peritoneum (approximately 30 mL of purulent fluid). Histopathological examination of the appendix confirmed mucormycosis infection with necrosis and perforation (Figure 1a). Postoperatively, the patient was treated with vancomycin (15mg/kg Q6h), meropenem (20mg/kg q8h), and voriconazole (10mg/kg qd). Although the abdominal pain improved and C-reactive protein levels decreased, the patient continued to experience low-grade fever. On postoperative day 5, the antifungal regimen was switched to liposomal amphotericin B(5mg/kg, qd), imipenem (15mg/kg q6h), and linezolid (10mg/kg q8h).

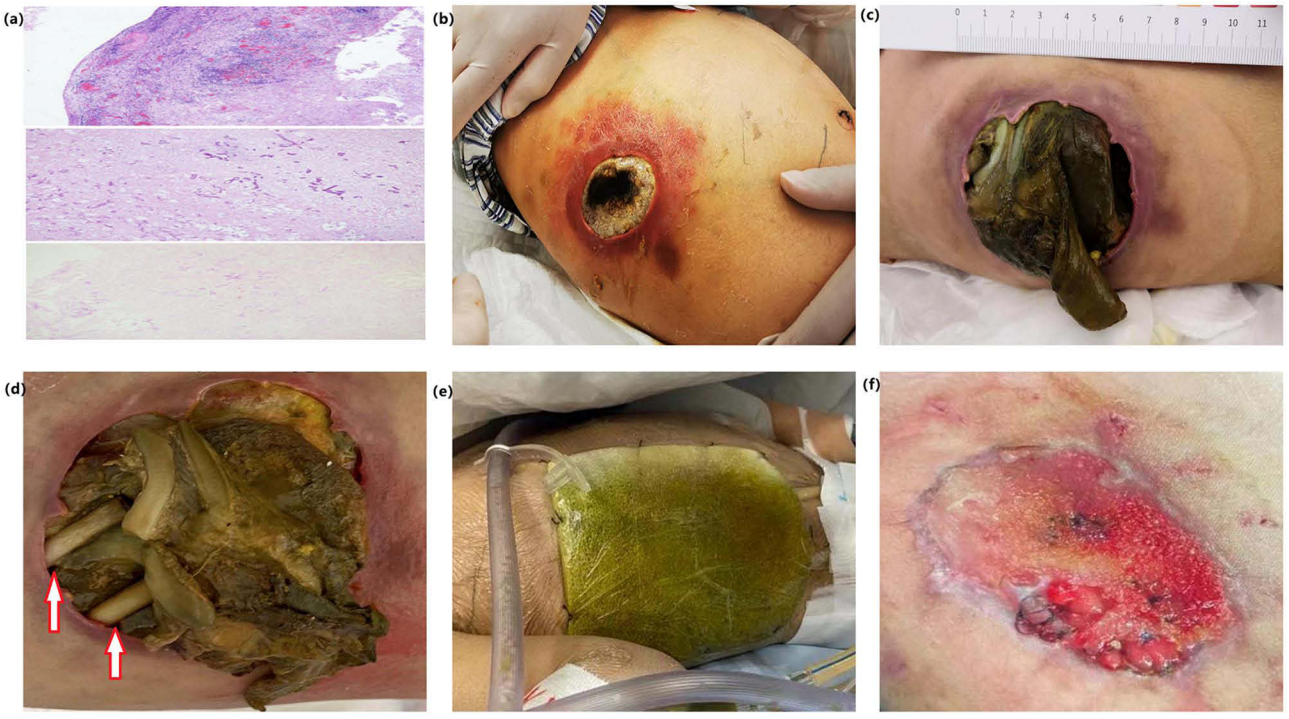

Figure 1 Clinical and histopathological progression of appendiceal perforation and abdominal wall infection caused by invasive mucormycosis in a child with acute leukemia. **a**. Histopathological appendix: Significant localized hemorrhage and necrosis of the appendix, with scattered infiltration of lymphocytes and neutrophils. Abundant hyphae present throughout the entire wall and within the blood vessels, PAS(+). **b**. Postoperative wound at the site of right abdominal puncture measuring approximately 4×1 cm, with blackened tissue and surrounding erythema measuring about 8×9 cm. **c**. Progression of right abdominal wall infection, characterized by the discharge of yellow-green feculent material, raising the suspicion of an enterocutaneous fistula. **d**. Worsening of the right abdominal wound infection with necrosis of the skin and subcutaneous tissue, exposing the ribs and penetrating the abdominal muscle layer, with visible liver tissue and fistula leakage. The arrow indicates the exposed rib. **e**. Postoperative image showing the colostomy bag following vacuum sealing drainage and enterostomy. **f**. Healing of the infection site, with granulation tissue formation visible.

On postoperative day 8, the patient developed fever (38.1°C) and paroxysmal abdominal pain. Physical examination revealed a blackened area (4×1 cm) at the site of puncture drainage in the right abdomen, with surrounding skin redness (8×9 cm) (Figure 1b). The infection progressed during treatment, and on postoperative day 18, the patient developed respiratory failure and was transferred to the pediatric intensive care unit (PICU) for mechanical ventilation. Over time, the right abdominal wall infection worsened (Figure 1c), with yellow-green fecal-like discharge, raising concerns about an enterocutaneous fistula. Local disinfection and debridement were performed, and a stoma bag was placed. Following extubation, the patient's vital signs gradually stabilized, but the abdominal wall infection continued to deteriorate. Necrosis of the skin and subcutaneous tissues extended to the fascia, exposing ribs and hepatic tissue, with leakage of fistula fluid (Figure 1d). The child was hospitalized for a total of 56 days. The patient was transferred to an external hospital for vacuum sealing drainage and enterostomy (Figure 1e), followed by treatment with liposomal amphotericin B for mucormycosis. The infection was successfully controlled, and the wound gradually healed, and the patient was eventually discharged in an improved condition (Figure 1f).

Discussion

There are currently no effective preventive measures for mucormycosis, apart from active treatment of underlying diseases and the avoidance of environments with a high concentration of airborne spores for high-risk individuals. Mucormycosis has historically been associated with high mortality rates until the introduction of amphotericin B and surgical debridement, which have significantly reduced fatality.[10] The key to treatment lies in controlling the underlying disease, excising necrotic tissue, and early administration of antifungal drugs. First-line therapy includes amphotericin B, with lipid-based formulations available for patient's intolerant to the traditional preparation.

A review of the literature reports that gastrointestinal mucormycosis accounts for 5% to 13% of all cases of mucormycosis.[11,12] Gastrointestinal mucormycosis is one of the rarest forms of the disease, and infection can result from the ingestion of contaminated foods, such as fermented milk products and dry bread. A retrospective study revealed that the most affected site in gastrointestinal mucormycosis is the intestine (52%), followed by the stomach (42%).[13] Mucormycosis requires early recognition, especially in immunocompromised patients, such as those undergoing chemotherapy for acute leukemia. In this case, the patient presented with gastrointestinal mucormycosis that progressed to appendiceal perforation and abdominal wall infection, a very rare manifestation in pediatric patients. The lack of specific clinical features in mucormycosis makes early identification particularly challenging. In immunocompromised states, mucormycosis often mimics more common conditions such as bacterial or viral infections, leading to delayed diagnosis. However, persistent symptoms such as abdominal pain and fever, coupled with clinical deterioration despite broad-spectrum antibiotics and initial surgical intervention, should raise suspicion for fungal infections such as mucormycosis. Furthermore, as observed in this patient, the presence of necrotic tissue, persistent abscesses, or darkened lesions in the abdominal wall are key clinical signs that warrant suspicion for mucormycosis. Early recognition and prompt intervention are critical to improving outcomes in such cases.

The progression of the disease in this child was rapid, leading to necrosis of the skin and muscle tissues as well as the development of intestinal fistula. Local tissues were also complicated by secondary bacterial infections, resulting in rapid systemic deterioration characterized by septic shock and respiratory failure. Although local infection was partially controlled through aggressive debridement and negative-pressure wound therapy, ischemic necrosis of the abdominal wall muscles continued to progress, and the child's overall condition failed to improve fundamentally. Mucormycosis can cause vascular obstruction and tissue necrosis, and when antifungal agents alone cannot penetrate the lesions effectively, surgical resection or debridement must be considered.[14] In this case, the child developed acute appendicitis during chemotherapy for leukemia. Bone marrow suppression following chemotherapy led to neutropenia and thrombocytopenia. Although surgical removal of the appendix was suggested, it was relatively contraindicated due to the child's immunosuppression and thrombocytopenia. Furthermore, mucormycosis as the causative agent of the appendiceal infection was not anticipated preoperatively.

In the early stages of abdominal pain, surgery was not performed promptly, delaying timely intervention. As intra-abdominal infection worsened and spread, surgery was eventually performed, confirming mucormycosis-associated appendicitis. However, the delay in surgical intervention resulted in the loss of the optimal timing for effective treatment.

This case emphasizes the importance of timely and thorough debridement of abdominal wall infections to prevent the spread of mucormycosis, reduce the duration of illness, and improve treatment outcomes.

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Ethical Approval Statement/Patient Consent

Written informed consent was obtained from the patient's parents for publication of the clinical images and case description.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicting interests.

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