

Educational Case: Acute Appendicitis

Emily Breeding, BA¹ and Richard M. Conran, MD, PhD, JD¹ 

The following fictional case is intended as a learning tool within the Pathology Competencies for Medical Education (PCME), a set of national standards for teaching pathology. These are divided into three basic competencies: Disease Mechanisms and Processes, Organ System Pathology, and Diagnostic Medicine and Therapeutic Pathology. For additional information, and a full list of learning objectives for all three competencies, see <http://journals.sagepub.com/doi/10.1177/2374289517715040>.¹

Keywords

pathology competencies, organ system pathology, gastrointestinal tract, mechanical disorders, appendix, appendicitis, abdominal pain

Received December 06, 2019. Received revised February 19, 2020. Accepted for publication April 11, 2020.

Primary Objective

Objective GT8.4: Appendicitis. Describe the clinicopathologic features of acute appendicitis and discuss the clinical differential diagnosis and potential complications of this disorder.

Competency 2: Organ System Pathology; Topic GT: Gastrointestinal Tract; Learning Goal 8: Mechanical Disorders of Bowel.

Patient Presentation

A 25-year-old woman with no previous medical history reported to the emergency department with abdominal pain, anorexia, nausea, and vomiting. Pain began 8 hours ago in the periumbilical region and is now localized to the right lower quadrant. She denied hematemesis, diarrhea, hematochezia, and melena.

Diagnostic Findings, Part I

Physical examination revealed a low-grade fever of 101 °F and pain and tenderness on palpation of the right lower quadrant.

Questions/Discussion Points, Part I

Based on the Clinical Presentation, What Disorders Are in the Differential Diagnosis of Right Lower Quadrant Pain?

The differential diagnosis of right lower quadrant pain includes abdominal disturbances, common abdominal/retroperitoneal

conditions, and systemic disorders. Common abdominal conditions that must be excluded before making a diagnosis include acute intestinal obstruction, acute pancreatitis, ischemic colitis, intussusception or volvulus, and general peritonitis. Malignancy and renal disorders, for example, urolithiasis and pyelonephritis, are other considerations. Abdominal disturbances, such as acute gastritis, gastroenteritis, and infective hepatitis, should be included in the differential as well. Meckel diverticulum and an acute exacerbation of Crohn disease may also mimic acute appendicitis. Both disease processes typically localize to the right lower quadrant. Meckel diverticulum is a congenital anomaly due to persistence of the vitelline duct and is typically found 2 ft from the ileocecal valve. The most common location for Crohn disease is the terminal ileum. Other inflammatory bowel diseases, such as ulcerative colitis, can extend to the ascending (right-sided) colon and should be included in the differential as well. Systemic conditions that may present with similar symptoms include influenza, diaphragmatic pleurisy, infectious enterocolitis, and acute porphyria. The differential diagnosis of abdominal pain

¹ Eastern Virginia Medical School, Norfolk, VA, USA

Corresponding Author:

Richard M. Conran, Pathology & Anatomy, Eastern Virginia Medical School, 700 West Olney Road, Norfolk, VA 23507, USA.

Email: conranrm@evms.edu



Table 1. Laboratory Test Results.

Laboratory test	Patient	Reference range
Complete blood count		
Hemoglobin (g/dL)	13.2	12-16
Hematocrit (%)	40.1	36-46
WBC count (cells/mm ³)	12,700	4500-11,000
Platelet count (cells/mm ³)	300,000	150,000-400,000
WBC differential		
Segmented neutrophils (%)	70	54-62
Band neutrophils (%)	8	3-5
Lymphocytes (%)	18	25-33
Monocytes (%)	3	3-7
Eosinophils (%)	1	1-3
Basophils (%)	0	0-1
CRP (mg/L)	34.0	<3
β-hCG	Negative	

Abbreviations: CRP, C-reactive protein; β-hCG, beta human chorionic gonadotropin; WBC, white blood cell.

in an adult woman also includes uterine colic, ovarian cyst, ectopic gestation, fibroids, twisted hydrosalpinx, salpingitis, and rupture of an endometrioma.²

Based on the Clinical Presentation, What Additional Studies Would You Order?

Complete blood count (CBC), C-reactive protein (CRP), pregnancy test (beta human chorionic gonadotropin [β-hCG]), and computed tomography (CT) scan of the abdomen.

Diagnostic Findings, Part 2

Laboratory Tests

The results from the CBC, CRP measurement, and pregnancy test are listed in Table 1.

Imaging

An abdominal CT scan demonstrated concentric thickening of the appendiceal wall with haziness of the surrounding fat consistent with an inflamed appendix. The appendiceal lumen was distended with an appendicolith.

Questions/Discussion Points, Part 2

What Is the Interpretation of the Laboratory Results?

Laboratory findings showed a neutrophilic leukocytosis with increased bands and an elevated CRP. These results are suggestive of an acute inflammatory process. A negative β-hCG rules out pregnancy complications (eg, ectopic pregnancy) as the cause of the patient's pain.



Figure 1. Acute appendicitis. The inflamed appendix is red, swollen and demonstrates a yellow purulent and fibrinous exudate on the serosal surface.

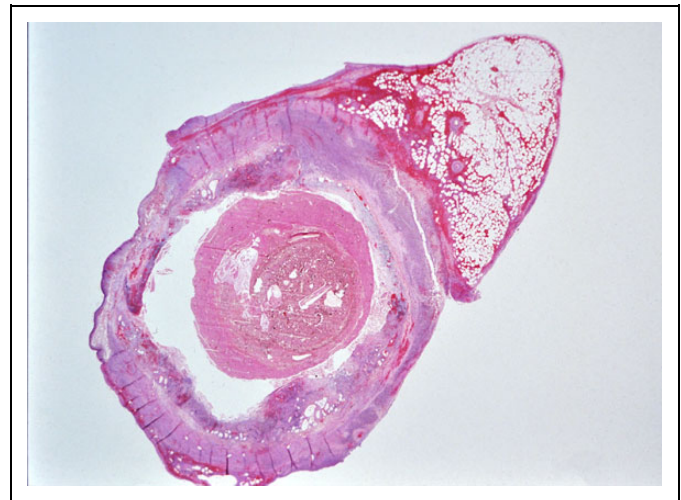


Figure 2. The appendiceal wall is thickened. An appendicolith is present in the appendiceal lumen (hematoxylin and eosin [H&E], low power).

What Would Be the Next Step Based on Laboratory and Imaging Findings?

The next step is laparoscopic surgery to remove the inflamed appendix. Intravenous metronidazole was given prior to surgery for coverage of Gram-negative bacteria.

Diagnostic Findings, Part 3

Describe the Findings Seen on the Resected Appendix

Gross morphology. The appendix is red, swollen, with a purulent fibrinous exudate on the serosal surface (Figure 1).

Histology. There is transmural acute inflammation with mucosal necrosis and hemorrhage extending into the serosal fat accompanied by an appendicolith in the lumen of the appendix. Fibrin deposition is present on the serosal surface (Figures 2–4).

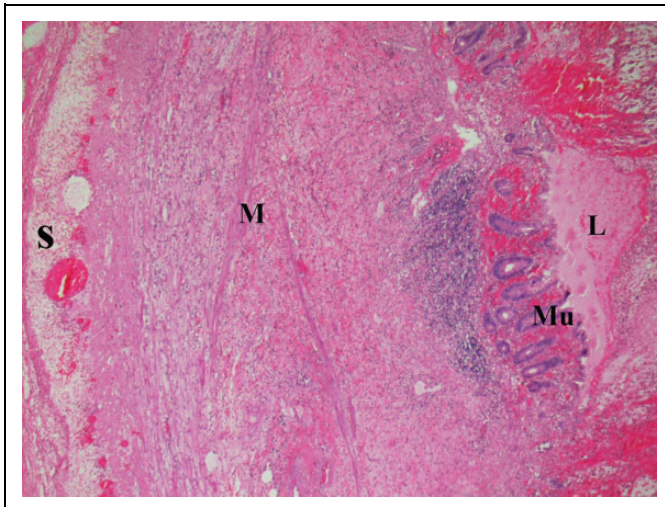


Figure 3. The appendix demonstrates a thickened wall accompanied by mucosal necrosis, transmural inflammation, and hemorrhage that extends into the serosal fat covered by a fibrinous layer (L—lumen, Mu—mucosa, M—muscularis, S—serosa; hematoxylin and eosin [H&E], low power).

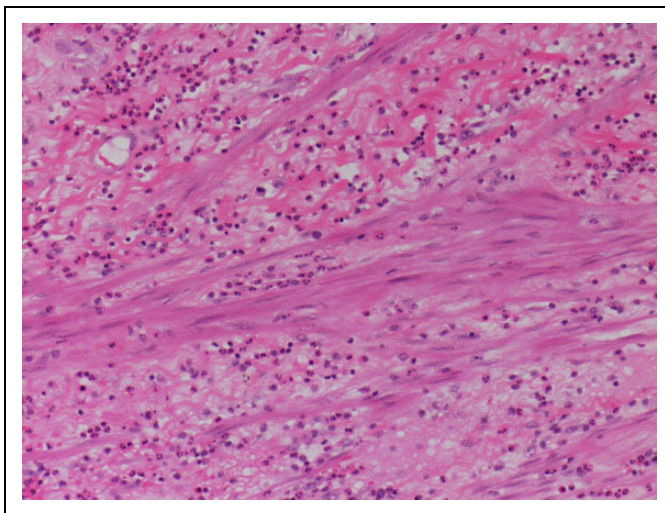


Figure 4. Inflamed appendix showing abundant neutrophils in the muscular layer of the appendix (hematoxylin and eosin [H&E], intermediate power).

Questions/Discussion Points, Part 3

Based on the Pathologic Findings, What Is the Diagnosis?

Based on the pathology, the diagnosis is acute appendicitis, which requires documentation of transmural acute inflammation.³

What Is the Underlying Pathogenesis of Acute Appendicitis?

The development of acute appendicitis is thought to be due to processes that increase intraluminal pressure and compromise venous outflow, resulting in mucosal necrosis and acute

inflammation.³ As the disease progresses, the inflammatory process spreads through all layers of the appendiceal wall. The necrosis and inflammation may lead to gangrene of the appendix and ultimately perforation, which is often associated with abscess formation.^{4,5}

Approximately 50% to 80% of cases are associated with direct luminal obstruction, commonly by appendicolith (fecalith), lymphoid hyperplasia, or impacted stool.^{4,6} Other less common causes of obstruction include a gallstone, tumor, or parasite.⁴ The most common parasite found in the appendix is *Enterobius vermicularis* (pinworm), although its role in the development of appendicitis is unclear. Viral infections of the appendix lead to lymphoid hyperplasia, causing obstruction and inflammation. Adenovirus is the most commonly described viral cause of appendicitis, especially in children. Other viral associations include cytomegalovirus and measles.⁷

Within the diseased appendix, bacterial overgrowth and invasion of the appendiceal wall occurs. This further propagates migration of neutrophils, which leads to a purulent reaction on the serosal surface and causes irritation of the surrounding parietal peritoneum.³ Early in the disease process aerobic organisms predominate, whereas mixed infections are more common in late appendicitis.⁸ *Escherichia coli*, *Peptostreptococcus*, *Bacteroides fragilis*, and *Pseudomonas* species predominate with gangrenous and perforated appendicitis.⁹

In What Order Do Symptoms of Acute Appendicitis Appear?

In most cases of appendicitis, pain is first referred to the epigastric or umbilical region because the enlargement of the appendix leads to the stimulation of afferent visceral nerve fibers at the T8 to T10 spinal cord level.¹⁰ Since this pain is visceral rather than somatic in origin, it is referred pain that is poorly localized. Other symptoms that occur in the early stages of acute appendicitis include vomiting, nausea, and anorexia. Local tenderness over the appendix is often elicited after general abdominal pain has subsided. Tenderness is most often detected on deep palpation two-thirds of the distance from the umbilicus to the right anterior superior iliac spine, which corresponds to the base of the appendix (McBurney point). Tenderness that is elicited on palpation of the right lower quadrant indicates irritation of the parietal peritoneum, which stimulates somatic nerves causing pain at the site of irritation.²

How Does the Anatomical Position of the Appendix Relate to Clinical Presentation?

The appendix is most commonly found behind the ileocecal junction with the tip pointed toward the spleen (retrocecal). Due to differences in embryological rotation of the midgut, the appendix may technically be found in any position. The second most common position of the appendix is within the true pelvis, over the right pelvic brim. Signs and symptoms of appendicitis vary based on the anatomical position of the appendix. Local tenderness is often present when the appendix is positioned by

the side of the ascending colon (paracecal) or within the iliac fossa. If the appendix is in the retrocecal position, the gut lying over the appendix may mask the inflammatory process. Vomiting is less frequent with a retrocecal appendix and muscular rigidity is less prominent. A rectal examination will often produce pain in the case of an appendix situated within the pelvis. In addition, localizing signs will vary depending on the location of the appendix after perforation.²

What Conditions Can Mimic Acute Appendicitis?

The diagnosis of acute appendicitis can often be difficult to confirm due to the absence of classical physical findings such as McBurney sign. Conditions that may mimic the clinical signs and symptoms of acute appendicitis include mesenteric lymphadenitis, acute salpingitis, ectopic pregnancy, mittelschmerz (pain due to pelvic bleeding during ovulation), and Meckel diverticulum.³ Imaging modalities such as abdominal ultrasound and CT are important for establishing the cause of appendicitis preoperatively for these conditions. Ectopic pregnancy can be excluded with a negative β -hCG value.¹¹ Mesenteric lymphadenitis is the most common alternative diagnosis for patients with suspected acute appendicitis, especially in children and young adults. Diagnosis of mesenteric lymphadenitis is confirmed by the presence of multiple, enlarged, and hypoechoic mesenteric lymph nodes on ultrasound. The cause of mesenteric lymphadenitis is often due to an underlying viral or zoonotic infection, such as *Yersinia enterocolitica* or *Salmonella*.¹²

What Are Possible Complications of Appendicitis?

If the appendix is not resected in time, it may perforate and put the patient at a greater risk of death. Other complications associated with appendicitis include pylephlebitis, portal venous thrombosis, liver abscess, and bacteremia.³ The most common complication associated with both open and laparoscopic appendectomy is wound infection. There is an increased risk of wound infection if the appendix has been perforated or if pus was present. Another postsurgical complication is the formation of a pelvic abscess. In this case, patients usually present several days after discharge with fever, malaise, abdominal pain, and loose stools. Depending on the size of the abscess, management includes antibiotics and/or drainage. Rare postsurgical complications include bleeding, fecal fistula, and incisional hernia.⁵

Teaching Points

- Acute appendicitis is more common in children and adolescents than adults.
- The pathogenesis of appendicitis is thought to be due to processes that increase intraluminal pressure and compromise venous outflow.
- Clinical features of appendicitis include early periumbilical pain that localizes to the right lower quadrant,

nausea, vomiting, low-grade fever, and a mildly elevated white blood cell count.

- The classic physical examination finding associated with appendicitis is the McBurney sign, which is deep tenderness to palpation of the right lower quadrant, specifically located two-thirds of the distance from the umbilicus to the right anterior superior iliac spine.
- Laboratory tests used to evaluate suspected appendicitis include a CBC with differential, CRP, and serum pregnancy test in women of childbearing age.
- Computed tomography is the recommended imaging modality to aid in making a diagnosis of acute appendicitis. Ultrasound and magnetic resonance imaging can be used in radiosensitive populations such as pregnant women or children.
- In order to make a formal diagnosis of acute appendicitis, transmural neutrophilic infiltration of the appendix is required on histology.
- Complications include perforation, pylephlebitis, portal venous thrombosis, liver abscess, and bacteremia.

Acknowledgements

Images were obtained during the scope of US government employment for Dr Conran.


Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Richard M. Conran  <https://orcid.org/0000-0002-4053-1784>

References

1. Knollmann-Ritschel BEC, Regula DP, Borowitz MJ, Conran R, Prystowsky MB. Pathology competencies for medical education and educational cases. *Acad Pathol*. 2017;4. doi:10.1177/2374289517715040
2. Silen W, Cope Z. *Cope's Early Diagnosis of the Acute Abdomen*. 22nd ed. Revised by William Silen. Oxford University Press; 2010:67-104.
3. Kumar V, Abbas AK, Aster JC, eds. *Robbins and Cotran Pathologic Basis of Disease*. 9th ed. Elsevier/Saunders; 2015:751:800-816.
4. Kumar V, Abbas AK, Aster JC, Robbins SL, eds. *Robbins Basic Pathology*. 9th ed. Elsevier/Saunders; 2013:600-601.
5. Froggatt P, Harmston C. Acute appendicitis. *Surgery (Oxford)*. 2011;29:372-376. doi:10.1016/j.mpsur.2011.05.016
6. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis,

- diagnosis, and management. *Lancet*. 2015;386:1278-1287. doi:10.1016/S0140-6736(15)00275-5
7. Lamps LW. Infectious causes of appendicitis. *Infect Dis Clin North Am*. 2010;24:995-1018. doi:10.1016/j.idc.2010.07.012
 8. Lau WY, Teoh-Chan CH, Fan ST, Yam WC, Lau KF, Wong SH. The bacteriology and septic complication of patients with appendicitis. *Ann Surg*. 1984;200:576-581. doi:10.1097/00000658-198411000-00003
 9. Bennion RS, Baron EJ, Thompson JE, et al. The bacteriology of gangrenous and perforated appendicitis—revisited. *Ann Surg*. 1990;211:165-171. doi:10.1097/00000658-199002000-00008
 10. Birnbaum BA, Wilson SR. Appendicitis at the millennium. *Radiology*. 2000;215:337-348. doi:10.1148/radiology.215.2.r00ma24337
 11. Hatipoglu S. Acute right lower abdominal pain in women of reproductive age: clinical clues. *World J Gastroenterol*. 2014;20:4043. doi:10.3748/wjg.v20.i14.4043
 12. Helbling R, Conficconi E, Wytttenbach M, et al. Acute nonspecific mesenteric lymphadenitis: more than “no need for surgery.” *Biomed Res Int*. 2017;2017:1-4. doi:10.1155/2017/9784565