Seminars in Pediatric Surgery 26 (2017) 367–372

Contents lists available at ScienceDirect

Seminars in Pediatric Surgery

journal homepage: www.elsevier.com/locate/sempedsurg

Management of acute severe ulcerative colitis in children

Vei Shaun Siow[a], Riha Bhatt[b], Kevin P. Mollen[a,c,*]

[a] Department of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
[b] Division of Gastroenterology, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, Pennsylvania
[c] Division of Pediatric Surgery, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, Pennsylvania

ARTICLE INFO

Keywords:
Pediatric inflammatory bowel disease
Toxic megacolon
Pediatric Ulcerative Colitis Activity Index (PUCAI)
Ulcerative colitis

ABSTRACT

The incidence of pediatric-onset ulcerative colitis (UC) is rising. Children often present with a more severe disease phenotype as compared to adults with over a third requiring hospitalization for the management of acute severe ulcerative colitis (ASUC). Further, in pediatric patients presenting with inflammatory bowel disease (IBD) limited to the colon, a definitive diagnosis of UC vs. Crohn's disease is often unclear. Here, we review the unique aspects of pediatric ASUC including the epidemiology, diagnosis, medical, and surgical management of this disease.

Introduction

Epidemiologic studies show that the incidence of inflammatory bowel disease (IBD) is increasing.[1] About 20% of all patients with ulcerative colitis (UC) are diagnosed in childhood (≤18 years) with an incidence between 1 and 4 cases per 100,000/year.[1–4] Pediatric-onset UC is often more severe and extensive at diagnosis, presenting as pancolitis in 60–80% of patients as compared to 20–30% of patients diagnosed as adults.[5–7] Approximately 25–35% of children with UC will require hospitalization for acute severe ulcerative colitis (ASUC) during a period of 3 years after initial diagnosis, roughly double the rate seen in adult-onset disease.[5,6] Childhood-onset UC is also less responsive to steroids as compared to adult-onset UC, with a higher steroid-refractory rate (34% vs. 29%)[8,9]. Furthermore, 10-year colectomy rates in pediatric patients range from 30% to 40% as compared to 15–25% in adults.[10–12]

Defining severity

The best validated and most widely used index for the diagnosis of adult ASUC is the European Crohn's and Colitis Organization adaptation of the 1955 Truelove and Witts' classification.[13,14] It defines ASUC as an exacerbation of disease with at least 6 bloody stools daily and one of the following: tachycardia (> 90 b.p.m.), temperature > 37.8°C, anemia (hemoglobin < 10.5 g/dL) or an elevated erythrocyte sedimentation rate (> 30 mm/h).

However, the use of these criteria have never been evaluated in the children with severe colitis who rarely present with fever.[15] Further, pulse rate and hemoglobin are subject to age-related variations.[9] Instead, the Pediatric Ulcerative Colitis Activity Index (PUCAI)[16] as developed by Turner et al. is more widely used for children. This scoring index defines severe disease as a PUCAI score of at least 65 points (Table). The PUCAI has been validated in an independent cohort study and proven to predict clinically relevant outcomes in pediatric patients with ASUC.[6,15] Unlike the Truelove and Witts' classification, which is only useful in diagnosing the acute presentation of disease, the PUCAI yields a range of scores that can also be used to monitor disease severity and treatment progress.

Initial diagnostic considerations

Initially, the diagnosis of IBD should be established according to accepted pediatric criteria.[17,18] Patients without a prior diagnosis of UC or Crohn's disease that present with acute colitis should undergo an extensive workup including a thorough history and physical exam, stool studies, cross-sectional imaging and endoscopic evaluation with biopsies.

Endoscopic evaluation

In the setting of acute colitis, a flexible sigmoidoscopy should be performed instead of a full colonoscopy during the initial evaluation due to a high procedure-associated risk.[19,20] However,

* Corresponding author at: Division of Pediatric Surgery, Children's Hospital of Pittsburgh of UPMC, 4401 Penn Ave, Faculty Pavilion Suite #7000, Pittsburgh, Pennsylvania 15224.
E-mail address: kevin.mollen@chp.edu (K.P. Mollen).

http://dx.doi.org/10.1053/j.sempedsurg.2017.10.006
1055-8586/

Table
Pediatric Ulcerative Colitis Activity Index (PUCAI). Please refer to original study for the user's guide.[16] Generally, a PUCAI score <10 indicates remission, 10–34 mild disease, 35–64 moderate disease and ≥65 severe disease.

Item	Points
(1) Abdominal pain	
No pain	0
Pain can be ignored	5
Pain cannot be ignored	10
(2) Rectal bleeding	
None	0
Small amount only, in less than 50% of stools	10
Small amount with most stools	20
Large amount ($>50\%$ of the stool content)	30
(3) Stool consistency of most stools	
Formed	0
Partially formed	5
Completely unformed	10
(4) Number of stools per 24 hours	
0–2	0
3–5	5
6–8	10
>8	15
(5) Nocturnal stools (any episode causing wakening)	
No	0
Yes	10
(6) Activity level	
No limitation of activity	0
Occasional limitation of activity	5
Severe restricted activity	10
Sum of PUCAI (0–85)	

a follow-up ileocolonoscopy and upper endoscopy with biopsies should be performed to definitively diagnose pediatric IBD.[21,22]

Cross-sectional imaging

Imaging modalities are of limited utility in the setting of acute colitis when a firm diagnosis of UC has been previously established (unless complications i.e. toxic megacolon are suspected).[9] However, if the diagnosis of Crohn's disease has yet to be ruled out, imaging of the entire gastrointestinal tract via computer tomography or magnetic resonance enterography should be performed to help distinguish between UC and Crohn's.[9,21] Interestingly, a study by Mege et al.[23] showed that in adults with acute severe colitis complicating IBD, admission abdominal CT scan had no impact on the decision to continue medical therapy or proceed to surgery. A similar study has not been performed in children.

Evaluation for infectious causes

Clostridium difficile (C. difficile)

Patients with IBD are more susceptible to *C. difficile* infection compared to the general population.[24–27] Nylund et al.[28] found that children with IBD were 11 times more likely to have a diagnosis of *C. difficile* compared to patients without IBD. *C. difficile* infection has been shown to worsen disease severity, prolong hospital stay, increase the need for parenteral nutrition and blood transfusions, as well as increase colectomy rates and colitis relapses.[29–31] Adults that are admitted with both *C. difficile* and IBD were found to have longer hospitalizations and a mortality rate 4 times greater than adults with either condition alone.[26]

Nucleic acid amplification tests (NAATs) such as PCR for *C. difficile* toxin genes have surpassed toxin A and toxin B enzyme immunoassays (EIA) as the preferred method for diagnosing *C. difficile*. They have been shown to be both sensitive (85–95%) and specific (89–95%) in detecting toxigenic *C. difficile* in patients with documented diarrhea.[32–34]

In the setting of ASUC where the colitis is severe, treatment with oral vancomycin (40 mg/kg per day, orally, divided into four doses) is preferred due to several adult studies showing greater response rates to vancomycin as compared to metronidazole in the setting of severe colitis.[35–38] However, this may not be suitable in the setting of a coexisting ileus or toxic megacolon and in that instance intravenous metronidazole (30 mg/kg in four divided doses) with vancomycin delivered via enema has been recommended.[39,40] Treatment should be administered for at least 10-days.[32,39]

Cytomegalovirus (CMV)

There is significant heterogeneity in the experimental design of studies on ulcerative colitis, steroid-resistance and CMV. Several investigators have demonstrated that CMV infection is detected more often in patients with steroid-refractory ulcerative colitis and is associated with increased rates of colectomy.[41–43] A CMV infection rate as high as 67% is seen in steroid-refractory ulcerative colitis compared to 33% in patients with steroid-responsive disease.[44] Additionally, Roblin et al.[45] showed that a CMV DNA load above 250 copies/mg in colonic tissue was predictive of resistance to three successive treatment regimens for UC. However, despite CMV being detected more often in steroid-resistant colitis, it is unclear whether CMV positivity is a causative factor contributing to disease severity or simply a marker of more severe disease.[46,47] Blood testing for CMV is not reliable and the diagnosis is usually made via polymerase chain reaction or immunohistochemistry of intestinal tissue biopsies.[21] A consensus study recommends that children with steroid-resistant disease undergo endoscopy and biopsy to exclude CMV infection. The decision to initiate antiviral therapy if CMV is detected should be made in conjunction with infectious disease specialists.[22] Additionally, a meta-analysis of 8 studies showed that the risk of colectomy was significantly lower in patients with corticosteroid-refractory UC treated with antivirals as compared to their counterparts who did not received antiviral therapy (OR = 0.20; 95% CI: 0.08–0.49).[48]

Toxic megacolon

Toxic megacolon (TMC) is characterized by total or segmental non-obstructive colonic dilation plus systemic toxicity. Common etiologies aside from IBD include infectious colitis (*C. difficile*, Salmonella, Shigella, Campylobacter, and Entamoeba) and ischemic colitis.[49] Although the exact incidence of toxic megacolon in pediatric IBD is not known, data from three decades ago report the incidence around 1–5%.[50] Mortality has been reported as 19–50% in adult patients with TMC, however data is lacking in children. One small retrospective study reported no mortality in pediatric patients with TMC, however, the authors noted that 7/10 patients required colectomy.[51] The most common diagnostic criteria for TMC in adults was introduced by Jalan et al.,[52] which includes the presence of fever, dehydration, hypotension, an altered level of consciousness, hematologic and biochemical abnormalities as well as radiographic evidence of a dilated colon.

Although colonic dilation on radiography alone is insufficient to diagnose TMC, one retrospective study suggested that a transverse colon diameter of ≥56 mm (>40 mm in children less than 11 years old) was strongly suggestive of TMC.[51] It is important to note