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Laparoscopic Surgery for Acute Appendicitis in Children With Cancer

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ABSTRACT

Introduction: Abdominal pain during cancer chemotherapy may be caused by medical or surgical conditions. A retrospective review of 5 children with cancer who had appendicitis while receiving chemotherapy was performed.

Case Descriptions: Three had acute lymphoblastic leukemia, and 1 each had T-cell lymphoblastic lymphoma and rhabdomyosarcoma. Two of the patients had a Pediatric Appendectomy Score of 6, and 1 each had a score of 7, 5, and 2. All had evidence of appendicitis on computed tomography. Laparoscopic appendectomy was performed without any perioperative complication.

Discussion: Appendicitis is an important diagnosis in children with cancer, and laparoscopic appendectomy is safe and the procedure of choice.

Key Words: Appendicitis, Laparoscopic appendectomy, Pediatric cancer.

INTRODUCTION

Appendicitis is the most common condition that necessitates emergent abdominal surgery in children.[1] Anorexia, abdominal pain, fever, and emesis are classic clinical manifestations. However, younger children may present with nonspecific symptoms, making a diagnosis of appendicitis challenging. Moreover, in children with leukemia, the incidence of appendicitis is low (0.5–1.5%), and most patients may present with vague, nonspecific symptoms, resulting in delay of diagnosis, which may result in perioperative complications and death.[2,3] A blunted immune response may occur because of myelosuppression and/or immunosuppression. Computed tomography has a high sensitivity and specificity in the evaluation of immunocompetent children with suspected appendicitis.[4] Despite the use of improved diagnostic imaging, the rates of negative appendectomy and perforation have not been lower,[5,6] although one study found a sustained decrease in the rates of false-positive diagnoses of appendicitis and appendiceal perforation.[7] Moreover, early use of computed tomography may assist in distinguishing appendicitis from typhlitis, because the management of the former is surgery and of the latter is total parenteral nutrition and broad-spectrum antibiotics.[8] As in the general pediatric population, laparoscopic appendectomy is the preferred surgical approach.

CASE REPORTS

Case 1

A 12-year-old girl with T-cell acute lymphocytic leukemia (ALL), who was receiving maintenance chemotherapy, presented with intermittent periumbilical pain that migrated to the right lower quadrant. She was afebrile and eating and denied constipation, diarrhea, and nausea. The physical examination indicated diffuse abdominal pain with guarding. The leukocyte count was 2600, and the absolute neutrophil count (ANC) was 1700. The Pediatric Appendicitis Score (PAS) of Alvarado and of Samuel was 6 (2 each for pain with cough, percussion, or hopping and right lower quadrant tenderness and 1 each for migration of pain and fever). Abdominal computed tomography dem-

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onstrated an enlarged appendix with significant periappendiceal and pericecal fat stranding, consistent with appendicitis. The patient underwent laparoscopic appendectomy and partial omentectomy. Histopathology was consistent with acute appendicitis and periappendicitis. Postoperative recovery and wound healing were uneventful.

Case 2

An 8-year-old boy with T-cell ALL, who was receiving maintenance chemotherapy, presented with a sudden onset of severe right lower quadrant abdominal pain. His temperature was 101.5. The physical examination indicated a soft abdomen with tenderness on deep palpation of the right lower quadrant. The leukocyte count was 4700 and the ANC was 3700. The PAS was 6 (2 each for pain with cough, percussion, or hopping and right lower quadrant tenderness and 1 each for nausea or vomiting and fever). Abdominal computed tomography demonstrated a dilated appendix with thickening and hyperemia of the distal appendiceal wall. The patient underwent laparoscopic appendectomy. Histopathology was consistent with appendicitis and periappendicitis. Postoperative recovery and wound healing were uneventful.

Case 3

A 12-year-old boy with ALL, who was receiving consolidation chemotherapy, presented with a 1-day history of abdominal pain, located in the periumbilical region and right lower quadrant. The physical examination indicated diffuse abdominal pain with guarding in the right lower quadrant. The leukocyte count was 3600, and the ANC was 1900. The PAS was 7 (2 each for pain with cough, percussion, or hopping and right lower quadrant tenderness and 1 each for anorexia, nausea or vomiting, and fever). Abdominal computed tomography demonstrated that the appendiceal wall was thickened and enlarged. The patient underwent laparoscopic appendectomy. Histology was consistent with appendicitis and periappendicitis. Postoperative recovery and wound healing were uneventful.

Case 4

A 6-year-old boy with metastatic (lung) prostatic embryonal rhabdomyosarcoma developed fever and abdominal pain. The physical examination indicated severe oral mucositis and right lower quadrant pain on deep palpation. The leukocyte count was 0.1 and the ANC was 0. The PAS was 5 (1 each for anorexia, nausea or vomiting, and fever, and 2 for right lower quadrant tenderness). Abdominal computed tomography demonstrated inflammatory changes in the right lower quadrant adjacent to the cecum, corresponding to the site of the appendix. A normal air- and contrast-filled appendix was not demonstrated. The patient underwent laparoscopic appendectomy. Histopathology demonstrated appendicitis. Postoperative recovery and wound healing were uneventful.

Case 5

A 17-year-old boy with refractory T-cell mediastinal lymphoblastic lymphoma developed fever. The physical examination showed signs of peripheral neuropathy. The leukocyte count was 0.1 and the ANC was 0. The PAS was 2 (1 each for anorexia and fever). Abdominal computed tomography, obtained to evaluate neutropenic fever, showed a hyperemic appendix with periappendiceal inflammation. The patient underwent laparoscopic appendectomy. Histopathology demonstrated acute appendicitis. Postoperative recovery and healing were uneventful.

DISCUSSION

Gastrointestinal complications and acute surgical abdomen can become life-threatening conditions in immunocompromised/myelosuppressed children with cancer. The differential diagnosis comprises infections, colitis, typhlitis, and appendicitis. Differentiating appendicitis from typhlitis is challenging. Indeed, appendiceal thickening is observed in association with typhlitis. McCarville et al[9] identified typhlitis and appendiceal thickening in 4 of 90 pediatric oncology patients. Two of 4 patients with appendiceal thickening needed surgical intervention, whereas only 1 of 86 without this finding underwent surgery. The authors concluded that appendiceal thickening does not prolong the course of typhlitis, but may indicate an increased need for surgical intervention. Hobson et al[3] reported that children with typhlitis present with fever, diarrhea, abdominal pain, and typical computed tomography findings, whereas those with appendicitis present atypically. However, Angel et al[2] described 16 children with cancer and appendicitis. Six diagnoses were delayed, and 3 of the 6 patients presented with nonlocalized pain, abdominal distention, and lack of abdominal guarding, fever, dehydration, diarrhea, and upper gastrointestinal bleeding. Indeed, Skibber et al[10] stated that laparotomy may be the only effective method of differentiating typhlitis from appendicitis.

There are 2 pediatric appendicitis scoring systems that use history, physical examination, and leukocyte count. Samuel[11] found that the mean PAS score was significantly

higher in children with appendicitis (9.1 ± 0.1) than in children without appendicitis (3.1 ± 1.1; $P = .001$). A score of ≥6 indicated a high probability of appendicitis. Alvarado[12] found that a score of 5 or 6 is compatible with a diagnosis of appendicitis, 7 or 8 indicates probable appendicitis, and 9 or 10 very probable appendicitis. A prediction rule for identifying children at low risk for appendicitis based on presenting ANC may not be appropriate in immunocompromised/myelosuppressed children.[13,14] In our series of 5 immunocompromised children, 3 were categorized as having a high probability of appendicitis, 1 had symptoms compatible with appendicitis, and 1 had a low probability of appendicitis.

Diagnostic imaging plays a critical role in the evaluation of children for appendicitis. The American College of Radiology recommends beginning with ultrasonography and then proceeding to computed tomography if the appendix is not visualized or the study is nondiagnostic. In two recent studies, the authors concluded that increased use of ultrasonography, with or without computed tomography, is associated with a negative appendectomy rate and that ultrasonography has universally high sensitivity and specificity when the appendix is visualized.[15,16] Although the trend toward the use of ultrasonography may apply to immunocompetent patients, this current clinical wisdom may not apply to patients with both immunocompromise and myelosuppression, and physicians must exercise caution and maintain a high index of suspicion when evaluating patients who are so affected. Magnetic resonance imaging is a valuable technique for the evaluation of children with nonperforated acute appendicitis. Hörmann et al[17] used ultrasonography and magnetic resonance imaging in 45 immunocompetent children during an evaluation of clinically suspected acute appendicitis. Acute appendicitis was diagnosed by ultrasonography in 40% of the children and by magnetic resonance imaging in 100%. On T2-weighted ultra-fast turbo spin–echo images, the appendix appeared with a markedly hyperintense center, a slightly hyperintense thickened wall, and markedly hyperintense periappendiceal tissue. Moreover, in a study comparing imaging strategies with conditional contrast-enhanced computed tomography and unenhanced magnetic resonance imaging in patients with suspected appendicitis, the authors concluded that the accuracy of conditional or immediate magnetic resonance imaging is similar to that of conditioned computed tomography.[18] In our patients, computed tomography was indispensable in differentiating appendicitis from other intra-abdominal conditions that might have been present in patients with cancer.

Laparoscopic appendectomy has emerged as the operation of choice for appendicitis. U. S.[19] and Canadian[20] trends and outcomes studies from 2004 through 2011 have indicated that the frequency of laparoscopic appendectomy has doubled and hospital stays are shorter. A prospective randomized study of laparoscopic versus open appendectomy for complicated appendicitis concluded that the laparoscopic approach is safe and that operation time, hospital stay, and rates of wound sepsis, reoperations, and readmissions did not differ between the 2 approaches.[21] Kim et al[22] reviewed their experience with acute appendicitis in 7 Korean children with acute leukemia. Five of the 7 underwent laparoscopic appendectomy, and 2 underwent an open procedure. All experienced an uneventful recovery, but 1 in the laparoscopic group had an umbilical wound infection. Moreover, 2 patients had ANC of 0 at the operation. Forghieri et al[23] described their experience with 2 adult patients with hematologic malignancies (1 with multiple myeloma, the other with acute myeloid leukemia; French–American –British [FAB] classification, M2) who developed acute appendicitis while neutropenic. Both surgical procedures started laparoscopically (1 was converted to a minilaparotomy because of a gangrenous appendix) and each recovered uneventfully. In our cohort, laparoscopic appendectomy was performed safely, and no perioperative complications were observed. Notably, our patients in cases 4 and 5 had prolonged myelosuppression (lasting 3 and 4 wk after surgery, respectively) and severe mucositis. Because of the fear of perforation and sepsis, we proceeded with appendectomy. European randomized trials have suggested that an antibiotics-first strategy is not associated with an increased risk of perforation or higher rate of perioperative complication; however, there are early treatment failures in those patients so treated and all have a risk of recurrent appendicitis that may ultimately require appendectomy.[24] Wiegering et al[25] described 5 children with lymphoid malignancy that was managed with broad-spectrum antimicrobial coverage, which resulted in complete resolution in clinically stable patients with neutropenic cancer.

Clinicians and surgeons should not overlook the possibility of appendicitis in children with cancer. The application of appendicitis scores and early use of diagnostic imaging may facilitate the diagnosis of appendicitis and differentiate it from typhlitis. Diagnostic imaging recommendations (ultrasonography followed by either computed tomography or magnetic resonance imaging, if ultrasonography is not diagnostic) for immunocompetent patients may not be adequate for immunocompromised/myelosuppressed pa-

tients. We recommend abdominal computed tomography with a pediatric protocol to assist in diagnosis and reduce radiation exposure.

References:

1. Janik JS, Firor HV. Pediatric appendicitis: a 20-year study of 1640 children at Cook County (Illinois) Hospital. *Arch Surg*. 1979;111:717–719.

2. Angel CA, Rao BN, Wrenn E, Lobe TE, Kumar AP. Acute appendicitis in children with leukemia and other malignancies: still a diagnostic dilemma. *J Pediatr Surg*. 1992;27:476–479.

3. Hobson MJ, Carney DE, Molik KA, et al. Appendicitis in childhood hematologic malignancies: analysis and comparison with typhlitis. *J Pediatr Surg*. 2005;40:214–219.

4. Bachur RG, Dayan PS, Bajaj L, et al. The effect of abdominal pain duration on the accuracy of diagnostic imaging for pediatric appendicitis. *Ann Emerg Med*. 2012;60:582–590.

5. Martin AE, Vollman D, Adler B, Caniano DA. CT scans may not reduce the negative appendectomy rate in children. *J Pediatr Surg*. 2004;39:886–890.

6. Partrick DA, Janik JE, Janik JS, Bensard DD, Karrer FM. Increased CT scan utilization does not improve the diagnostic accuracy of appendicitis in children. *J Pediatr Surg*. 2003;38: 659–662.

7. Raman SS, Osuagwu FC, Kadell B, Cryer H, Sayre J, Lu DSK. Effect of CT on false positive diagnosis of appendicitis and perforation. *N Engl J Med*. 2008;358:972–973.

8. Gorschluter M, Mey U, Strehl J, et al. Neutropenic enterocolitis in adults: systemic analysis of evidence quality. *Eur J Haematol*. 2005;75:1–13.

9. McCarville MB, Thompson JJ, Li C, et al. Significance of appendiceal thickening in association with typhlitis in pediatric oncology patients. *Pediatr Radiol*. 2004;34:245–249.

10. Skibber JM, Matter GJ, Pizzo PA, Lotze MT. Right lower quadrant pain in young patients with leukemia: a surgical perspective. *Ann Surg*. 1987;206:711–716.

11. Samuel M. Pediatric appendicitis score. *J Pediatr Surg*. 2002; 37:877–881.

12. Alvarado A. A practical score for the early diagnosis of acute appendicitis. *Ann Emerg Med*. 1986;15:557–564.

13. Kharbanda AB, Dudley NC, Bajaj L, et al. Validation and refinement of a prediction rule to identify children at low risk for acute appendicitis. *Arch Pediatr Adolesc Med*. 2012;166:738–744.

14. Anandalwar SP, Callahan MJ, Bachur RG, et al. Use of white blood cell count and polymorphonuclear leukocyte differential to improve the predictive value of ultrasound for suspected appendicitis in children. *J Am Coll Surg*. 2015;220;1010–1017.

15. Bachur RG, Hennelly K, Callahan MJ, Monuteaux MC. Advanced radiologic imaging for pediatric appendicitis, 2005–2009: trends and outcome. *J Pediatr*. 2012;160:1034–1038.

16. Mittal MK, Dayan PS, Macias CG, et al. Performance of ultrasound in the diagnosis of appendicitis in children in a multicenter cohort. *Acad Emerg Med*. 2013;20:697–702.

17. Hörmann M, Paya K, Eibenberger K, et al. MR imaging in children with nonperforated acute appendicitis: value of unenhanced MR imaging in sonographically selected cases. *AJR Am J Roentgenol*. 1998;171:467–470.

18. Leeuwenburgh MMN, Wiarda BM, Wiezer MJ, et al. Comparison of imaging strategies with conditional contrast-enhanced CT and unenhanced MR imaging in patients suspected of having appendicitis: a multicenter diagnostic performance study. *Radiology*. 2013;268:135–143.

19. Masoomi H, Nguyen NT, Dolich MO, Mills S, Carmichael JC, Stamos MJ. Laparoscopic appendectomy trends and outcomes in the United States: data from the Nationwide Inpatient Sample, 2004–2011. *Am Surg*. 2014;80:1074–1077.

20. Cheong LH, Emil S. Pediatric laparoscopic appendectomy: a population-based study of trends, associations, and outcomes. *J Pediatr Surg*. 2014;49:1714–1718.

21. Thomson JE, Kruger D, Jann-Kruger C, et al. Laparoscopic versus open surgery for complicated appendicitis: a randomized controlled trial to prove safety. *Surg Endosc*. 2015;29:2027–2032.

22. Kim EY, Lee JW, Chung NG, Cho B, Kim HK, Chung JH. Acute appendicitis in children with acute leukemia: experience of a single institution in Korea. *Yonsei Med J*. 2012;53:781–787.

23. Forghieri F, Luppi M, Narni F, et al. Acute appendicitis in adult neutropenic patients with hematologic malignancies. *Bone Marrow Transplant*. 2008;42:701–703.

24. Flum DR. Acute appendicitis: appendectomy or the "antibiotics first" strategy. *N Engl J Med*. 2015;372:1937–1943.

25. Wiegering VA, Kellenberger CJ, Bodmer N, et al. Conservative management of acute appendicitis in children with hematologic malignancies during chemotherapy-induced neutropenia. *J Pediatr Hematol Oncol*. 2008;30:464–467.