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Anorectal Abscess in a Patient with Neutropenia and Refractory Acute Myeloid Leukemia: To Operate or not to Operate?

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Manuscript Preparation E
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Patient: Male, 56-year-old
Final Diagnosis: Perianal abscess
Symptoms: Fever • gluteal pain • septic shock
Medication: —
Clinical Procedure: Debridement • fistulotomy • incision and drainage
Specialty: Hematology • Infectious Diseases • Surgery

Objective: Rare disease**Background:** Anorectal infections occur in 5% to 9% of patients with hematological malignancies, including acute myeloid leukemia, and cause febrile neutropenia and sepsis. Surgical treatments of anorectal abscesses tend to be avoided in patients with leukemia owing to persistent neutropenia and bleeding risks.**Case Report:** A 56-year-old man presented with an ischioanal abscess. Preoperative laboratory test results revealed leukocytopenia and anemia. He was diagnosed with acute myeloid leukemia. He developed septic shock. Antibiotic treatment was ineffective, and fever persisted. One week later, the abscess was treated by incision and drainage. Two days later, induction chemotherapy was initiated. No pus was drained; cellulitis spread to both buttocks. Pain worsened, and oxycodone was administered. Achievement of complete remission failed. Reinduction therapy was started, followed by fistulotomy of the abscess with extensive debridement of cellulitis on day 6. Granulation was observed on day 17. The patient's fever resolved on day 21. Although hematopoietic recovery was observed, bone marrow examination demonstrated partial remission. Two additional courses of chemotherapy were administered. Abscess recurrence was not observed, even during febrile neutropenia. The surgical wound shrank to a skin defect along the gluteal cleft. He achieved complete remission and was transferred to another hospital, where he underwent 3 allogeneic stem cell transplants. He died of leukemia progression.
Conclusions: Surgical treatments can prevent fatal progression of anorectal abscess, even during neutropenia. Incision and drainage are suitable for fluctuant abscesses. For a non-fluctuant abscess aggravated by sepsis and cellulitis, it is worth considering more invasive surgical interventions, including debridement and fistulotomy.**Keywords:** Abscess • Anus Diseases • Colorectal Surgery • Febrile Neutropenia • Leukemia, Myeloid, Acute • Rectal DiseasesFull-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/931589>

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Background

Anorectal abscesses are caused by infection of the anal glands and are characterized by redness, swelling, and pain of the anal skin. Fistulas, in contrast, are formed by chronic inflammation and the epithelialization of a tract connecting the inciting anal gland with the perianal skin and are characterized by secretions from around the anus [1-3]. Treatments for anorectal abscesses in the general population are prompt incision upon diagnosis and complete drainage [1-3]. These procedures alleviate pain and prevent progressive inflammation (including life-threatening pelvic sepsis and Fournier gangrene), abscess recurrence, and fistula formation. Antibiotic treatment is not required for patients who are immunocompetent but should be administered in the presence of extensive cellulitis in the perianal/perineal area, signs of systemic infection, or other complications (diabetes, valvular heart disease, or immunosuppression, such as human immunodeficiency virus infection and leukemia) [1-3]. Antibiotic therapy can prevent fistula formation after incision and drainage [3], as was shown in a randomized single-blind clinical trial [4] and meta-analysis [5]. Fistulotomy at the time of incision and drainage of a perianal abscess is associated with a significant decrease in abscess recurrence, persistence of fistula or abscess, and the need for subsequent surgery; however, a statistically insignificant increase of continence impairment has been reported [6]. Therefore, primary fistulotomy can be performed in cases of superficial fistulas, by experienced surgeons. Otherwise, it should be performed as a secondary procedure [1-3].

The frequency of anorectal infections in patients with hematological malignancies, including leukemia, has been reported as 5% to 9% [7-12]. When febrile neutropenia develops in patients with hematological malignancies who suffer from anorectal infections, broad-spectrum antibiotic treatment must be immediately prescribed, with modifications made based on the site of the infection and the identified pathogens [13]. Guidelines for anorectal abscesses and fistulas also recommend that antibiotic treatment be used for patients who are immunocompromised [1-3,14].

However, the indications for surgical intervention of anorectal abscesses during neutropenia are still debated. Surgical treatments tend to be avoided in patients with leukemia owing to persistent neutropenia, slow granulation, and bleeding risks. There is no strong evidence-based treatment guideline because there have been no prospective randomized studies on this topic to date [14].

We report the case of a patient with refractory acute myeloid leukemia (AML) during prolonged myelosuppression who successfully underwent radical abscess surgery (fistulotomy) and extensive debridement for widespread cellulitis after incision and drainage of the ischioanal abscess.

Case Report

The patient was a 56-year-old man with an unremarkable past medical history. He denied a history of tobacco use, alcohol use, and substance abuse. He experienced anal pain for 2 weeks before presenting at our hospital. A perianal abscess found on the right buttock had caused spontaneous perforation a week before, and he visited our hospital for colorectal surgery. The abscess was accompanied by erythema and yellow discharge. On admission, laboratory test results showed a low white blood cell count ($1.57 \times 10^3/\mu\text{L}$, neutrophils 2.0%, blasts 80.5%) and anemia. Bone marrow aspiration revealed 77% blasts, which led to the diagnosis of AML (subtype M1). His temperature was 40.3°C. We promptly began administering 1 g intravenous (i.v.) doripenem 3 times daily for febrile neutropenia. The gluteal pain was persistent and worsened in a sitting position. For this reason, the patient was always in the lateral decubitus position. The day after admission, septic shock manifested. Pelvic magnetic resonance imaging revealed an ischioanal abscess. Immunoglobulin 5 g i.v. once daily for 3 days and vancomycin 1 g i.v. twice daily were also administered. *Escherichia coli* was detected in blood and urine cultures, and *E. coli* and *Enterococcus faecalis* were detected in the perianal abscess culture. The fever and gluteal pain persisted. On day 8 of hospitalization, an incision and drainage were performed, with the patient under general anesthesia (Figures 1, 2). The day after surgery, septic shock manifested again. Induction chemotherapy with daunorubicin 38 mg/m² i.v. once daily for 5 days and continuous cytarabine 100 mg/m² i.v. for 7 days (body surface area 1.8 m²) was performed on the second day after surgery. The patient's fever resolved 3 days after surgery. However, cellulitis developed and spread to both buttocks, forming a horseshoe abscess. The gluteal pain worsened, requiring analgesia by oral oxycodone. Liposomal amphotericin B 100 mg i.v. once daily was also administered. The patient had fever on day 23 and thereafter. No pus was observed draining from the abscess. The neutropenia persisted, and bone marrow aspiration revealed no response (blasts 72%).

High-dose cytarabine (HD-Ara-C) 2 g/m² i.v. twice daily for 4 days was initiated as a reinduction therapy. As the cellulitis worsened and sepsis continued after incision, drainage, and prolonged antibiotic therapy, radical fistulotomy and debridement of the abscess were performed on day 6. The abscessed skin and the infected granulation tissues were extensively removed (Figure 2). Perioperatively, the platelet counts were maintained above 50 000/ μL with platelet transfusions. *E. coli*, *E. faecalis*, methicillin-resistant coagulase-negative staphylococci (MRCNS) and anaerobic gram-negative bacilli were cultured from the removed drainage tube, while only MRCNS was cultured from the blood. The patient's fever persisted after the surgery. Laboratory test results showed elevated hepatic enzyme

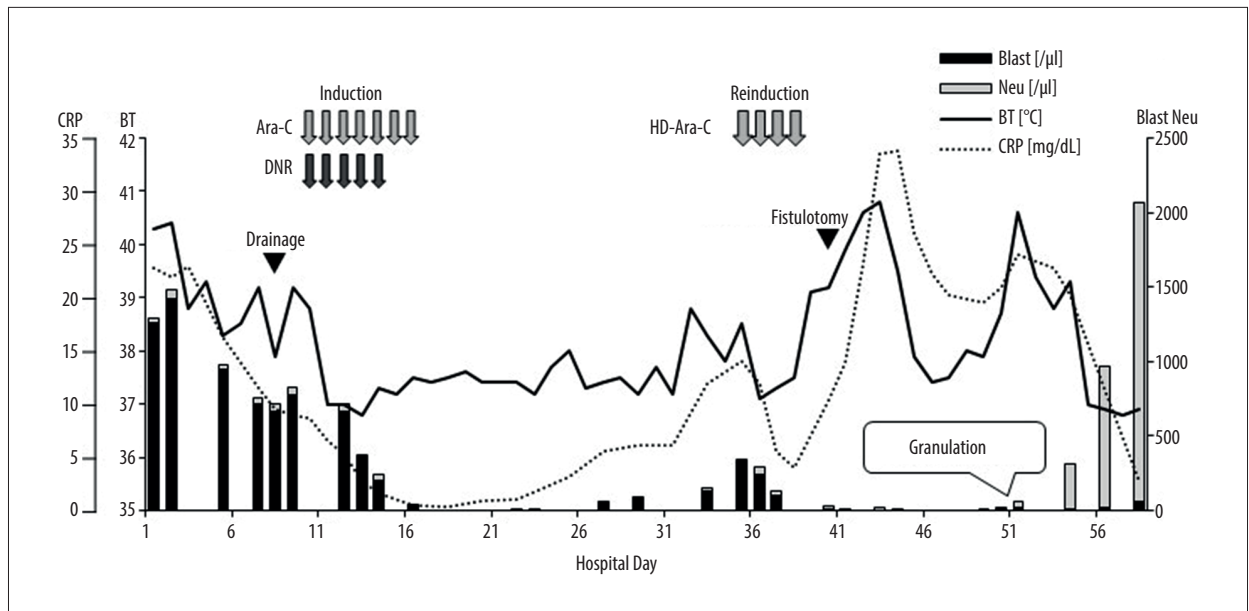


Figure 1. Clinical course of induction and reinduction chemotherapy. On the X axis, hospital day 1 was set as the day of admission. Ara-C – cytarabine; BT – body temperature; CRP – C-reactive protein; DNR – daunorubicin; HD-Ara-C – high-dose cytarabine; Neu – neutrophils.



Figure 2. Macroscopic appearance of the perianal abscess and the surgical wound. HD – hospital day; HD-Ara-C – high-dose cytarabine; POD – postoperative day.

levels, for which endotoxin adsorption was performed. Silver sulfadiazine was applied to the open wound. Large volumes of malodorous exudate were observed every day. However, no further extension of cellulitis was observed. On day 17, healthy granulation tissue appeared in the wound, and the gluteal pain improved. The patient's fever resolved on day 21. The neutrophil levels recovered to $>500/\mu\text{L}$ on day 22, and a bone marrow examination demonstrated partial remission (blasts 25%).

Because the reinduction chemotherapy was effective for debulking (reducing blasts from 72% to 25%), chemotherapy treatment of HD-Ara-C i.v. for 5 days (1 day longer than previously) was repeated as the third chemotherapy. The surgical wound continued to shrink. The gluteal pain improved, and oxycodone (maximum dose, 25 mg twice daily) was tapered off. From the wound swab, alpha-hemolytic *Streptococcus*, coryneform bacteria, *Enterobacter cloacae*, and anaerobic gram-negative bacilli were cultured during myelosuppression, while *Enterococcus faecium* was cultured during the bone marrow recovery. The neutrophil levels recovered to $>500/\mu\text{L}$ on day 20. Febrile neutropenia was observed on days 11 to 22. The bone marrow examination showed refractory disease (blasts 26%).

Another reinduction chemotherapy was administered: modified FLAGM (subcutaneous granulocyte colony-stimulating factor 300 μg on day 1+i.v. fludarabine 1.5 mg/m^2 twice daily on days 2 to 5+i.v. HD-Ara-C 2 g/m^2 twice daily on days 2 to 5+i.v. mitoxantrone 9.4 mg/m^2 once daily on day 6). *E. faecalis* was detected in blood cultures on day 3. Coryneform bacteria and *E. faecalis* were detected in the wound culture on day 4, and *Morganella morganii* was detected in the blood culture on day 11. The surgical wound was closed to the gluteal cleft (Figure 2). Neutrophil levels recovered to $>500/\mu\text{L}$ on day 23. Febrile neutropenia was observed on days 10 to 22. The patient achieved complete remission and was transferred to another hospital for transplantation. However, soon after the transfer, the leukemia relapsed. He underwent an allogeneic peripheral-blood stem cell transplant, followed by 2 cord-blood transplants. There was no abscess recurrence or fistula formation. The patient did not develop fecal incontinence. He died of leukemia 16 months after diagnosis.

Discussion

Surgical treatments for anorectal infection include incision and drainage, debridement, fistulotomy, and surgeries for other complications, such as fasciotomy for Fournier gangrene and colostomy for a rectovaginal fistula. Incomplete drainage might lead to worsening of cellulitis and sepsis, abscess recurrence, and fistula formation [1-3]. In patients with neutropenia and hematological malignancies, surgical treatments tend to be avoided because of concerns about delayed wound healing, secondary infections, and bleeding risks [8,12,15].

There are several retrospective studies comparing patient outcomes, with or without surgery, that draw conflicting conclusions. Owing to the retrospective nature of these studies, there were no predefined indications for surgical treatment or principles of antibiotic use, and the clinical course of the underlying disease (de novo, refractory/relapsed, or complete remission) and neutrophil counts could have affected treatment decisions. Some researchers believe surgery is not recommended because there is insufficient data on the impact of surgical interventions on recurrence or survival could not be statistically demonstrated owing to the small number of cases and variable clinical severity [8,12]. However, they do not deny the efficacy of surgical treatments or provide enough evidence to deem surgery inappropriate.

The minimally invasive surgical treatments of anorectal abscess are incision and drainage, which are recommended in cases of abscesses that are fluctuant or resistant to antibiotics, even during stages of neutropenia [7,9-11,16-18], including cases of stem cell transplantation [17,18].

The evidence on the application of more invasive surgical treatments (debridement and fistulotomy) for anorectal infections during neutropenia is scarce. These procedures are performed for anorectal non-fluctuant abscesses, induration, cellulitis, and fistulas. In the retrospective studies mentioned above, some patients did undergo these invasive procedures, but detailed information of each case was not available [8,9,12,17,18]. However, Barnes et al reported in detail about 16 patients with acute leukemia with non-fluctuant perirectal infections during severe neutropenia [10]. Eight patients who underwent incision and debridement showed wound healing and granulation, and all but 1 patient were discharged. The patients were receiving induction chemotherapy for de novo acute leukemia or reinduction therapy for relapse, and the time to neutrophil level recovery of $>500/\mu\text{L}$ ranged between 2 and 15 days after surgery [10]. Loureiro et al reported anorectal infections in 27 patients (abscess in 9 patients, fistula in 13 patients, cellulitis in 5 patients) with hematological malignancies [19]. Of the patients treated with antibiotics alone, 9 of 12 showed improvement or resolution of symptoms, while 14 of 15 patients treated with antibiotics plus surgery (cannulation, seton placement, and fistulotomy in 10 patients and surgical drainage and debridement in 5 patients) showed improvement or resolution of symptoms, suggesting a favorable outcome in the latter group [19]. In the present report, with refractory AML, a horseshoe abscess progressed to cellulitis, sepsis persisted during prolonged myelosuppression, and extensive debridement and fistulotomy were performed. Bleeding was managed by platelet transfusion. Antibiotic treatment was continued even after the surgery because the patient was immunocompromised, with extensive disease and signs of infection [1-3,13]. The time from debridement and fistulotomy to a

neutrophil recovery level > 500/ μ L was 16 days (neutropenia continued for 56 days after admission) (Figure 1). Although the wound closure time was longer than 98 days, the wound was in good enough condition for the patient to undergo 3 transplants without a recurrent abscess.

These results demonstrate that surgical interventions can prevent progression to a life-threatening infection. Thus, it is important to consider surgical procedures, including debridement and fistulotomy, in patients with leukemia, even in those with persistent neutropenia, if cellulitis, sepsis, and complications worsen despite antimicrobial treatment. Deciding on the appropriate timing for surgery can be challenging but it should be resolved through collaboration between hematologists and surgeons.

Wound culture is not necessary in all patients but is typically performed in patients who are at risk of having methicillin-resistant *Staphylococcus aureus* (MRSA) infection, who have recurrent infection or nonhealing wounds, or who are immunosuppressed (due to HIV infection or leukemia) and can have resistant or unusual bacteria [1]. Therefore, multiple culture tests were performed from our patient's abscess and surgical wound.

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Conclusions

For anorectal abscesses in patients with neutropenia and hematological malignancies, antibiotic treatment is mandatory. A fluctuant abscess is a good indication for incision and drainage. If the abscess is (or becomes) non-fluctuant, is accompanied by cellulitis or sepsis, and shows antibiotic resistance, it is worth considering further surgical intervention, including debridement and fistulotomy. Surgical interventions can prevent the progression of infection and can be lifesaving; thus, they should not be deemed a contraindication for patients with neutropenia. Prospective multicenter studies are warranted to establish a clear treatment algorithm for this rare disease.

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Conflicts of Interest

None.