

Appendiceal Abscess in Cystic Fibrosis

A Diagnostic Challenge

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A patient with cystic fibrosis who developed appendicitis, rupture, and a periappendiceal abscess is presented. A retrospective chart review revealed 5 other cases that demonstrate a spectrum of clinical presentation of periappendiceal abscess in patients with cystic fibrosis. Three patients were symptomatic for <5 days, but the remaining 3 patients were symptomatic for 8, 12, and 30 days before diagnosis. There were two deaths due to respiratory failure. Other complications included a perirectal fistula and 2 cases of recurrent abscess. This demonstrates the difficulty with which this diagnosis is reached in this patient population and the relatively high incidence of abscess formation compared with normal populations. A retrospective autopsy review of 51 cystic fibrosis patients showed that in 49 of 51 instances, the mucosa of the appendix was hyperplastic, and the mucosal glands were distended with eosinophilic secretions. In 12 cases (24%), the appendix itself was grossly firm, dilated, and distended, although the mucosal wall was free of inflammation. This lends credence to the suggestion that these inspissated secretions may be protective against the occurrence of appendicitis, the incidence of which may be as low as 1%–2% among cystic fibrosis patients.

Hyperplasia and hypersecretion of the intestinal tract goblet cells is characteristic of patients with

cystic fibrosis (CF), often leading to distention and inspissation of the appendix. Appendicitis and its complications, however, have been described primarily as incidental findings at laparotomy for recurrent abdominal pain or at autopsy (1–3). When appendicitis does occur, symptomatology is often mistaken for the more common gastrointestinal complications seen in these patients, such as meconium ileus equivalent and intussusception. This diagnostic dilemma can lead to a late diagnosis and often a course complicated by abscess formation. The authors present 6 cases (1 case in detail) that illustrate a spectrum of clinical presentation.

Case Report

A 19-yr-old white woman with CF and severe pulmonary insufficiency, cor pulmonale, and hypersplenism presented with a 5-day history of constant dull periumbilical pain that became localized to the right lower quadrant 2 days before admission. There was a 3-day history of anorexia and low grade temperature; there had been no nausea or vomiting. There was no diarrhea. She had normal amounts of flatus, no melena, and no prior history of abdominal obstruction. There had been no interruption in the use of pancreatic supplements. Oral pulmonary prophylaxis consisted of dicloxacillin, 500 mg, four times daily, and tetracycline, 500 mg, four times daily.

On physical examination, temperature was 37.0°C orally, pulse was 100 beats/min. Breathing was labored and rales were heard in both lung bases. Abdominal examination showed normal bowel sounds without rushes. There was generalized rebound tenderness, and a tender 10 × 10-cm fixed right lower quadrant mass was palpated. Rectal examination revealed an anterior midline mass.

Laboratory data on admission showed a white blood cell

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Abbreviations used in this paper: CF, cystic fibrosis.

count of 13,700 cells per mm^3 with 54% polymorphonuclears, 28% bands, 12% lymphocytes, and 6% monocytes. Flat plate and upright roentgenogram of the abdomen showed marked splenomegaly and a large soft tissue mass in the pelvis, extending to the right. A gastrograffin enema showed that the entire colon filled, as did the cecum and terminal ileum. There was flattening of the base of the cecum due to an extrinsic cause which also displaced the terminal ileum superiorly (Figure 1). The appendix was not visualized.

The patient was started on tobramycin, ticarcillin, and clindamycin intravenously. At surgery, a periappendiceal abscess was located, incised, and drained; the appendix was not removed. The area of the abscess was irrigated at surgery with 1% kanamycin and a drain was inserted that was not removed until postoperative day 29. Cultures grew *B. fragilis* sensitive to chloramphenicol and clindamycin, and antibiotics were continued for a full 10-day postoperative course. On day 7, the patient complained of abdominal fullness. On day 10, her albumin fell to 1.9 g/dl and abdominal ultrasound demonstrated ascites, and a 5×5 -cm echo-free mass in her right lower quadrant. She developed a temperature ranging between 37.2° and 38.3°C , but also showed signs and symptoms of a pulmonary exacerbation for which she was treated. On day 34, a repeat ultrasound showed a fluid collection in the area of prior abscess formation (Figure 2). It was decided not to subject the patient to further surgery. On day 41, she developed acute respiratory distress with an increase in heart size

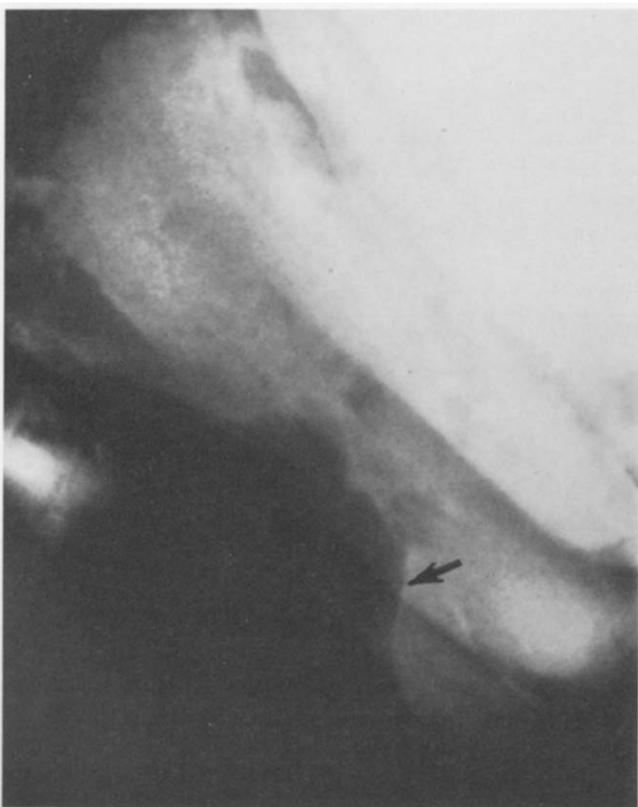


Figure 1. Gastrograffin enema demonstrates flattening of the base of the cecum due to an extrinsic mass (arrow).

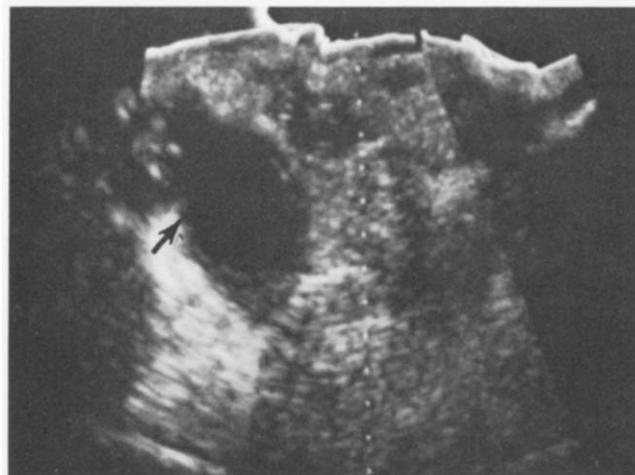


Figure 2. Abdominal ultrasound demonstrates an area of fluid accumulation (arrow) in the abdomen at the site of prior abscess formation.

and on day 42, expired due to respiratory failure. At autopsy there was a peritoneal abscess in the right lower gutter, surrounding the appendix.

Results

A retrospective chart review of all patients with CF followed at the National Institutes of Health revealed 4 cases of appendicitis and periappendiceal abscess among 256 patients followed between 1960 and 1981. A fifth case had been followed by one of the authors (di S.A.) at Columbia Presbyterian Medical Center in New York. A sixth case, just presented in full, had been followed by one of the authors (E.H.M.) at the Center for Health Sciences, University of Wisconsin, at Madison.

The patient population consisted of 3 men and 3 women, aged 6–21 yr. Brasfield scores (4), assessed retrospectively on the basis of their admission chest roentgenogram, were available for only 5 of 6 patients and ranged from 3 to 23. The clinical status of their primary disease appeared to have no bearing on the actual onset of appendicitis, however, clinical status affected the outcome of surgical recovery in 2 cases. Five of 6 patients were on some form of oral antibiotic prophylaxis at the time the appendiceal abscess was diagnosed. A prior history of meconium ileus equivalent was obtained in 2 cases.

Cramping abdominal pain was the most common symptom, occurring in all 6 patients, and it became localized to the right lower quadrant in 5 patients. The duration of pain before admission ranged from 2 to 30 days. All 6 patients complained of anorexia. Nausea, vomiting, and difficulty upon defecating occurred in 3 patients each, diarrhea did not occur in any of the 6 patients.

At the time of presentation, 4 of 6 patients had a temperature $<38^{\circ}\text{C}$ (range $36.9\text{--}39.0^{\circ}\text{C}$). The 4 patients with lower temperatures at the time of admission had been symptomatic for 5, 8, 12, and 30 days before admission. All 6 patients had a heart rate ≥ 100 beats/min. Right lower quadrant tenderness was present in all 6 patients as was a lower quadrant mass. A mass was detected on rectal examination in 6 cases, but rectal tenderness was present in only 4. Bowel sounds were present in 5 cases at the time of admission.

Laboratory findings on admission showed an average white blood cell count of 15,000 (range 10,500–21,000). Polymorphonuclear cells ranged from 47%–79% (average 65%) and bands ranged from 0% to 30% (average 17%) of the total count. A contrast enema was performed in 5 cases and revealed a nonspecific cecal deformity in 4 of 5 cases. In the fifth case, several gastrograffin enemas had been nondiagnostic.

All 6 cases of appendicitis were complicated by perforation and periappendiceal abscess formation. In this review, there were no cases of appendicitis not associated with abscess formation. In one instance, where clinical deterioration of pulmonary status precluded early surgical intervention, a rectal fistula was an added complication. In 2 cases, there was recurrent abscess formation. There were two deaths, both due to respiratory failure secondary to cystic fibrosis.

A retrospective autopsy review revealed 51 patients for whom pathological reports and histologic slides were available. Upon reviewing the gross anatomic evaluations of the appendix from autopsy or surgical pathology reports, there were 12 cases in which the appendix had been noted to be firm, dilated, and distended with mucoid material. In two of these cases, fecal material was also found within the lumen of the appendix; however, there was no evidence of mural inflammation in any of these specimens. All other specimens were reported as being grossly normal with patent lumens. Microscopically, 49 of 51 specimens showed hyperplasia and mucous distention of the mucosal glands of the appendix (Figure 3).

Discussion

The goblet cells in the intestinal mucous glands of patients with CF are increased in number and distended with eosinophilic mucoid secretions (2,3). These same histologic findings are found in the appendix, which may become thick, firm, and fingerlike due to an accumulation of inspissated secretions. Indeed, routine appendectomy performed at exploratory laparotomy on patients with recurrent

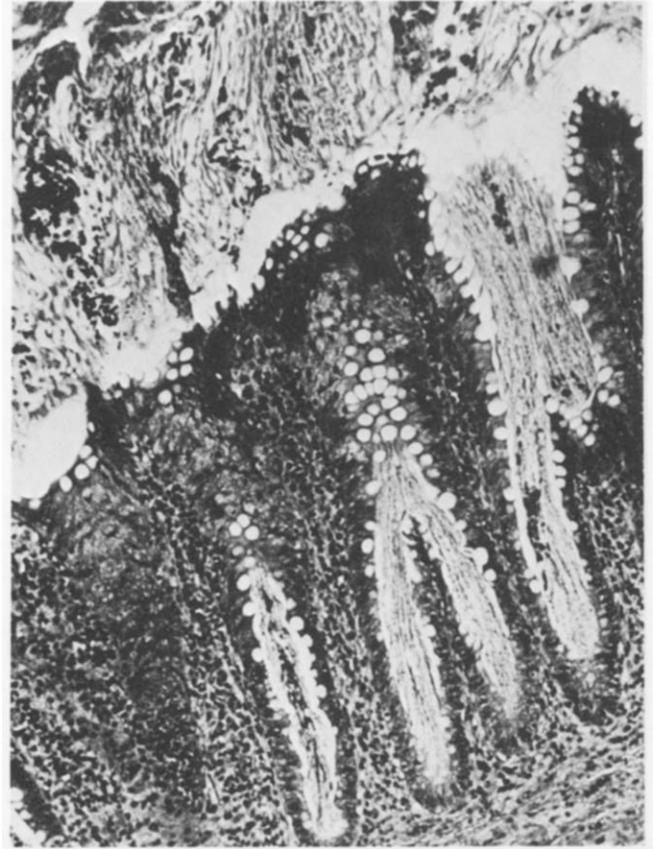


Figure 3. Microscopic section of the appendix demonstrates hypertrophy of the goblet cells with accumulation of mucous secretions within the crypts, and extrusion into the appendiceal lumen.

abdominal pain has led to the diagnosis of CF on the basis of these findings, before the clinical diagnosis was ever considered (1). As inspissated secretions collect within the appendix, it may become swollen and distended, presenting clinically as a nontender asymptomatic mass. Larger masses may occur as secretions extrude into the cecum (5). The results of our own autopsy review affirm these findings. In all but 2 of 51 instances, a hyperplastic secretory mucosa was observed, and in 12 instances (24%), the appendix was grossly distended and dilated with mucoid secretions but free of mural inflammation.

With luminal obstruction, a functional appendiceal mucosa will normally secrete fluid, develop a high secretory pressure, and exhibit the histologic appearance of acute appendicitis (6). When distended by a volume of 5-ml fluid, perforation ensues in 36–48 h (7). It is interesting that appendiceal complications do not occur more frequently in CF patients in face of a hypersecretory mucosa, frequent cecal fecaliths, and an increased occurrence of intestinal obstruction due to fecal material. It is possible that the secretion of mucous, with subsequent dilation and distention of the appendix is not associated

with either total luminal occlusion or the acute build up of intraluminal pressure necessary for ischemia, venous occlusion, and subsequent inflammation.

Despite the apparent frequency with which inspissation of the appendix occurs, appendicitis and perforation have been described mainly as "incidental findings" on autopsy. Two cases, out of 700 patients, most of whom were young children; were briefly mentioned in 1959 by di Sant'Agnese and Andersen (8). Jaffe et al. (9) found 4 cases of acute appendicitis among 250 patients with CF; 3 of these had an appendiceal abscess. In 1976, Holsclaw et al. (10) described 3 cases of "occult" appendiceal abscess in patients with CF. In the present study, 2 cases were seen elsewhere, but the other 4 patients were among the 256 patients followed at the NIH between 1960 and 1981. This occurrence rate of appendicitis of 1%–2% among patients with CF is lower than the 7% incidence in the general population. This would suggest that the filling of the appendix with inspissated secretions may play a protective role in preventing acute appendiceal inflammation.

The high incidence of abscess formation and the duration of symptoms before making a correct diagnosis clearly attest to the fact that making the clinical diagnosis of acute appendicitis in patients with CF is a diagnostic dilemma. Three of 4 patients seen by Jaffe (9) and all 6 patients in this review had a periappendiceal abscess complicate the course of acute appendicitis. This is clearly higher than the 3% incidence in the general population described by Lewis et al. (11). In breaching this difficulty in CF patients, the differential diagnoses need to be briefly considered.

Palpable abdominal masses in the right lower quadrant are frequently due to fecaliths, meconium ileus equivalent, and more rarely, intussusception. Fecaliths are usually mobile, asymptomatic, found on routine physical examination, and pass spontaneously. Meconium ileus equivalent, which occurs in as many as 20% of patients with CF (12), and intussusception can be tender on palpation and cause crampy abdominal pains. Pain associated with palpable masses can also be due to ovarian cysts (13) and hepatic enlargement. Abdominal pain may be secondary to the muscular aches associated with coughing, cholelithiasis, pancreatitis, and volvulus. Tenderness on rectal examination is usually only associated with fecaliths, meconium ileus equivalent, intussusception, and ovarian cysts. Other symptoms often associated with abdominal pathology such as fever, leukocytosis, anorexia, and vomiting (due to increased coughing) may be present in a patient with CF who has a severe degree of respiratory involvement.

It may be difficult to distinguish clinically between a symptomatic fecalith, meconium ileus equivalent, intussusception, and appendiceal abscess even by contrast radiography. Hypaque or gastrograffin enema is often diagnostic and therapeutic for meconium ileus equivalent or intussusception, but may only show a filling defect in the case of periappendiceal abscess. If a periappendiceal abscess is strongly suspected, or when a gastrograffin enema is nondiagnostic and a patient has either local findings or is critically ill, the more recent diagnostic methods of ultrasound and computed tomographic scanning should be utilized (14).

In patients with a classic history of anorexia, crampy abdominal pain that localizes to the right lower quadrant, and physical findings of a tender right lower quadrant mass symptomatic on rectal examination, a periappendiceal abscess should be considered, especially if the patient has been symptomatic for a period of time. In these patients, fever may be present early, but is often absent at admission, even when patients have been symptomatic for prolonged periods of time. Leukocytosis should also suggest this diagnosis, as it is an uncommon finding with asymptomatic masses or impactions.

Five of the 6 patients described herein were on some form of oral antibiotic therapy at the time of the diagnosis. The antibiotics did not prevent abscess formation, and may have even had an adverse effect. Prescribed antibiotics or self-medicated usage of antibiotics may mask or even improve a patient's general condition until abscess formation or peritonitis is grossly obvious (15). The often quoted work of Alexander and Altemeier (16) demonstrated that antibiotics administered intravenously before bacterial challenge lessen the incidence of abscess formation after perforation. It is unlikely, however, that common oral antibiotic regimens used in patients with CF would provide necessary bactericidal levels and proper coverage of the bacterial flora responsible for the infectious complications of appendicitis.

Among the 6 patients presented, there were 3 who had been symptomatic for 5 days or less, and 3 who had been symptomatic for >5 days. Generally, only 1% of children treated for appendicitis present 5 or more days after onset and have a palpable mass but no generalized peritonitis. This patient population is usually managed nonoperatively with fluids, bed rest, and antibiotics and readmitted for an interval appendectomy anywhere from 4 to 20 wk later (17–19). Immediate drainage of an abscess is performed in these patients only if there is a worsening of symptoms or a recurrence of abscess formation. In patients with CF, pulmonary insufficiency or the risks and potential complications of general anesthesia, or any combination thereof, may make a second

elective procedure prohibitive. An appendectomy should be performed whenever possible if surgical drainage of an abscess is done. In CF patients who are critically ill, or in whom there are substantial risks due to respiratory compromise, ultrasound and computed tomography may also be used to plan a route for percutaneous catheter drainage of an abdominal abscess that is accessible (20).

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