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MINIREVIEWS

Appendicitis in children less than five years old: A challenge for the general practitioner

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Abstract

Acute appendicitis is one of the most common indications for abdominal surgery in pediatrics with peak incidence in the second decade of life. Acute appendicitis in the first years of life is an uncommon event. The clinical presentation is often varied and the diagnosis may be overshadowed by other medical conditions. Gastroenteritis is the most common misdiagnosis, with a history of diarrhea present in 33% to 41% of patients. Pain is the most common presenting symptom in children less than 5 years old, followed by vomiting, fever, anorexia and diarrhea. The most common physical sign is focal tenderness (61% of the patients) followed by guarding (55%), diffuse tenderness (39%), rebound (32%), and mass (6%). Neonatal appendicitis is a very rare disease with high mortality; presenting symptoms are nonspecific with abdominal distension representing the main clinical presentation. The younger the patient, the earlier perforation occurs: 70% of patients less than 3 years develop a perforation within 48 h of onset of symptoms. A timely diagnosis reduces the risk of complications. We highlight the epidemiology, pathophysiology, clinical signs and laboratory clues of appendicitis in young children and suggest an algorithm for early diagnosis.

Key words: Appendicitis; Children; Early diagnosis; Newborn; Appendicitis complications

Core tip: Acute appendicitis in the first years of life is an uncommon event but with a high incidence of early perforation the younger the patient. We highlight the epidemiology, pathophysiology, clinical signs, and laboratory clues of appendicitis in young children. The challenge for the practitioner is to perform a timely diagnosis of acute appendicitis in first years of life before complications occur.

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INTRODUCTION

Acute appendicitis has the highest incidence during the second decade of life[1], and represents a frequent indication for abdominal surgery in pediatrics[2]. It is more common in males than in females (ratio 1.4:1)[2]. While up to 33% of affected children may present not distinct abdominal pain with consecutive pain localization in the right lower quadrant, nausea and vomiting, young children could show atypical or delayed symptoms presentation[3-5]. When the diagnosis is performed, perforation could be already present in 30%-75% of children, with young children being at higher risk[6]. Perforated appendicitis increases the morbidity with intra-abdominal abscess being an important complication[7]. In young children, appendicitis is an uncommon event with a varied presentation and complications that can develop rapidly[8,9]. A timely diagnosis although necessary can be difficult, representing a challenge for the physician.

EPIDEMIOLOGY

In a study over a 12-year period, 1836 pediatric appendectomies were reviewed. Three hundred and twenty (17%) patients were under 5 years of age, 103 (5%) were less than 3 years, with only 7 patients (0.38%) younger than 1 year[7]. Perforation was more frequent in young children (the perforation rate was 86% in children less than 1 year of age, 74% between 1 and 1.9 years, 60% between 2 and 2.9 years, 64% between 3 and 3.9 years, and 49% between 4 and 4.9 years), while the rate in older patients was 5%[7]. Seven patients under 1 year of age were included so that the statistical relevance of the differences in the perforation rate of the different age groups would be limited[7]. Moreover, male patients present more risk of perforation than female patients also if the symptoms have a similar duration[10].

A single pediatric center study over a 28-year period reported a similar rate of appendicitis in patients under 1 year of age (0.34%) and 2.3% in patients under 3 years[11].

Andersen *et al*[9], in a cohort of Danish children, reported an annual incidence of 2.22/10000 among boys less than 4 years and 1.82/10000 among girls less than 4 years with a perforation rate of 0.64 and 0.62, respectively. The annual incidence among 10-19 years old boys and girls was 22/10000 and 18/10000 respectively, with a perforation rate of one third the rate of young children[9].

The risk of perforation increases with diagnostic delay. In children 5-12 years old, if the diagnosis is made in less than 24 h from the outbreak of symptoms, the reported perforation rate is 7%, if between 24-48 h 38%, and if more than 48 h 98%[8]. In patients < 3 years, the perforation rate is high (70%), even if the time to diagnosis is less than 48 h[4].

A timely diagnosis is more difficult in toddlers because of presentation to emergency department delayed since the outbreak of symptoms of 1.6 d for patients less than 5 years[7], and 3 d in patients less than 3 years[11].

ANATOMIC AND PATHOPHYSIOLOGIC ELEMENTS

Differences in the appendicitis clinical presentation could be explained by age-related variations in appendiceal anatomy and development. In the neonatal period, the appendix is 4.5 cm long reaching the length of 9.5 cm in adults[12]. Acute appendicitis is rare in neonates because they present a funnel-shaped appendix[13,14], have liquid diet, supine posture, low frequency of gastrointestinal and upper respiratory tract infections[15]. Furthermore, there is evidence that breast-feeding could reduce the risk of appendicitis[16].

Between 1-2 years of age, the appendix becomes similar to that of an adult and the susceptibility to inflammation increases. Lymphoid follicle hyperplasia and follicular size gradually increase with the major expression during adolescence, corresponding to the period of the highest rate of appendicitis[1]. Young children have an undeveloped omentum that is not able to limit the purulent material effusion from a perforation[17]. For this reason, diffuse peritonitis following a perforation is more likely in young children[18]. The mobility of fetal and infant appendices is accentuated and the probability of appendix to be fixed by mesenteric connections to the cecum, ascending colon, or abdominal wall is lower[19]. This could explain why the incidence of localized abscesses in young children is infrequent.

HISTORY AND CLINICAL EXAMINATION

In preverbal toddlers and preschoolers, the anamnesis about the pain is difficult to examine[20]. In preverbal children, clinicians need to relay on the physical examination and on detecting contingent signs of pathology evaluating how children eat, move around, play, sleep, and defecate[20]. Many children, in particular young children, can be easily influenced. Even though their conflicting significances, questions such as "Does it hurt here?" and "This feels fine, right?" may lead to the same positive answer[20]. Abdominal pain usually begins as vague mid-abdominal or periumbilical pain migrating to the right lower quadrant during an interval of hours to days, and many school-aged children can accurately report and localize their pain movement. However, young children may not be able to describe accurately their symptoms, and the clinicians could locate the pain exclusively asking the children to show the painful abdominal point[20].

Pain is the most frequent presenting symptom in children less than 5 years old. In a cohort of 120 patients less than 5 years, 94% presented with pain,

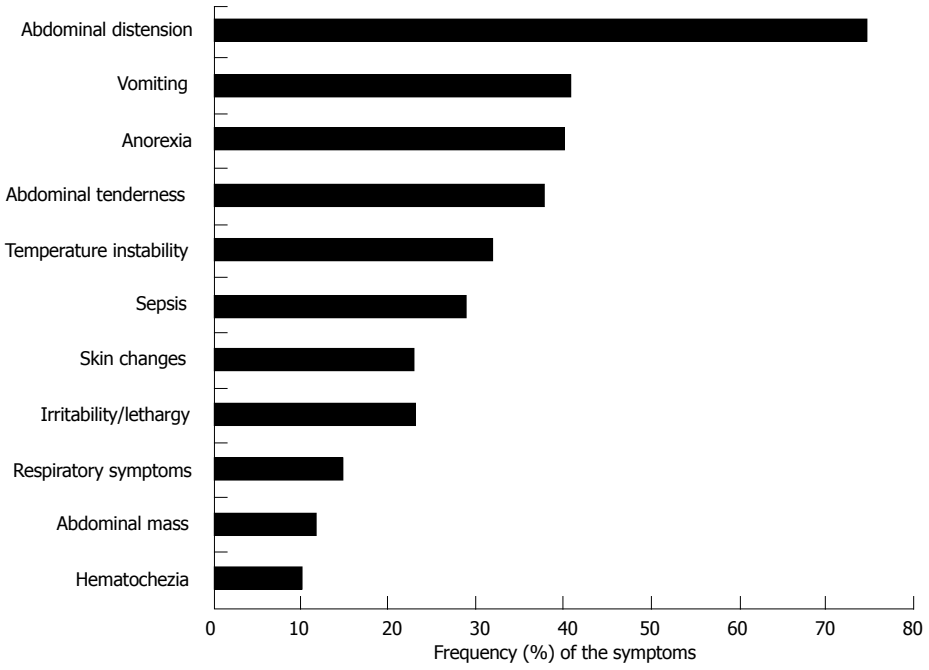

Figure 1 Neonatal appendicitis: frequency of symptoms at presentation (modified from ref.[24]).

83% with vomiting, 80% with fever, 74% with refusal to eat, and 32% with diarrhea[21]. When the data was restricted to children less than 3 years, vomiting, fever and diarrhea were more frequent[11]. If the appendicitis is non-perforated the most common physical sign is localized tenderness (61%) followed by guarding (55%), diffuse tenderness (39%), rebound (32%), and mass (6%)[21]. If the appendicitis is perforated, the most frequent sign is the guarding (79%) followed by diffuse tenderness (62%), rebound (39%), localized tenderness (33%), mass (9%), and rigidity (7%)[21].

In the neonatal period, the signs and symptoms are nonspecific with irritability or lethargy (22%), abdominal distension (60%-90%), and vomiting (59%)[15,22]. Other symptoms include a palpable mass (20%-40%)[15], abdominal wall cellulitis (12%-16%), hypotension, hypothermia, and respiratory distress[22-25]. The most common clinical presenting signs and symptoms are reported in Figure 1[24].

LABORATORY EVALUATION

White blood cell count (WBC) and C-reactive protein (CRP) are commonly used when an acute appendicitis is suspected. Conventional WBC count presents both low sensitivity and specificity, in fact it could increase in 70% of the patients presenting abdominal pain for causes different from appendicitis[26]. A high WBC count or a left shift (represented by higher than 80% polymorphonuclear cells along with bands) has good sensitivity (79%), while the coexistence of both positive WBC count and left shift present the greatest specificity (94%)[27]. The sensitivity and specificity of WBC counts range from 70%-80% and 60%-68%, respectively[28]. Up to 20% of children with pathologically proven appendicitis present a WBC in the normal range[29], while the leukocyte response declines in children younger than 5 years old with appendicitis[30].

CRP is more specific than WBC count, even if in the early stage of acute appendicitis the sensitivity is lower[26,31]. The reported sensitivity and specificity are of 57% and 87% respectively[28]. CRP presents higher sensitivity in discovering appendiceal perforation and abscess formation[26,31]. Recently, it has been demonstrated that the use of both WBC count and CRP may lead to enhanced negative predictive value[6,32]. Yokoyama *et al*[33] showed as indicative of surgical intervention a CRP cut-off value of 4.95 mg/dL (sensitivity 84% and specificity 76%). Procalcitonin is not helpful in the acute appendicitis diagnosis presenting a diagnostic accuracy lower than CRP and WBC[31]. When a complicated appendicitis is present the pooled procalcitonin sensitivity and specificity are 62% and 94%, respectively[31].

RADIOLOGICAL EVALUATION

Computed tomography (CT) has been considered the radiological gold standard to confirm clinical suspicion of appendicitis with high sensitivity and specificity[34,35]. Repeated CT carries an established risk of increased incidence of cancer in children and its use should therefore be limited to clear indications with a well-defined risk to benefit ratio[36]. Less operator dependence, easier visualization of retrocecal appendix, less interference of bowel gas, obesity, or patient pain and tenderness with image quality are included among CT advantages. For these reasons, CT remains the most common primary imaging method before

Table 1 Conditions mimicking childhood and neonatal appendicitis (modified from ref.[8])

Condition	Diagnostic clues
Gastroenteritis	Continuous abdominal pain
	Poor clinical condition with mild or no dehydration, continuous, focal abdominal pain, and lack of movement in infants and young children distinguishes appendicitis from gastroenteritis
	Acute appendicitis is more common during viral epidemics and bacterial gastroenteritis[44]
Upper respiratory tract infection[1]	The presence of concomitant signs of upper respiratory infection are common in toddlers and does not rule out the possibility of appendicitis
Pneumonia	Basal pneumonia may mimic appendicitis pain[45]
	Simultaneous pneumococcal pneumonia and appendicitis is well reported in the literature[46]
Sepsis	An acute appendicitis should be suspected and ruled out in any case of sepsis associated with abdominal pain and or abdominal tenderness[47]
Urinary tract infection	Peritoneal inflammation may cause voiding disturbances and bladder symptoms[48]
Blunt abdominal trauma	Acute appendicitis may be associated with blunt abdominal trauma[49-51]
Intussception	Abdominal US is highly operator dependent
	In presence of fever, localized pain and guarding in infants and young children, appendicitis should be ruled out[52]
NEC	With a history of NEC outside prematurity and signs of abdominal cellulitis, neonatal appendicitis should be ruled out[53]

[1]Includes diagnoses of otitis media, sinusitis, pharyngitis and upper respiratory tract infection. US: Ultrasonography; NEC: Necrotizing enterocolitis.

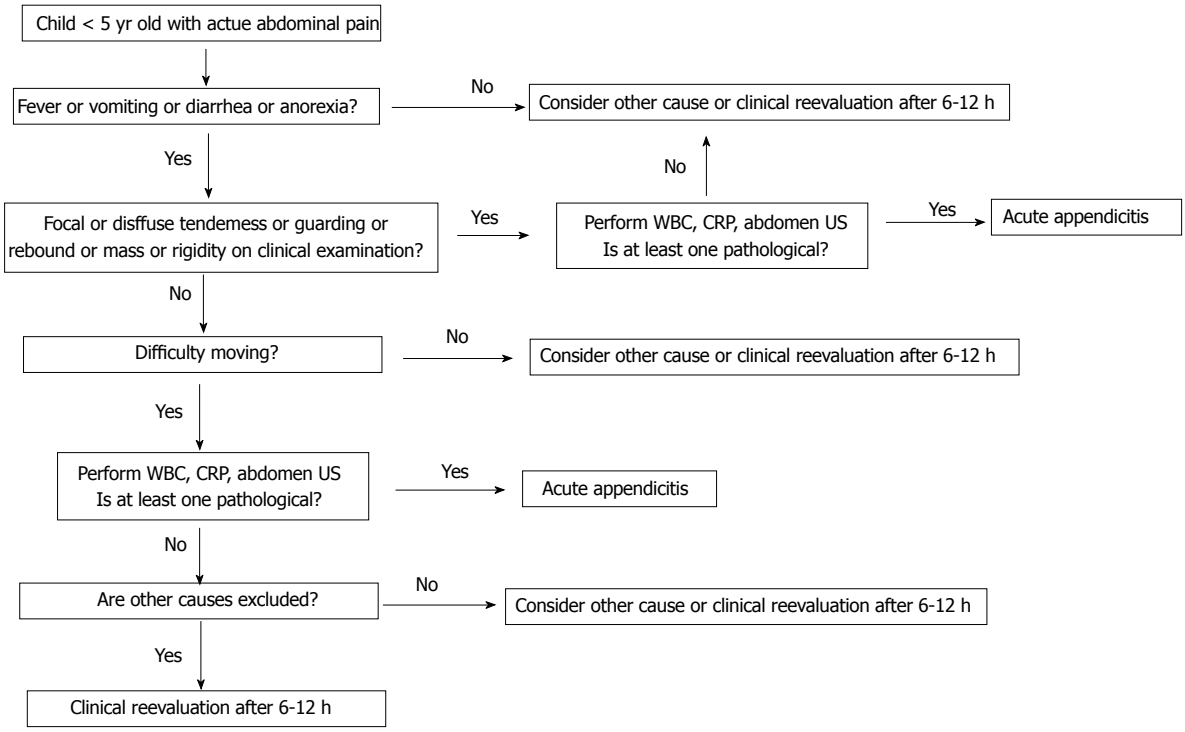

Figure 2 Diagnostic algorithm to assess acute appendicitis in young children. WBC: White blood cell count; CRP: C-reactive protein; US: Ultrasonography.

appendectomy in children[25,37]. To increase sensitivity of diagnosis but decrease radiation exposure, CT used in conjunction with equivocal ultrasonography (US) has been recommended as the most judicious diagnostic imaging pathway[38].

Using US for the acute appendicitis diagnosis is convenient and safe, but is highly operator dependent with a wide reported sensitivity range (44%-100%)[34,36,39]. There is evidence that the diagnostic accuracy can be improved[40] using specific US criteria and using repeated scans[41].

Magnetic resonance imaging (MRI) may also be used in young children[42]. Diagnostic imaging with US selectively followed by MRI is possible and comparable to CT, without differences in time to antibiotic administration and appendectomy, negative appendectomy and perforation rate, or length of stay[43]. Aspelund *et al*[43] showed an high US-MRI pathway specificity (99%) with a sensibility of 100%.

DIFFERENTIAL DIAGNOSIS

Appendicitis in young children is a diagnostic challenge. In a case series of 27 children less than 3 years, 67% had been visited by one or more clinicians without the diagnosis of acute appendicitis had been performed[11].

At this age the diagnosis of appendicitis may be hided by other medical conditions (Table 1). Gastroenteritis is the most common misdiagnosis (possible red flags to suspect appendicitis mimicking a gastroenteritis are shown in Table 1), in fact diarrhea may be present in 33%-41% of patients[4,26]. Importantly, as prior infective diseases may play a role in the physiopathology of acute appendicitis[54], diagnosis of a gastrointestinal, respiratory or urinary infection, should not rule out concomitant acute appendicitis[55].

CONCLUSION

A timely diagnosis of acute appendicitis in young children is a challenge due to the rarity of the disease, the varied presentation, and the rapid development of complications. A high level of suspicion and the knowledge of specific red flags can increase diagnostic skill. We present a diagnostic algorithm (Figure 2) that could be used to assess acute appendicitis in young children, optimizing diagnostic sources and limiting the CT use.

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