NASPGHAN Clinical Report on the Evaluation and Treatment of Pediatric Patients With Internal Penetrating Crohn Disease: Intraabdominal Abscess With and Without Fistula

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(JPGN 2013;57: 394-400)

OVERVIEW

Natural History of Pediatric Crohn Disease

he natural history of pediatric Crohn disease (CD) remains unpredictable, although some trends are observed that differentiate children from adults. Pediatric CD often presents with more severe disease and more frequent need for immunosuppressive therapy (1). Growth failure, present in 15% to 20% of patients, is a unique characteristic of pediatric CD not seen in adult-onset CD (2). Colonic disease distribution is common in patients younger than 10 years (1). The need for surgical intervention also varies, with 1 study reporting the actuarial risk of having undergone an extensive intestinal resection being $48.6\% \pm 5\%$ in a childhood-onset group versus $14.6\% \pm 2\%$ in the adult-onset group (P < 0.001) (1). More recently, long-term follow-up of patients enrolled in pediatric registries shows a cumulative surgical rate of 14% to 17% at 5 years and 28% at 10 years (3,4).

Pathogenesis of Internal Penetrating Disease in CD

The postoperative evolution of recurrent CD is a helpful model to understand the pathogenesis of internal penetrating CD (5,6). In this model, a primary focal inflammatory infiltrate forms in the ileum proximal to the anastomosis. Aphthous ulcers may appear within 3 months of the operation. The superficial ulcers may evolve into deeper and more extensive transmural lesions.

Received May 31, 2013; accepted June 1, 2013.

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The authors report no conflicts of interest.

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DOI: 10.1097/MPG.0b013e31829ef850

Transmural inflammation can progress to the formation of an inflammatory mass, or phlegmon, adjacent to the affected loop of bowel. A phlegmon is an acute suppurative inflammation of the subcutaneous tissue. The phlegmon may undergo liquefaction necrosis, resulting in an abscess, which is a circumscribed collection of pus. The tissue destruction involved in an enlarging abscess may lead to fistula formation. A fistula is an abnormal passage or tract resulting from a break in the integrity, or perforation, of the bowel wall, which then allows leakage of intestinal contents into the peritoneum or another adjacent organ. Deep ulceration and transmural inflammation may be followed by the formation of a stricture (7). Symptoms often are delayed for 2 to 3 years after the development of inflammatory lesions. These data indicate that the main risk factors for fistula formation appear to be severe luminal disease, ileal disease, and the presence of strictures. Perianal disease is related to perianal glands and is beyond the scope of this report.

One of the special features of the ileum is the abundant lymphoid tissue in the Peyer patch. Patients with CD have been reported to have defects in the follicle-associated epithelium and an increase in the adherence of commensal bacteria (8). Adherentinvasive Escherichia coli bind to CEACAM6 on the gut mucosa and replicate in epithelial cells and macrophages and stimulate production of tumor necrosis factor (TNF) (9). The outer membrane porin molecule, pili, and flagella play a role in adherence, and these interactions may explain the presence of antibodies to these molecules as markers in CD (10). NOD2, a genetic marker for stricturing ileal disease, is a key sensor for intracellular bacteria (11). Recent evidence shows that NOD2 and the autophagy gene, also associated with CD, form a complex at the cytoplasmic membrane (12). Recognition of muramyl peptidase by NOD2 induces autophagy and bacterial clearance. Defects in autophagy prevent the killing of intracellular bacteria. Bacteria proliferate in epithelial cells, macrophages, and dendritic cells, which may provide the breach in the mucosa necessary for the start of an abscess or fistula. Opportunistic bacteria may then follow. The production of metalloproteases by these opportunistic bacteria, such as Clostridium perfringens, degrades basement membrane type IV collagen and the extracellular matrix, resulting in further tissue destruction (13). Morphologic studies show that internal fistulae from patients with CD have a lining of flattened intestinal epithelium without goblet cells (14). Nonepithelialized fistulae have a layer of myofibroblasts forming a new basement membrane. All fistulas are surrounded by granulation tissue and, in CD, inflammatory cells including memory T cells, B cells, and macrophages. This lining may prevent further invasion and dissemination, but it may also prevent complete healing without operative removal of the fistula tract.

Risk Factors for Developing Complicated CD

Longitudinal registry data show that children diagnosed between the ages of 13 and 16 years have an increased risk of bowel surgery compared with younger children (4). These surgeries included bowel resection, ostomy, strictureplasty, and appendectomy. The disease extent at baseline was associated with the occurrence of intestinal complications. Relative to a patient with colonic disease, a patient with isolated terminal ileal disease or ileocolonic disease was at a higher risk (6- to 9-fold) of developing stricturing or penetrating disease (15). The cumulative incidence at 5 years of stricturing or penetrating complications was 27% of 989 pediatric patients and complicated disease was lowest in isolated colonic disease (16). Children with esophageal involvement compared with children with nonesophageal CD had greater disease severity (Pediatric Crohn Disease Activity Index of 40 vs 24, respectively, P < 0.001) and more penetrating disease behavior (12% vs 2% respectively, P = 0.001) and greater frequency of perianal disease (51% vs 33% respectively, P = 0.005) at diagnosis (17). In comparing 270 cases with and without fistulas, cases with fistulas tended to have more intraabdominal abscesses (P = 0.044), more frequent operations for perianal fistulae and abscesses (P = 0.001) as well as a higher incidence of combined small bowel and colonic disease (18).

In a study of serologic markers in 196 pediatric patients with CD, 28% developed internal penetrating and/or stricturing disease. The odds of developing internal penetrating/stricturing disease were highest in patients who were positive for all 4 immune responses (odds ratio 11, 95% confidence interval [CI] 1.5–80, P=0.03). Patients positive for ≥ 1 immune response progressed to internal penetrating/stricturing disease soon after diagnosis as compared with those negative for all immune responses (P<0.03) (19). Mutations in the NOD2 gene have been associated with ileal disease location and fibrostenotic behavior, but not penetrating disease behavior.

EVALUATION

Clinical Presentation: History and Physical Examination

The commonly reported presenting symptoms and findings of internal penetrating disease include abdominal pain (84%), fever (49%), nausea and vomiting (41%), diarrhea (25%), and fistula (14%) (20). An abscess may present subacutely or with acute onset of abdominal pain and sepsis. Occasionally, there may be signs and symptoms of partial bowel obstruction, including colicky pain, abdominal distension, vomiting, and intermittent constipation (21). The right lower quadrant, specifically the ileocecal area, is the most common site of the abscess, with the pelvis being the next most common (22).

Urinary symptoms may be present if the abscess is adjacent to the bladder. Refusal to walk may indicate irritation of the psoas muscles from the inflammatory process surrounding ileal disease. There can be shortness of breath and abdominal or shoulder pain with deep breathing when there is irritation of the diaphragm.

Physical examination may reveal localized tenderness and possibly a mass. There may be peritoneal signs, suggested by rebound tenderness. An abscess resulting from ileal disease may be difficult to distinguish from appendicitis or a ruptured appendix with abscess, with pain in the right lower quadrant and psoas signs, including pain with heel tap or straight leg raise. On rectal

examination, there may be a warm, tender bulge into the rectum if the abscess is in the pelvis. With either abscess or fistula, there may be additional signs of active CD, including weight loss, poor growth or development, oral aphthous ulcers, erythema nodosum, arthritis, or perianal signs such as tags, fissures, or perianal fistula.

Laboratory Evaluation

Laboratory investigation should include a complete blood cell count with differential white blood cell count to look for signs of inflammation, anemia, and thrombocytosis. Erythrocyte sedimentation rate and C-reactive protein can be useful, especially when recent values can be compared. Measurement of the serum albumin level may be helpful to support a diagnosis of protein wasting or chronic malnutrition. In the patient with abdominal pain and vomiting, liver and pancreatic function tests should be evaluated as well. A urinalysis should be obtained if there is dysuria, urinary frequency, or pneumaturia. Blood and urine cultures should be obtained in an acutely ill patient with fever.

Radiologic Evaluation

Cross-sectional imaging plays an important role in patients suspected to have complicated CD. When complicated CD is suspected in the acute setting of an intraabdominal abscess, both ultrasonography (US) or computed tomography (CT) can be used as the initial imaging evaluation. US has the inherent advantage of imaging without the use of ionizing radiation, but is relatively operator dependent. CT is readily available and frequently used in the acute setting when US does not answer the clinical question. CT can readily demonstrate bowel wall thickening, bowel dilation, and mesenteric fat proliferation, and unlike US, CT is not limited by bowel gas. Magnetic resonance (MR) and CT enterography carry the added value of identifying the presence of a fistula that may be feeding into the intraabdominal abscess. The sensitivities of CT enterography (83%-95%) and MR enterography (90%-100%) are comparable with the small bowel follow-through (65%-90%) in the detection of active small bowel disease but are more sensitive for the detection of extraenteric complications involving the solid organs (23). CT enterography and MR enterography have similar sensitivity rates in the evaluation of active disease, with CT having a slight advantage in the evaluation of bowel wall enhancement because of less artifact from peristalsis (24). Expertise in CT enterography may be more readily accessible than MR enterography, but the latter is the preferred modality when available. Because of the increased risks of ionizing radiation in patients with CD, and the potential for this patient population to be exposed to a large number of imaging studies during the course of their lifetime, MR enterography is frequently the imaging modality of choice. Ultrasonography or MR imaging should be used to follow-up a previously identified abscess to avoid additional radiation exposure (24-26).

Endoscopy

Few studies in the literature define the role of endoscopy in fistulizing CD. Endoscopy may be necessary to further characterize disease extent and severity, to evaluate possible infectious complications of immunosuppression (cytomegalovirus, *Clostridium difficile*), and to facilitate therapeutic decision making, especially in light of impending surgical intervention. The optimal timing for performing colonoscopy following treatment of an intraabdominal abscess is also unclear, although some clinicians recommend waiting 4 to 6 weeks (27).

Infectious Disease Evaluation

Empiric antibiotics should be initiated in the presence of an intraabdominal abscess, and abscess drainage for both therapeutic and diagnostic purposes should be pursued to allow specific antimicrobial coverage. Aerobic and anaerobic cultures of blood and abscess fluid should be sent, with at least 1 mL of fluid for reasonable culture yield. Culture yield can be increased with larger samples. Abscess fluid should be placed in clearly labeled blood culture bottles and sent to the microbiology laboratory immediately. Yeast (*Candida*) will grow in a routine blood culture, so dedicated fungal cultures are not necessary under most circumstances.

TREATMENT

Medications

Antimicrobials

Initial Choice of Antimicrobials. Recently updated guidelines published jointly by the Surgical Infection Society and the Infectious Diseases Society of America are helpful in the management of abdominal infections, including in the setting of CD, and should be followed (28). Most patients with CD with an abdominal abscess will have had multiple experiences with the health services system and should be classified as health care associated; hence, coverage for potential nosocomial organisms (Gram-negative aerobic and facultative bacilli: Pseudomonas aeruginosa, Enterobacter species, Klebsiella species), in addition to community-acquired pathogens (coliforms and anaerobes: Escherichia coli, Enterococcus species, Bacteroides species, Peptostreptococcus species), should be provided initially. Initial empiric antibiotics should be selected from one of the accepted broad-spectrum intravenous regimens: a carbapenem (imipenem, meropenem, or ertapenem), a β-lactam/ β-lactamase-inhibitor combination (piperacillin-tazobactam or ticarcillin-clavulanate), or an advanced-generation cephalosporin (ceftazidime, cefepime) with metronidazole (28) (Table 1). Enterococcal species (eg, Enterococcus faecalis) are the most susceptible to the penicillins and vancomycin. Vancomycin should be used empirically if the patient has had recent cephalosporin exposure, a history of previous infection, or colonization with enterococcal organisms (28). Drainage with aerobic and anaerobic cultures of the abscess material should be attempted and antibiotics tailored when culture and susceptibility reports become available. Generally, aggressive therapy for methicillin-resistant Staphylococcus aureus, enterococcus, or fungus should be prompted only by a positive culture, methicillin-resistant S aureus colonization, or a previous infection. Fluoroguinolones should only be used if >90% of E coli are susceptible; a carbapenem- or piperacillin-based regimen with adjunct aminoglycoside therapy should be chosen if there is a significant frequency of resistance to extended-spectrum β-lactamase or ceftazidime at the local facility (28).

Use of Oral Antimicrobials. Oral therapy is reasonable to consider in the context of decreasing fever, controlled pain, ability to tolerate oral fluids, and ability to ambulate (28). The oral agent used must be active against all microbiologic isolates. Suggested oral regimens include a second- or third-generation cephalosporin combined with metronidazole, or amoxicillin-clavulanate if the isolated organisms are susceptible. A fluoroquinolone (ciprofloxacin or levofloxacin) may be used to treat susceptible Pseudomonas, Enterobacter, Serratia, and Citrobacter species (28). If ciprofloxacin or levofloxacin is used, metronidazole should be added. A generally accepted principle is to reserve fluoroquinolones for more resistant enteric organisms. Resistance to fluoroquinolones can develop on therapy, so they must be used with caution and with close follow-up of the patient's clinical condition. When fluoroquinolones are the best option for the circumstance, this should be explained and discussion with the child's family about the extremely small potential for tendonitis or tendon rupture should take place, but should not prevent the child from receiving the antibiotics (29). In patients younger than 19 years, the relative risk (RR) of verified tendon or joint disorders was not different in those who received ofloxacin and ciprofloxacin (RR 1.04, 95% CI 0.55-1.84) compared with those who received azithromycin (RR 1.04, 95% CI 0.72-1.51), likely reflecting the background incidence of these disorders in children (30).

Duration of Antimicrobial Therapy. Seven days of antimicrobial therapy is sufficient for situations in which complete (percutaneous or surgical) drainage is achieved (28). In most cases of abdominal abscess in the setting of CD, however, source control is difficult to achieve. An abdominal abscess in the setting of CD cannot be considered definitively treated until complete resolution has been documented by an imaging study. For a completely drained abscess, antibiotics should be continued for at least 3 to 7 days. Resolution of the abdominal pain and intestinal obstructive symptoms, along with defervescence, signify response to therapy. A longer course of antibiotics, along with re-imaging, should be considered if clinical improvement is not seen within 3 to 5 days of initiating therapy (27).

CD-Specific Therapies

Aminosalicylate. There are no data indicating that aminosalicylates are useful in the treatment of internal penetrating CD. For the most part, these agents are continued for the management of active bowel disease.

Corticosteroid. There are no controlled studies evaluating the use of steroids for Crohn fistula. Corticosteroids should generally be avoided in fistulizing disease because of an increased risk of abscess (31). In patients who are already receiving corticosteroid therapy at

TABLE 1. Common initial antimicrobials for treatment of pediatric Crohn intraabdominal abscess

Antimicrobial	Dosage	Frequency of dosing
Piperacillin-tazobactam	200-300 mg · kg ⁻¹ · day ⁻¹ of piperacillin component	Every 6-8 h
Ticarcillin-clavulanate	$200-300 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ of ticarcillin component (not for severe infection)	Every 4–6 h
Meropenem	$60 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$	Every 8 h
Cefepime or ceftazidime with metronidazole combination	Cefepime 100 mg \cdot kg ⁻¹ \cdot day ⁻¹	Every 12 h
	Ceftazidime 150–200 mg \cdot kg ⁻¹ \cdot day ⁻¹ Metronidazole 30–40 mg \cdot kg ⁻¹ \cdot day ⁻¹	Every 6–8 h Every 8 h

the time of abscess diagnosis, there does not seem to be additional morbidity in continuing corticosteroid therapy for as long as the abscess is appropriately treated (27), although one should attempt to wean the dose to <20 mg/day, but not below twice the physiologic steroid replacement, to avoid the increased risk of perioperative complications should a surgical intervention be necessary (32).

Immunomodulators. Pediatric studies have shown the efficacy of immunomodulators (6-mercaptopurine, azathioprine, and methotrexate) in maintaining remission in pediatric CD (33–36). Additional studies in adults show that at least 30% of fistulas achieve complete or partial closure with immunomodulators. Long-term therapy, however, is necessary to maintain fistula closure (37,38). Uncontrolled studies in adults show that intravenous cyclosporine is effective in fistula closure but will not maintain response over the long term (38).

Biologic Therapy. In the absence of randomized, prospective clinical trials, uncertainty persists about how beneficial TNF-α inhibitors may be in the acute setting of an abdominal abscess in aiding resolution. Clinicians are often faced with the dilemma of whether to continue or hold anti-TNF therapy in the setting of an intraabdominal abscess. A series of 100 patients with opportunistic infections showed that most opportunistic infections from immunosuppressive drugs used for inflammatory bowel disease were from viruses, fungi, or mycobacteria, pathogens requiring a strong T-cell response for control (39). The ACCENT II study data were analyzed to determine whether fistula-related abscess development was affected by infliximab exposure (40). Twenty-seven (19%) of the patients in the placebo maintenance group compared with 21 (15%) patients in the infliximab maintenance group developed at least 1 new fistula-related abscess (P = 0.526), indicating that maintenance infliximab does not result in increased abscess development in fistulizing CD. In adults, there was no increase in postoperative abdominal abscesses observed after surgery performed while patients were on TNF- α inhibitors, and the authors suggested that there may be a drug-associated benefit in the setting of an acute abdominal abscess (40-42). It has, therefore, been proposed that TNF- α inhibitors be continued in the setting of treatment of an active CD-related abscess (42). Expert opinion among adult gastroenterologists indicates that immunosuppressive therapy can be started soon after successful percutaneous drainage of the abscess (27). This question deserves research attention so that reliable practice parameters can be established in the pediatric population.

Infliximab has been shown to be effective in the treatment of CD draining abdominal, perianal, or rectovaginal fistula in multicenter, randomized, double-blind, placebo-controlled trials (43,44). There are no randomized studies evaluating the efficacy of infliximab for internal fistulas. A case report described the beneficial effects of infliximab in 5 children with CD and enterovesicular fistulas, 3 of whom were asymptomatic and 2 required surgical resection (45).

Percutaneous Interventional Management

Percutaneous abscess drainage (PAD) was formerly avoided in patients with CD because of the fear of creating a postdrainage enterocutaneous fistula. Present studies indicate that PAD is an effective treatment for intraabdominal abscesses in CD. Simple, unilocular abscesses respond well to PAD, with success rates up to 90% and lower rates for complex abscesses. Multiple abscesses and postoperative collections can be drained successfully in the nontoxic patient (46,47).

PAD should generally be considered as initial therapy in collections > 2 cm in size (to accommodate a drain's distal pigtail), although percutaneous aspiration can be used for smaller collections to obtain a specimen for culture. Most abdominal abscesses will require US guidance, whereas abscesses in the pelvis will likely require CT guidance or a transrectal approach combined with US and fluoroscopic guidance. A standard Seldinger technique is commonly used in which the fluid collection is punctured with an 18-gauge needle using image guidance. A fluid sample is obtained followed by insertion of a 0.035-inch guidewire. After tract dilation, a pigtail locking drain (6F-12F) is inserted. The drain is flushed, secured to the skin with suture, and connected to gravity drainage. Daily irrigation with normal saline is performed and drain outputs followed. When outputs fall to <10 mL/day (5 mL/day in infants) and the patient is clinically improved, the drain can be removed (48). If there is persistent drain output, then an abscessogram is performed with contrast injection to evaluate for the presence of a fistula. In some cases, PAD along with medical therapy may avoid the need for surgical intervention in the acute setting, especially when a fistula is not present.

PAD with prolonged catheter drainage (17–41 days), bowel rest, medical therapy, and parenteral nutrition have been used to treat fistulae with varying results (49–51). Advances in the technique of PAD with prolonged catheter drainage in addition to intravenous antimicrobials and bowel rest may result in spontaneous closure of the fistula, hence avoiding the need for surgery in the acute setting. This conservative management has led to some adult patients avoiding operations in the long term (21,52,53) for as long as the fistula remains closed, and the active Crohn inflammation is controlled. If the fistula persists, having the drain in place still offers the advantage of less intraabdominal inflammation and fewer adhesions as well as improvement of the general status of the patient to allow for elective surgical removal of the diseased segment of bowel. Operative intervention is necessary when conservative therapy fails.

Surgical Management

Abdominal Abscess Source Control

One particularly challenging aspect in fistulizing CD is "source control," or effectively removing the driving force of the abscess. Source control requires drainage of the abscess along with antimicrobial therapy. Challenges in achieving source control probably account for the majority of treatment failures and recurrent abscesses. Several reports in adults have described a higher long-term success rate when fistulae are addressed definitively (54,55).

Operative intervention is indicated for an abscess that is refractory to a combination of percutaneous drainage, antimicrobial, and CD therapy.

Indications and Timing of Operation

Hemodynamic instability and diffuse peritonitis are indications for urgent abdominal exploration. A prerequisite to operative management of an intraabdominal abscess is to reduce the infectious burden, which can be achieved with the use of broad-spectrum antibiotics and PAD. Once source control is achieved, definitive operation to resect the region of perforation with treatment of the associated abscess space and inflammatory mass can proceed.

The time interval between successful PAD and elective surgical resection of diseased bowel varies from center to center and may occur from several days to weeks after initial presentation (56).

General Principles

Above all, the guiding principle in the surgical management of CD is preservation of intestinal length. In the case of enteroenteric or enterovesical fistulas, the primary goal is interruption of the fistula with limited intestinal resection. In general, loss of colonic length is less dire than loss of small bowel. In either case, macroscopically disease-free resection margins are ideal (57).

Over time, the trend in abdominal surgery has been toward the use of laparoscopy. The benefits of laparoscopy include faster postoperative recovery, decreased risk of wound-related complications, formation of fewer intraabdominal adhesions, and better cosmesis in pediatric patients (58). Laparotomy, however, continues to be a safe and reasonable approach to treat the complications of CD in the surgical patient who cannot tolerate insufflation of the abdomen with carbon dioxide, a necessary step in laparoscopy. Diverting ileostomy or colostomy is rarely necessary but is considered in the following scenarios: significant intraabdominal soilage—particularly with colonic perforation, inflammatory thickening of intestinal wall, and intraoperative hemodynamic instability precluding safe additional operative time needed to construct an anastomosis.

Modifiable risk factors for perioperative complications should be identified and treated. The most commonly encountered risk factors are the use of steroids and malnutrition (32). The presence of either increases the risk for technical, anastomotic, wound healing, and infectious complications (59). Every effort should be made to wean the steroid dose as much as the patient will tolerate, with a goal of <20 mg daily. Patients who were receiving a higher corticosteroid dose were at least 9 times more likely to develop an abscess.

Tolerance of steroid wean is usually directly related to disease activity with luminal narrowing. Consequently, low residual diet and/or total parenteral nutrition can be used to facilitate the

steroid wean as well as enhance nutritional rehabilitation in the setting of inflammatory luminal narrowing (32,60).

Emerging experience and case series reports also suggest that some patients may be managed medically with complete resolution of the intraabdominal abscess without need for further elective surgery (27). Of 16 adult patients with Crohn-related intraabdominal abscesses that were treated medically, 7 patients did not have recurrence of the abscess during a mean follow-up of 45 months for the entire study group (54). A recent report of 13 adult patients with a phlegmon, 12 of whom had an associated abscess, were successfully treated with a combination of antibiotics and anti-TNF (61). Only 2 of these patients eventually required surgery, >1 year following initiation of anti-TNF therapy.

Although reported, resolution of an intraabdominal abscess with present medical therapy alone appears to remain an exception rather than the rule. Clearly, larger studies with prospective data are needed, but it appears that some Crohn-related intraabdominal abscesses may respond to conservative management without need for intestinal resection. An important concept to remember in children is that definitive management of their underlying pathology may avoid long-term disruptions to their psychosocial environment in the form of need for rehospitalization or chronic percutaneous drainage, antibiotic or parenteral nutrition management. It is unclear, at this point, whether the benefit of preservation of a short segment of intestine involved in penetrating CD outweighs chronic disruption of normal psychosocial development in children. Definitive management of the perforation and abscess with resection of the intestine may, in fact, get a child back to school and age-appropriate activities more quickly.

Nutrition

Objective measures of nutritional repletion should be obtained, including historical weights (a clue to duration of

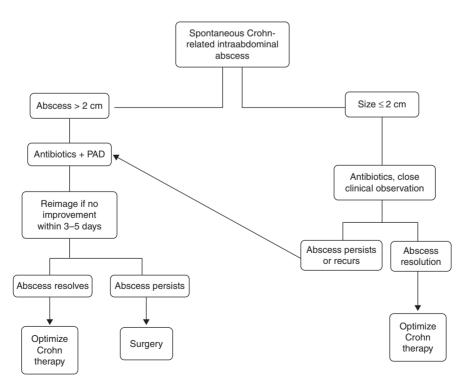


FIGURE 1. Proposed algorithm for initial management of spontaneous intraabdominal abscess in pediatric Crohn disease. PAD = percutaneous abscess drainage.

disease and degree of catabolism), daily weights, serum albumin, and prealbumin. Consideration should be given to bowel rest until the abscess is drained. Once the abscess has been drained and shown to not reaccumulate, a trial of enteral feeding is warranted and often successful.

The presence of an actively flowing fistula is another indication for bowel rest. Feeding a patient with an ongoing fistula will increase the flow across the fistula. Feeding should be restarted once the clinical picture is consistent with closure of the fistula. A liquid diet is an option to be considered along with parenteral nutrition, and can be administered safely at a lower cost as an outpatient. In the event of intolerance of enteral feeding, parenteral nutrition should be used and definitive operation should be undertaken in a timely fashion upon normalization of nutritional parameters.

RECOMMENDATIONS

Intraabdominal abscess in pediatric CD should, at the least, be managed with antimicrobials. Maximal doses of antimicrobials should be used for abscesses that cannot be drained. An abscess >2 cm is amenable to percutaneous drainage. In the setting of clinical improvement and a decrease in percutaneous drain output to <10 mL/day, the drain is discontinued and the patient is discharged to complete the parenteral antimicrobial with instructions to return for re-imaging in 1 to 2 weeks. Absence of clinical improvement 3 to 5 days following percutaneous drain placement, however, should prompt re-imaging of the abscess. Persistence of the abscess will require surgical drainage with resection of the affected intestinal segment (Fig. 1). Corticosteroid should ideally be weaned to a goal of <20 mg of prednisone per day, before surgery. Medical therapy of CD should be optimized and may include continuation of biologic therapy to target the severe intestinal inflammation or fistula that initiated the intraabdominal abscess. Expert opinion indicates that immunosuppressive therapy can be started soon after successful percutaneous drainage of CD-related abscess to enable healing of the diseased bowel and prevent abscess recurrence (27).

Definitive surgical management of the abscess and diseased intestinal segment should be used when small bowel obstruction or intraabdominal sepsis persists in spite of medical therapy, thereby allowing the child afflicted with complicated CD to return to normal growth and psychosocial development.

Acknowledgments: The authors appreciate Joseph F. Fitzgerald, MD, and Francine Breckler, PharmD, for their comments, and Ms Vicki Haviland-Wilhite for detailed attention in the preparation of this manuscript.

REFERENCES

- Pigneur B, Siksek P, Viola S, et al. Natural history of Crohn's disease: comparison between childhood and adult-onset disease. *Inflamm Bowel Dis* 2010;16:953

 –61.
- Shamir R, Phillip M, Levine A. Growth retardation in pediatric Crohn's disease: pathogenesis and management. *Inflamm Bowel Dis* 2007;13: 620–8.
- Gupta N, Cohen SA, Bostrom AG, et al. Risk factors for initial surgery in pediatric patients with Crohn's disease. *Gastroenterology* 2006;130: 1069–77.
- Schaefer ME, Machan JT, Kawatu D, et al. Factors that determine risk for surgery in pediatric patients with Crohn's disease. Clin Gastroenterol Hepatol 2010;8:789–94.
- Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative course of Crohn's disease. Gastroenterology 1990;99:956–63.
- Olaison G, Smedh K, Sjodahl R. Natural course of Crohn's disease after ileocolic resection: endoscopically visualized ileal ulcers preceding symptoms. Gut 1992;33:331–5.

- Oberhuber G, Stangl PC, Vogelsang H, et al. Significant association of strictures and internal fistula formation in Crohn's disease. Virchows Arch 2000;437:293–7.
- Keita AV, Salim SY, Jian T, et al. Increased uptake of non-pathogenic E. coli via the follicle-associated epithelium in long standing ileal Crohn's disease. J Pathol 2008;215:135–44.
- 9. Chassaing B, Darfeuille-Michaud A. The commensal microbiota and enteropathogens in the pathogenesis of inflammatory bowel disease. *Gastroenterology* 2011;140:1720–8.
- Zholudev A, Zurakowski D, Young W, et al. Serologic testing with ANCA, ASCA, and anti-OmpC in children and young adults with Crohn's disease and ulcerative colitis: diagnostic value and correlation with disease phenotype. Am J Gastroenterol 2004;99: 2235-41.
- Hugot JP, Chamaillard M, Zouali H, et al. Association of NOD2 associated with susceptibility to Crohn's disease. *Nature* 2001;411: 603-6
- Travassos LH, Carneiro LA, Ramjeet M, et al. Nod1 and Nod2 direct autophagy by recruiting ATG16L1 to the plasma membrane at the site of bacterial entry. *Nat Immunol* 2010;11:55–62.
- Pruteanu M, Hyland NP, Clarke DJ, et al. Degradation of the extracellular matrix components by bacterial-derived metalloproteases: implications for inflammatory bowel disease. *Inflamm Bowel Dis* 2011; 17:1189–200.
- Bataille F, Klebl F, Rumele P, et al. Morphological characterization of Crohn's disease fistulae. Gut 2004;53:1314–21.
- Thia K, Sandborn J, Harmsen W, et al. Risk factors associated with progression to intestinal complications of Crohn's disease in a population-based cohort. *Gastroenterology* 2010;139:1147–55.
- Gupta N, Bostrom A, Kirschner B, et al. Incidence of stricturing and penetrating complications of Crohn's disease diagnosed in pediatric patients. *Inflamm Bowel Dis* 2010;16:638–44.
- 17. Ammoury R, Pfefferkorn M. Significance of esophageal Crohn disease in children. *J Pediatr Gastroenterol Nutr* 2011;52:291–4.
- Yoon Y, Yu C, Yang S, et al. Intra-abdominal fistulas in surgicallytreated Crohn's disease patients. World J Surg 2010;34:1924–9.
- Dubinsky M, Lin Y, Dutrifge D, et al. Serum immune responses predict rapid disease progression among children with Crohn's disease: immune responses predict disease progression. Am J Gastroenterol 2006;101:360-7.
- Garcia JC, Persky SE, Bonis PAL, et al. Abscesses in Crohn's disease outcome of medical versus surgical treatment. *J Clin Gastroenterol* 2001;32:409–12.
- 21. Jawhari A, Kamm M, Ong C, et al. Intra-abdominal and pelvic abscess in Crohn's disease: results of non-invasive and surgical management. *Br J Surg* 1998;85:365–71.
- Ayuk P, Nicholson DA, Williams N, et al. Management of intraabdominal abscesses in Crohn's disease. Ann R Coll Surg Engl 1996; 78:5-10.
- Lee SS, Kim AY, Yang S-K, et al. Crohn's disease of the small bowel: comparison of CT enterography, MR enterography, and small-bowel follow-through as diagnostic techniques. *Radiology* 2009;251:751–61.
- Siddiki HA, Fidler JL, Fletcher JG, et al. Prospective comparison of state-of-the-art MR enterography and CT enterography in small bowel Crohn's disease. Am J Roentgenol 2009;193:113–21.
- Parente F, Maconi G, Bollani S, et al. Bowel ultrasound in assessment of Crohn's disease and detection of related small bowel strictures: a prospective comparative study versus X-ray and intraoperative findings. *Gut* 2002;50:490–5.
- Spencer JA, Chapple K, Wilson D, et al. Outcome after surgery for perianal fistula: predictive value of MR imaging. Am J Roentgenol 1998;171:403–6.
- 27. Feagins L, Holubar S, Kane S, et al. Current strategies in the management of intra-abdominal abscesses in Crohn's disease. *Clin Gastroenterol Hepatol* 2011;9:842–50.
- 28. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis* 2010;50:133–64.
- Bradley JS, Jackson MA. The use of systemic and topical fluoroquinolones. Committee on Infectious Diseases. *Pediatrics* 2001;128:e1034–45.

- Yee CL, Duffy C, Gerbino PG, et al. Tendon or joint disorders in children after treatment with fluoroquinolones or azithromycin. Pediatr Infect Dis J 2002;21:525–9.
- Present D. Crohn's fistula: current concepts in management. Gastroenterology 2003:1629–36.
- 32. Alves A, Panis Y, Bouhnik Y, et al. Risk factors for intra-abdominal septic complications after a first ileocecal resection for Crohn's disease: a multivariate analysis in 161 consecutive patients. *Dis Colon Rectum* 2007;50:331–6.
- Markowitz J, Grancher K, Kohn N, et al. A multicenter trial of 6-mercaptopurine and prednisone therapy in children with newly diagnosed Crohn's disease. *Gastroenterology* 2000;119:895–902.
- Jaspers GJ, Verkade HJ, Escher JC, et al. Azathioprine maintains first remission in newly diagnosed pediatric Crohn's disease. *Inflamm Bowel Dis* 2006;12:831–6.
- 35. Mack DR, Young R, Kaufman SS, et al. Methotrexate in patients with Crohn's disease after 6-mercaptopurine. *J Pediatr* 1998;132:830–5.
- Turner D, Grossman AB, Rosh J, et al. Methotrexate following unsuccessful thiopurine therapy in pediatric Crohn's disease. Am J Gastroenterol 2007;102:2804–12.
- 37. Mahadevan U, Marion J. Fistula response to methotrexate in Crohn's disease: a case series. *Aliment Pharmacol Ther* 2003;18:1003–8.
- Present DH. Crohn's fistula: current concepts in management. Gastroenterology 2003;124:1629–35.
- Toruner M, Loftus EV Jr, Harmsen WS, et al. Risk factors for opportunistic infections in patients with inflammatory bowel disease. *Gastroenterology* 2008;134:929–36.
- Sands BE, Blank MA, Diamond RH, et al. Maintenance infliximab does not result in increased abscess development in fistulizing Crohn's disease: results from the ACCENT II study. Aliment Pharmacol Ther 2006;23:1127–36.
- Colombel JF, Loftus EV Jr, Tremaine WJ, et al. Early postoperative complications are not increased in patients with Crohn's disease treated perioperatively with infliximab or immunosuppressive therapy. Am J Gastroenterol 2004:99:878–83.
- 42. Fleshman JW. Pyogenic complications of Crohn's disease, evaluation, and management. *J Gastrointest Surg* 2008;12:2160-3.
- Present DH, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med 1999;340:1398– 405.
- Sands B, Anderson F, Bernstein C, et al. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med 2004;350:876–85.
- Teitelbaum J, Saeed S, Triantafyllopoulou M, et al. Infliximab in pediatric Crohn disease patients with enterovesicular fistulas. *J Pediatr Gastroenterol Nutr* 2007;44:279–82.

- Cinat ME, Wilson SE, Din AM. Determinants for successful percutaneous image guided drainage of intraabdominal abscess. *Arch Surg* 2002;137:845–9.
- Rypens F, Dubois J, Garel L, et al. Percutaneous drainage of abdominal abscesses in pediatric Crohn's disease. *Am J Roentgenol* 2007;188: 579–85.
- Hogan MJ, Hoffer FA. Biopsy and drainage techniques in children. Tech Vasc Interv Radiol 2010;13:206–13.
- Gervais DA, Hahn PF, O'Neill MJ, et al. Percutaneous abscess drainage in Crohn's disease: technical success and short and long term outcomes during 14 years. *Radiology* 2002;222:645–51.
- Schuster MR, Tu RK, Scanlan KA. Abdominal abscesses associated with enteric fistulas: percutaneous management. J Vasc Interv Radiol 1992;3:359–63.
- LaBerge JM, Brandt ML, Lebecque P, et al. Nonoperative treatment of enteric fistulas: results in 53 patients. J Vasc Interv Radiol 1992;3: 353-7
- Lambiase R, Cronan J, Dorfman G, et al. Percutaneous drainage of abscesses in patients with Crohn disease. Am J Roentgenol 1988;150: 1043-5.
- 53. Safrit H, Mauro M, Jacques P. Percutaneous abscess drainage in Crohn's disease. *Am J Roentgenol* 1987;148:859–62.
- 54. Garcia JC, Persky SE, Bonis PA, et al. Abscesses in Crohn's disease: outcome of medical versus surgical treatment. *J Clin Gastroenterol* 2001;32:409–12.
- Gutierrez A, Lee H, Sands BE. Outcome of surgical versus percutaneous drainage of abdominal and pelvic abscesses in Crohn's disease. Am J Gastroenterol 2006;101:2283–9.
- Da Luz Moreira A, Stocchi L, Tan E, et al. Outcomes of Crohn's disease presenting with abdominopelvic abscess. *Dis Colon Rectum* 2009;52: 906–12.
- 57. Henriksen M, Jahnsen J, Lygren I, et al. Clinical course in Crohn's disease: results of a five-year population-based follow-up study (the IBSEN study). *Scand J Gastroenterol* 2007;42:602–10.
- Laituri CA, Fraser JD, Garey CL, et al. Laparoscopic ileocecectomy in pediatric patients with Crohn's disease. *J Laparoendosc Adv Surg Tech* 2011;21:193–5.
- Agrawal A, Durrani S, Leiper K, et al. Effect of systemic corticosteroids on risk for intra-abdominal or pelvic abscess in non-operative Crohn's disease. Clin Gastroenterol Hepatol 2005;12:1215–20.
- Evans JP, Steinhart AH, Cohen Z, et al. Home total parenteral nutrition an alternative to early surgery for complicated inflammatory bowel disease. J Gastrointest Surg 2003;7:562–6.
- 61. Cullen G, Vaughn B, Ahmed A, et al. Abdominal phlegmons in Crohn's disease: outcomes following antitumor necrosis factor therapy. *Inflamm Bowel Dis* 2012;18:691–6.