

Approach to chronic abdominal pain in Cystic Fibrosis



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Abstract

Abdominal pain in individuals with CF is challenging for the patient as well as the physician, as the differential diagnosis can be complex. Most gastrointestinal manifestations of CF present with regional abdominal pain. Pain localization, which requires knowledge of gut development and innervation, is crucial to understanding the pathophysiology of abdominal pain in CF. The location of the pain, together with the clinical presentation, shapes the differential diagnosis and thus guides the evaluation and management.

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1. Background

Prolonged survival of people with CF demands that attention be paid to the chronic manifestations of their disease as well as their quality of life. There have been several studies which demonstrate that children and adults with CF have a high incidence of undertreated pain throughout life, regardless of the severity of their disease [1–4]. A study of 73 children and 110 adults with CF found that the abdomen was the most prevalent location of chronic pain in children and the second most prevalent in adults, with 60% of children and 36% of adults in the study reporting chronic abdominal pain [3]. By comparison, the prevalence of occasional abdominal pain in otherwise healthy children is approximately 11% [5]. Across ages, pain is associated with more anxiety and depression, worse physical function, impairment of sleep, and restriction of activities and work [6].

In recent years, the natural history of chronic abdominal pain in CF, as well as the range of possible etiologies, has changed. This is mainly due to the fact that more people with CF are living into adulthood. One major difference between children and adults is the prevalence of exocrine pancreatic insufficiency

(PI), which is higher in children than in adults. The main reason for this difference is the better survival of PS patients [7]. Symptoms such as painful bloating and steatorrhea can be secondary to uncontrolled malabsorption related to exocrine pancreatic insufficiency. PS can be associated with painful episodes of pancreatitis, whereas PI patients can have symptoms such as painful bloating and steatorrhea but rarely develop pancreatitis [8,9]. Conditions that are commonly seen in children, such as intussusception, occur rarely in adults. However, gastrointestinal cancers are now being reported with increasing frequency in CF adults [7].

The mechanisms by which we perceive abdominal pain are varied and complicated. Abdominal pain is generally classified as visceral pain, parietal (also known as somatic or somatoparietal) pain, and referred pain. **Visceral** pain is elicited by stretch (mechano)receptors in the smooth muscle of hollow organs and exhibits slow transmission through C unmyelinated fibers. Examples include distension of the bowel by gas or liquid, as in diarrheal disorders or obstruction. Signals are propagated through bilateral pathways to the brain, and can involve multiple dermatomes. Accordingly, pain tends to be dull, crampy, insidious and poorly localized. This sort of pain is often accompanied by autonomic disturbances such as flushing, sweating and nausea. **Parietal** pain is elicited by cutting, tearing or inflammation in

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Table 1
Geography and developmental origin of abdominal pain.

Region of perception	Embryonic origin	Anatomic location
Epigastrium	Foregut	Proximal to ligament of Treitz, including hepatobiliary organs and spleen
Periumbilical	Midgut	Ligament of Treitz to hepatic flexure
Hypogastrum	Hindgut	Hepatic flexure to lower pelvis

organs covered by the parietal peritoneum. Transmission is rapid through A-delta myelinated neurons, usually unilateral, and propagated through the somatic spinal innervation. As a consequence, parietal pain tends to be intense and well-localized, although it may be referred. **Referred** pain occurs when visceral afferents share spinal cord segments with somatic afferents from a remote location. Referred pain is usually intense, and often lateralizing, sometimes complicating the differential diagnosis.

The common locations of abdominal pain are established developmentally. For example, pain in the epigastrium usually stems from organs of the embryonic foregut, proximal to the ligament of Treitz, including the lower esophagus, stomach, hepatobiliary organs and spleen. Periumbilical pain derived from organs of the embryonic midgut reflects disorders in organs from the ligament of Treitz to the hepatic flexure of the colon. Hypogastric pain derives from organs of the embryonic hindgut: the remaining colon, splenic flexure and rectum. Of course, depending on the stimulus, there may be more widespread pain or referred pain (Table 1).

Using this information, many disorders present with regional abdominal pain that aids in the differential diagnosis. Epigastric pain often occurs with GERD, esophagitis, gastritis, peptic ulcer, and pancreatitis. However, pancreatitis is also experienced in the right and left upper quadrants. Left upper quadrant pain is associated with gastritis and splenic infarct (which may also cause left shoulder pain), while right upper quadrant pain reflects hepatobiliary disease and pneumonia. Periumbilical pain is often due to gastroenteritis, early appendicitis, the distal intestinal obstruction syndrome (DIOS), small bowel bacterial overgrowth, and small bowel obstruction. Left lower quadrant pain is often found in people with fecal retention, urinary tract infection, and ovarian or renal pathology. While ovarian and renal disorders may also produce pain in the right lower quadrant, such pain is more likely from later appendicitis and DIOS. Diffuse abdominal pain is seen with intestinal obstruction, peritonitis, and gastroenteritis.

Table 2
“Red flags” for immediate referral to the emergency department.

Sign or symptom	Possible etiologies
Acute onset or sudden worsening of pain, especially in the right lower quadrant	Appendicitis, pancreatitis, bowel obstruction, intussusception, DIOS, biliary disease, renal stones
Bilious vomiting	Bowel obstruction, volvulus, DIOS
Fever in the presence of abdominal pain	Appendicitis, fulminant colitis
Bloody stools	Intussusception, infectious colitis, inflammatory bowel disease
Obstipation	Bowel obstruction, DIOS
Peritoneal signs – guarding or rebound	Appendicitis, pancreatitis, biliary disease
Hematemesis	Peptic ulcer disease, esophageal or gastric varices

2. Clinical presentation and differential diagnosis

It is important to note that while acute abdominal pain in people with CF can be a critical emergency (Table 2), we will only focus on a few etiologies.

As in any patient who presents with abdominal pain, it is critical to elicit a thorough history. Elements of the history which apply specifically to individuals with CF are:

- **Character of the pain:** common descriptors include burning, sharp, stabbing, cramping, achy, dull, pressure-like
- **Chronicity:** how long has the patient been experiencing pain? Is it constant or intermittent? Does it occur at a particular time of day? Is it associated with mealtimes or bowel movements?
- **Intensity:** is the pain interfering with activities of daily living or school / work attendance? Does the pain change with position?
- **Localization:**
 - Epigastric: GERD, gastritis, peptic ulcer disease, pancreatitis
 - Central/periumbilical: appendicitis (early), DIOS, gastroenteritis, bowel obstruction
 - Right upper quadrant: hepatobiliary, pancreatitis, acute pneumonia
 - Left upper quadrant: pancreatitis, gastritis, splenic infarct, acute pneumonia
 - Right lower quadrant: DIOS, appendicitis (late), ovarian, renal
 - Left lower quadrant: fecal impaction, urinary tract infection, ovarian, renal
 - Diffuse: intestinal obstruction, peritonitis, gastroenteritis
- **Associated symptoms:** may include nausea, vomiting, changes in frequency or consistency of bowel movements, worsening or relief with passage of stool or flatus
- **Pancreatic function:** is the patient PI or PS? If PI, is the pancreatic enzyme dose appropriate? If PS, has pancreatic function been screened for recently? If PS, consider serum amylase and lipase measurement for pancreatitis
- **Exposures:** has the patient been hospitalized or taken antibiotics? Sick contacts or foreign travel? Is there a family history of gastrointestinal disease?
- **Weight changes:** is there recent weight loss?
- **Surgical history:** focus on abdominal surgery, such as fundoplication, enteral feeding tube placement, intestinal resection (e.g., meconium ileus, volvulus, intussusception), or cholecystectomy

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