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# Appendectomy Challenge If There is Not Neutrophil!

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### Abstract:

Acute appendicitis is a rare gastrointestinal condition in neutropenic acute leukemia patients. Urgent surgery as appendectomy in these neutropenic patients is a procedure with risks of morbidity and mortality. We report a rare presentation of a neutropenic acute leukemia patient with acute appendicitis operated urgently without any complications.

### Keywords:

Acute appendicitis, acute leukemia, neutropenia

## Introduction

Advances in medicine contribute to the life expectancy of transplant patients and many patients with oncological and hematological malignancies.

When a surgical problem occurs in severely immunosuppressed patients, diseases related to immunosuppression and underlying diseases should be considered while making differential diagnosis.<sup>[1]</sup> Apart from immunosuppression caused by hematological malignancy in hematology, neutropenia secondary to the drugs used is frequently encountered. Neutropenia, especially when the absolute neutrophil count falls below 1000, causes various complications such as infection, which is very difficult to cope with. Studies have shown that 30% of infectious complications in patients receiving chemotherapy originate from the gastrointestinal system.<sup>[2,3]</sup>

Numerous problems may be encountered in neutropenic patients involving any part of the gastrointestinal system such as the esophagus, stomach, and small and large intestine. Acute appendicitis is a rare condition in neutropenic patients.

The diagnosis, treatment, and follow-up of this rare condition require attention. The differential diagnosis in such a neutropenic patient should include infections of atypical microorganisms, opportunistic neoplasms, and drug-related complications.<sup>[1]</sup>

When diagnosed with acute appendicitis in a healthy patient without comorbidity, the treatment modality is usually surgery. However, the treatment modality in neutropenic patients may vary depending on the patient and the underlying disease. Considering the advantages and disadvantages of surgery, it is a very challenging situation for both the surgeon and the clinician. Both clinicians and surgeons have to make critical decisions regarding these patients.

Here, we would like to present a patient diagnosed with acute myeloid leukemia (AML), who developed deep neutropenia after chemotherapy and subsequently had acute appendicitis. We also would like to share our experience in diagnosis and treatment approach.

## Case Report

A 31-year-old male was diagnosed with AML. The patient's diagnosis was classified

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as AML M4 according to the FAB classification. The disease's risk category was intermediate according to cytogenetics.

One session of leukapheresis was performed due to hyperleukocytosis (white blood cell: 106 180 K/ $\mu$ L, hemoglobin: 12.1 g/dL, and platelet: 31,000 K/ $\mu$ L) and signs of leukostasis such as cough, dyspnea, and hemoptysis. Following this, 7 + 3 remission induction chemotherapy was started. On the 11<sup>th</sup> day of the treatment, when the patient was in the deep cytopenia period, tachypnea, tachycardia and general condition disorder developed. He was on the 10<sup>th</sup> day of meropenem, teicoplanin on the 7<sup>th</sup>, and posaconazole on the 4<sup>th</sup> day, because of the neutropenic fever. Posaconazole was discontinued that day and micafungin was started.

Chest computed tomography (CT) was performed on the patient due to tachypnea. When suspicious findings were seen in the abdominal sections here, the sections were enlarged and abdominal CT was also performed. In CT images, there was an increase in pleural effusion in the right lung and in areas of consolidation-atelectasis containing air bronchogram in the lower lobe of the right lung. The diameter of the intestinal segment, which was thought to be the appendix in the right lower quadrant of the abdomen, was measured as 15 mm, and a hyperdense (fecalith?) formation with a size of 13 mm  $\times$  9 mm was observed distally. In the periappendiceal area, areas with heterogeneity, significant contamination, free fluid appearances, and increased density in the fatty tissue were observed. It was thought that the findings might be compatible with acute appendicitis.

In abdominal ultrasonography performed to support the diagnosis, the diameter of the aperistaltic bowel segment, which was thought to be an appendix, was measured 15 mm in its widest part, and a hyperechogenic appearance with acoustic shadowing was observed at its distal end with a diameter of 14 mm (fecalith?). It was also noted that there was contamination in periappendicular fatty area. Reactive wall thickening up to 6 mm was observed in the cecum and ileum, and there was some free fluid between the bowel loops and in the pelvis. Moreover, once more the appearance was evaluated sonographically to be compatible with acute appendicitis.

The patient, whose total leukocyte count was 80 and absolute neutrophil count was 0, was consulted to the general surgery department. Considering the patient's deep neutropenia, the patient was evaluated for the last time by the hematology and general surgery departments. Finally, the operation decision was made. Erythrocyte

and platelet transfusion was performed preoperatively in the patient with hemoglobin 7.5 g/dl and platelet  $40 \times 10^9$ /L. The patient was taken into operation. Appendectomy was performed with Mc Burney incision. No intraoperative complications developed.

Postoperative granulocyte colony-stimulating factor support was given to the patient. He was followed closely. Within days, an increase in neutrophil values was noted. He recovered from severe neutropenia 9 days after surgery and 20 days after the start of chemotherapy. The patient stabilized in terms of clinical and laboratory values. Follow-up bone marrow aspiration biopsy revealed that the patient was in remission.

Subsequently, three consolidation treatments were given. He is currently being watched in remission. Allogeneic stem cell transplant is planned.

## Discussion

Chemotherapy given in hematological malignancies can damage rapidly growing gastrointestinal mucosa cells. Bacterial invasion may occur in the intestinal wall with the effect of neutropenia. Various layers of the intestine may be affected by this infection and necrosis may develop. Any segment of the bowel may be involved, but mostly, the terminal ileum and cecum are affected.<sup>[4]</sup>

Diseases involving the abdomen in leukemic patients may be due to many chemotherapeutic agents, but they have been mostly associated with cytosine arabinoside and anthracycline drugs.<sup>[4]</sup> 7 + 3 chemotherapy protocol including idarubicin and cytosine arabinoside drugs was applied to our patient as an induction regimen.

Classical symptoms of appendicitis are known as abdominal pain (especially located in the right lower quadrant), nausea, vomiting, and anorexia. These classical symptoms may not be present in neutropenic patients, since sufficient inflammatory response cannot be achieved.<sup>[3,5]</sup> In the absence of typical signs of peritoneal irritation, even if a detailed physical examination is performed, diagnosis becomes difficult. Therefore, abdominal ultrasonography and abdominal CT gain importance in early diagnosis. Since the sensitivity and specificity of ultrasonography are low in acute appendicitis, abdominal CT is considered to be a better and appropriate method.<sup>[6]</sup>

On abdominal radiography, a decreased amount of gas in the fluid-filled dilated bowel loops can be observed in the right lower quadrant. Excessively thickened cecum mucosa can be seen in ultrasonography. On CT, decreased attenuation can be observed in thickened colon walls due to edema, necrosis, or extraluminal

fluid accumulation. Enteric pathogen positivity can be detected in blood cultures, and hypotension, bacteremia, or fungemia can also be observed.<sup>[1]</sup> In our case, no microorganisms were grown in aerobic or anaerobic blood cultures.

Abdomen CT is also valuable in the differential diagnosis of acute appendicitis from neutropenic enterocolitis (or Typhlitis). Typhlitis progresses with fever, abdominal pain especially in the right lower quadrant, nausea-vomiting, watery, or bloody diarrhea, in patients with neutropenia. Intestinal wall thickening occurs mostly in the cecum and ascending colon in Typhlitis, but sometimes the appendix may be affected.

If the treatment is uncomplicated in Typhlitis, differential diagnosis with acute appendicitis is very important since it is mostly conservative (resting the bowels, follow-up with a nasogastric tube, broad-spectrum antibiotic, and total parenteral nutrition) in Typhlitis.<sup>[6]</sup>

In addition, intussusception, obstructive ileus, pseudomembranous enterocolitis, and opportunistic enteric infections should be included in the differential diagnosis.<sup>[3]</sup>

Three treatment strategies can be followed in a neutropenic patient diagnosed with acute appendicitis:

1. Conservative medical treatment: It includes multiple intravenous broad-spectrum antibiotic therapy, bowel rest, intravenous hydration, or total parenteral nutrition support
2. Early surgery: It can be defined as “early surgical intervention” until 48 h after the onset of symptoms
3. Combined approach: The combined approach is the first line of intravenous antibiotic treatment and the application of delayed surgical treatments.<sup>[3]</sup>

We decided that the early surgery option would be more appropriate in our patient. In addition, broad-spectrum antibiotics and intravenous hydration support were also given. We planned a very close follow-up after surgery.

Supportive treatment including transfusion and broad-spectrum antibiotics can be given according to the patient’s follow-up. In the presence of intraabdominal infection, adding metronidazole effective to anaerobes to a broad-spectrum antibiotic such as carbapenem may be helpful.<sup>[6]</sup>

Cases without significant complications after appendectomy in early surgery have been reported.<sup>[3,5]</sup> Another option is supportive treatment in the form of close follow-up, hydration, and antibiotic support, which can be preferred in a neutropenic patient, and surgery performed at a later stage after this supportive

treatment.<sup>[3]</sup> However, there may be risks associated with prolonged hospital stay such as appendix perforation, unless appendectomy is performed.

In a study conducted by Scarpa *et al.*, thirty patients with an average age of 8.8 were included. Medical therapy was successful in seven patients. Early surgery was performed in six patients, antibiotic treatment was given to the remaining 17 patients, followed by delayed appendectomy (combined therapy). Although all treatments were successful, temporary complications were observed in three patients. Infection-related mortality was not observed.<sup>[3]</sup>

Ozyurek *et al.* also performed delayed surgery in a 13-year-old AML patient 5 days after the diagnosis of acute appendicitis, and the patient became stabilized by this strategy.<sup>[7]</sup>

Kim *et al.* reported that no significant complications were observed after appendectomy for acute appendicitis in four leukemia patients. Two patients (one acute lymphoblastic leukemia and the other AML) were in induction chemotherapy like our case. The others were an AML patient who received salvage chemotherapy and an aleukemic leukemia patient who received supportive therapy because his performance status was not sufficient.<sup>[4]</sup>

Histopathological examination of the appendix should be performed to confirm the diagnosis after appendectomy.<sup>[3]</sup> In our patient, the result of appendix pathology was reported as “acute appendicitis, localized peritonitis.”

Although there is no definite recommendation regarding the operation technique, there is a hypothesis that laparoscopic surgery may have less infectious or hemorrhagic complications.<sup>[5,6,8]</sup> However, it should be kept in mind that laparoscopic surgery also carries the risk of intraabdominal abscess formation in perforated or gangrenous appendicitis.<sup>[8]</sup>

In a neutropenic hematology patient, there is a risk of complications and mortality associated with urgent abdominal surgery as well as a conservative approach.<sup>[9]</sup> This risk increases even more, especially if the patient is not in remission.<sup>[2]</sup> Therefore, when making a treatment decision, an evaluation should be made on a patient basis.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in

the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

### References

1. Scott-Conner CE, Fabrega AJ. Gastrointestinal problems in the immunocompromised host. A review for surgeons. *Surg Endosc* 1996;10:959-64.
2. Koretz MJ, Neifeld JP. Emergency surgical treatment for patients with acute leukemia. *Surg Gynecol Obstet* 1985;161:149-51.
3. Scarpa AA, Hery G, Petit A, Brethon B, Jimenez I, Gandemer V, *et al.* Appendicitis in a neutropenic patient: A multicentric retrospective study. *J Pediatr Hematol Oncol* 2017;39:365-9.
4. Kim KU, Kim JK, Won JH, Hong DS, Park HS. Acute appendicitis in patients with acute leukemia. *Korean J Intern Med* 1993;8:40-5.
5. Ustun C. Laparoscopic appendectomy in a patient with acute myelogenous leukemia with neutropenia. *J Laparoendosc Adv Surg Tech A* 2007;17:213-5.
6. Forghieri F, Luppi M, Narni F, Morselli M, Potenza L, Bresciani P, *et al.* Acute appendicitis in adult neutropenic patients with hematologic malignancies. *Bone Marrow Transplant* 2008;42:701-3.
7. Ozyurek E, Arda S, Ozkiraz S, Alioglu B, Arikan U, Ozbek N. Febrile neutropenia as the presenting sign of appendicitis in an adolescent with acute myelogenous leukemia. *Pediatr Hematol Oncol* 2006;23:269-73.
8. Sweeney KJ, Keane FB. Moving from open to laparoscopic appendectomy. *Br J Surg* 2003;90:257-8.
9. Kang HJ, Kang SY, Kang WK, Lee DG, Lee JW. Treatment of acute appendicitis in the patients with severe neutropenia. *J Med Cases* 2013;4:799-802.