Atypical Clinical Features of Pediatric Appendicitis

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Abstract

Background: The diagnosis of appendicitis remains challenging in children. Delays in diagnosis, or misdiagnosis, have important medical and legal implications. The typical, or classic, presentation of pediatric appendicitis has been modeled after adult disease; however, many children present atypically with subtle findings or unusual signs.

Objectives: To determine the frequency of atypical clinical features among pediatric patients with appendicitis and to investigate which atypical features are the strongest negative predictors for appendicitis among patients being evaluated for appendicitis.

Methods: Children and adolescents with suspected appendicitis were enrolled over 20 consecutive months. Pediatric emergency physicians completed standardized data collection forms on eligible patients. Final diagnosis was determined by pathology or follow-up telephone call. Typical and atypical findings were defined strictly a priori.

Results: Seven hundred fifty-five patients were enrolled. The median age was 11.9 years (interquartile range [IQR]: 8.5, 14.9 yr); 36% of patients were diagnosed with appendicitis. Among patients with appendicitis, the most common atypical features included absence of pyrexia (83%), absence of Rovsing's sign (68%), normal or increased bowel sounds (64%), absence of rebound pain (52%), lack of migration of pain (50%), lack of guarding (47%), abrupt onset of pain (45%), lack of anorexia (40%), absence of maximal pain in the right lower quadrant (32%), and absence of percussive tenderness (31%). Forty-four percent of patients with proven appendicitis had six or more atypical characteristics. The median number of atypical features for patients with proven appendicitis was five (IQR: 4.0, 7.0). The greatest negative predictors, on the basis of likelihood ratios, were as follows: white blood cell count (WBC) of <10,000 per cubic millimeter (likelihood ratios [LR], 0.18), absolute neutrophil count (ANC) of <7,500 per cubic millimeter (LR, 0.35), lack of percussive tenderness (LR, 0.50), lack of guarding (LR, 0.63), and no nausea or emesis (LR, 0.65).

Conclusions: Appendicitis in pediatric patients is difficult to diagnose because children present with a wide variety of atypical clinical features. Forty-four percent of patients with appendicitis presented with six or more atypical features. Two atypical features are the strongest negative predictors of appendicitis in children: WBC of <10,000 per cubic millimeter and an ANC of <7,500 per cubic millimeter.

ACADEMIC EMERGENCY MEDICINE 2007; 14:124–129 © 2007 by the Society for Academic Emergency Medicine

Keywords: appendicitis, abdominal pain, diagnosis, surgery, white blood cell

In classic descriptions of appendicitis, the first symptom is periumbilical pain, followed by nausea, right lower quadrant pain, and later, vomiting with fever.[1–5] This sequence of events is noted in only 50% of adults, and it is even less common in children.[6,7] The classic symptoms are often not present in children, making the diagnosis difficult and sometimes leading to missed diagnoses with significant morbidity and mortality, as well as professional liability.[7,8] In addition to making the correct diagnosis, it is imperative to make the diagnosis in a timely manner. Delay in diagnosis ultimately leads to an increase in the perforation rate, with associated complications.[6,9] Recently, the medical literature has emphasized the use of advanced radiologic imaging (computed tomography [CT] or ultrasound [US]) to aid in the diagnosis of appendicitis, especially in cases in which examination findings or history are atypical.[10–16] These interventions can lead to delays in care as well as unnecessary radiation exposure. Often, patients with atypical findings are not candidates for

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Received May 27, 2006; revisions received July 25, 2006, and August 11, 2006; accepted August 13, 2006.

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ISSN 1069-6563
PII ISSN 1069-6563583

doi: 10.1197/j.aem.2006.08.009

immediate triage to the operating room. It would be helpful to know the frequency of atypical findings and which, if any, are strong negative predictors.

Most literature surrounding childhood appendicitis extrapolates the presenting signs and symptoms from adult patients. Presenting symptoms and signs will vary by age and the ability to achieve a reliable, but often limited, examination. In one small case series, approximately one third of children with appendicitis have atypical findings.[17]

The objectives of this investigation were to determine the frequency of atypical clinical features among pediatric patients with appendicitis and to investigate which atypical features are the strongest negative predictors for appendicitis.

METHODS

Study Design

This was a cross-sectional observational study. This study was approved by our institution's committee on clinical investigation. Consent was obtained from caretakers (assent for children older than age 7 yr) at the time of enrollment. Information regarding the names of the physicians completing the forms was documented at the request of our institution's committee on clinical investigation. The staff physicians who were responsible for completing the questionnaires were consented before the study. This study was compliant with the Health Insurance Portability and Accountability Act of 1996.

Study Setting and Participants

As part of a larger study to risk stratify patients with possible appendicitis,[18] patients with abdominal pain were enrolled for 20 consecutive months, beginning in April 2003, at a tertiary pediatric medical center with an emergency department (ED) volume of 52,000 visits per year. Children between 3 and 21 years of age with suspected appendicitis, as determined by an attending pediatric emergency physician (EP), were enrolled; these patients required surgical consultation for suspected appendicitis. Fifty-one fellowship-trained (attending pediatric EPs) individuals participated in this study. A surgical consult is requested per the hospital clinical-practice guidelines on patients who present with possible appendicitis before obtaining advanced radiologic imaging. Patients were excluded if they were pregnant, had undergone prior abdominal surgery, had chronic medical conditions (e.g., cystic fibrosis, inflammatory bowel disease, sickle cell anemia), or had had radiologic studies (CT or US) of the abdomen within the previous two weeks.

Study Protocol

Data Collection. Data collection forms were completed by the attending pediatric EP who was responsible for the patient's care. Forms were completed before diagnostic imaging and independent of the surgeon's evaluation. All participating physicians were introduced to the questionnaire and study definitions before commencement of the study. The standardized data-collection forms consisted of 24 demographic, historical, and physical examination variables. In addition, the patient's medical record was abstracted for laboratory, pathology, and operative reports. Enrollment was audited by review of the electronic medical ED log.

Definitions. On the basis of a review of the literature, including standard texts,[1,3,4] review articles,[2,5,19] and appendicitis scoring systems,[20,21] we defined a priori typical and atypical features of appendicitis for the purposes of this study (Table 1). Symptoms and signs were considered typical if *all* references listed the symptom or sign as "common, typical, classic," or "usual." Atypical findings were findings opposite of typical findings and not listed as "common, typical, classic," or "usual" in *any* of the above reference sources.

Outcomes. Final diagnosis (appendicitis or no appendicitis), was determined either by pathologic report, if the patient had surgery, or by a follow-up phone call at two weeks, if the patient did not have an operative diagnosis. The capture rate was assessed by reviewing the electronic medical records of our ED to make sure that no patient was missed. Determination of appendiceal perforation was based on the operative report. No patients with appendicitis were managed nonoperatively.

Data Analysis

Statistical analyses were performed by using SPSS (version 14.0; SPSS, Chicago, IL). Chi-square analysis was used to compare categorical variables, and independent samples t-test was used to compare means of continuous variables. The Mann-Whitney U test was used to compare nonparametric, continuous variables. A p-value of ≤ 0.05 was considered significant. Distribution and central tendency were reported as means and SDs for normally distributed data and as medians with interquartile ranges for nonparametric data. Confidence intervals

Table 1
Definitions of Typical and Atypical Features of Appendicitis

Feature	Typical	Atypical
Age (yr)	≥5	<5
History		
Anorexia	present	absent
Nausea or emesis	present	absent
Migration of pain	present	absent
Onset of pain	gradual	abrupt
Pain duration	<48 hours	>48 hours
Diarrhea	absent	present
Physical examination		
Pyrexia	present	absent
Guarding	present	absent
Percussive tenderness (or pain with walking or hopping)	present	absent
Bowel sounds	decreased	normal or increased
RLQ tenderness	present	absent
Rovsing's sign	present	absent
Rebound pain	present	absent
Laboratory		
WBC (per mm^3)	≥10,000	<10,000
Neutrophils (ANC), % (per mm^3)	≥75% (7,500)	<75% (7,500)

WBC = white blood cell count; ANC = absolute neutrophil count; RLQ = right lower quadrant.

(CIs) were calculated by using STATA (version 6; STATA, College Station, TX).

To add clinical relevance, we chose to calculate likelihood ratios, as opposed to simple sensitivity and specificity. Positive and negative likelihood ratios were calculated as sensitivity/(1 − specificity) and (1 − sensitivity)/specificity, respectively. Conceptually, a positive likelihood ratio is the likelihood of a positive test among those with disease (sensitivity), compared with the likelihood of a positive test among those without disease (false positive rate). Similarly, a negative likelihood ratio is the likelihood of a negative test among those with disease (false negative rate), as compared with the likelihood of a negative test among those without disease (specificity). A test with an LR of >1 increases the probability of disease when the test is positive (or condition is present); an LR of <1 decreases the probability of disease when the test is positive (or condition is present).[22]

Multivariable analysis was conducted by using stepwise logistic regression to identify independent predictors of appendicitis; variables left in the final equation are reported with adjusted odds ratios (ORs). All variables were initially entered. The entry criterion was 0.05, and the criterion for removal was 0.1.

RESULTS

Study Population

Over the study period, 755 patients were enrolled. The median age was 11.9 years (IQR: 8.5, 14.9 yr). Three hundred ninety-one (52%) patients were male; 270 patients (36%) were diagnosed with appendicitis. Forty-seven of the 270 patients (17%) with appendicitis had a perforated appendix. Follow-up was completed on 747 patients (99%). Over the study period, we had a capture rate of 92% of all patients with suspected appendicitis who had a surgical consult. The only patients not enrolled were those who met exclusion criteria, or those who did not consent to a follow-up phone call at the initial ED visit. The duration of abdominal pain was as follows: 28% of patients had pain for less than 12 hours, 32% had pain for 12–24 hours, 17% had pain for 24–48 hours, and 23% had pain for more than 48 hours.

Clinical Presentation

Univariate Analysis of Typical and Atypical Characteristics. Typical clinical characteristics of patients with suspected appendicitis, divided by their final diagnosis, are reported in Table 2. Although some differences were found, it is important to note that many patients without appendicitis had similar historical and clinical features. For example, whereas 67.8% of patients with appendicitis had maximal tenderness in the right lower quadrant (RLQ), 53.4% of patients *without* appendicitis also had tenderness in the RLQ. Pyrexia (T of ≥38°C) was also similar for both groups.

The frequencies of atypical characteristics among patients diagnosed with appendicitis are reported in Table 3. Among patients with appendicitis, the most common atypical features included absence of pyrexia (83%), absence of Rovsing's sign (68%), normal or increased bowel sounds (64%), absence of rebound pain (52%), and lack of migration (50%). A surprising finding was 32% of patients had absence of pain in the right lower quadrant.

The clinical value of each typical and atypical feature is represented by the positive and negative likelihood ratios in Table 4. For diarrhea, absence of diarrhea is considered a typical feature with a positive LR. As can be

Table 2
Typical Clinical Characteristics of Patients with Suspected Appendicitis, by Final Diagnosis

Characteristic	Appendicitis (*n* = 270)	No Appendicitis (*n* = 485)	p-value
Median age in yr (IQR)	12.8 (9.5–15.3)	11.6 (8.0–14.6)	0.045
History (%)			
Anorexia	59.6	47.4	<0.001
Nausea or emesis	71.1	55.7	<0.001
Migration of pain	50.2	27.5	<0.001
Gradual onset of pain	55.3	55.4	<1.0
Pain duration of <48 h	82.2	74.1	0.017
Absence of diarrhea	82.9	78.4	0.21
Physical examination (%)			
Guarding	63.6	42.3	<0.001
Percussive tenderness	69.3	39.0	<0.001
Bowel sounds decreased	36.3	14.3	<0.001
RLQ tenderness	67.8	53.4	<0.001
Pyrexia temperature of >38°C	17.3	19.7	0.49
Rovsing's sign	31.9	15.9	<0.001
Rebound pain	48.5	24.7	<0.001
Laboratory (%)			
WBC of >10,000 per mm^3	90.4	47.8	<0.001
ANC of >7,500 per mm^3	79.3	41.0	<0.001

IQR = interquartile range; RLQ = right lower quadrant; WBC = white blood cell count; ANC = absolute neutrophil count.

Table 3
Frequency of Atypical Findings in Patients with Appendicitis

Characteristic	*n*	Frequency (%)
Age <5 yr	270	2.4
History		
No anorexia	270	40.4
No nausea or emesis	222	28.9
No migration of pain	259	49.8
Abrupt onset of pain	217	45.1
Duration of pain of >48 h	241	17.7
Presence of diarrhea	217	15.9
Physical examination		
No pyrexia temperature of ≥38°C	270	82.7
No guarding	220	47.4
No percussive tenderness	270	30.7
Normal or hyperactive bowel sounds	190	64.4
Maximal tenderness not in RLQ	270	32.2
No Rovsing's sign	207	68.4
No rebound pain	270	51.5
WBC of <10,000 per mm^3	270	9.6
ANC of <7,500 per mm^3	270	14.7

RLQ = right lower quadrant; WBC = white blood cell count; ANC = absolute neutrophil count.

Table 4
Positive (LR+) and Negative (LR−) Likelihood Ratios for Clinical Features

Typical Characteristic	LR+ (95% CI)	Atypical Characteristic	LR− (95% CI)
Anorexia	1.26 (1.10, 1.44)	Lack of anorexia	0.77 (0.65, 0.91)
Nausea or emesis	1.28 (1.14, 1.43)	Lack of nausea or emesis	0.65 (0.53, 0.81)
Migration of pain	1.82 (1.51, 2.20)	No migration of pain	0.69 (0.60, 0.79)
Gradual onset of pain	1.00 (0.86, 1.16)	Sudden onset of pain	1.00 (0.83, 1.21)
Pain duration <48 h	1.11 (1.02, 1.20)	Pain duration of >48 h	0.69 (0.50, 0.94)
Absence of diarrhea	1.06 (0.98, 1.15)	Presence of diarrhea	0.79 (0.56, 1.12)
Guarding	1.50 (1.29, 1.75)	No guarding	0.63 (0.52, 0.77)
Percussive tenderness	1.78 (1.55, 2.04)	No percussive tenderness	0.50 (0.42, 0.61)
Bowel sounds decreased	2.53 (1.85, 3.48)	Bowel sounds normal or increased	0.74 (0.66, 0.83)
RLQ tenderness	1.27 (1.13, 1.43)	No RLQ tenderness	0.69 (0.57, 0.84)
Pyrexia	0.88 (0.64, 1.21)	Absence of pyrexia	0.97 (0.86, 1.11)
Rovsing's sign	2.01 (1.49, 2.72)	Absence of Rovsing's sign	0.81 (0.73, 0.90)
Rebound pain	1.96 (1.61, 2.39)	Absence of rebound pain	0.68 (0.60, 0.78)
WBC of ≥10,000 per mm^3	1.89 (1.71, 2.09)	WBC of <10,000 per mm^3	0.18 (0.13, 0.27)
ANC of ≥7,500 per mm^3	1.93 (1.71, 2.18)	ANC of <7,500 per mm^3	0.35 (0.28, 0.45)

RLQ = right lower quadrant; WBC = white blood cell count; ANC = absolute neutrophil count.

seen by the LRs in Table 4, the most important typical characteristics for diagnosing appendicitis are hypoactive bowel sounds (LR, 2.53), presence of Rovsing's sign (LR, 2.01), rebound pain (LR, 1.96), absolute neutrophil count (ANC) of ≥7,500 per cubic millimeter (LR, 1.93), white blood cell count (WBC) of ≥10,000 per cubic millimeter (LR, 1.89), migration of pain (LR, 1.82), and percussive tenderness (LR, 1.78). Similarly, the most significant atypical features (for absence of appendicitis) were as follows: WBC of <10,000 per cubic millimeter (LR, 0.18), ANC of <7,500 per cubic millimeter (LR, 0.35), lack of percussive tenderness (LR, 0.50), lack of guarding (LR, 0.63), and no nausea or emesis (LR, 0.65).

Among patients with appendicitis, Figure 1 demonstrates the likelihood of appendicitis with increasing numbers of typical and atypical features, respectively. Forty-four percent of patients with proven appendicitis had six or more atypical features.

Multivariate Analysis. Finally, multivariate analysis was performed by using stepwise logistic regression. Eight variables were retained in the logistic regression model; the adjusted ORs for these variables are shown in Table 5. Two variables, WBC of ≥10,000 per cubic millimeter and ANC of ≥7,500 per cubic millimeter, were noted to have greatest significance in pointing toward the diagnosis of appendicitis. The ORs for atypical features are the reciprocals; for example, the OR for WBC of <10,000 per cubic millimeter is 1/6.6 = 0.15, and for ANC of <7,500 per cubic millimeter, it is 1/3.4 = 0.29.

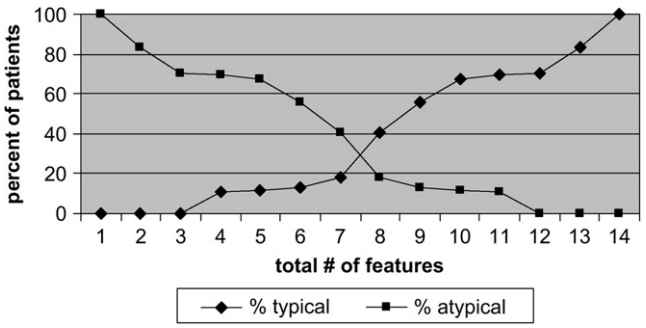

Figure 1. Likelihood of appendicitis among patients with increasing numbers of typical and atypical features.

DISCUSSION

Appendicitis is the most common condition requiring an emergency abdominal operation in childhood.[23] Four of every 1,000 children younger than 14 years of age will be diagnosed with appendicitis.[2,23] Despite the relatively high incidence of this common emergency, it remains a difficult diagnosis for the clinician. Pediatric patients are difficult to examine because they are often fearful of the examiner, cry or become uncooperative with the exam, or cannot articulate what aggravates them or offer exact historical progression of their symptoms. Over the past five years, there have been more than 250 medical articles in English-language journals that discuss pediatric appendicitis. Several articles mention atypical features, but no article's primary purpose was evaluating atypical features of appendicitis in children.

Because making the diagnosis of appendicitis can be difficult, the proper evaluation of these patients remains controversial. The pathways of evaluation and management are many and include the following: observation

Table 5
Adjusted Odds Ratios for Independent Predictors of Appendicitis as Determined by Logistic Regression

Variable	Odds Ratio (95% CI)
WBC of ≥10,000 per mm^3	6.6 (3.9, 11.0)
ANC of ≥7,500 per mm^3	3.4 (2.1, 5.2)
Migration of pain	2.1 (1.4, 3.2)
Maximal pain RLQ	2.1 (1.4, 3.3)
Hypoactive bowel sounds	2.1 (1.3, 3.1)
Nausea or emesis	2.0 (1.2, 3.2)
Rebound pain	1.9 (1.2, 2.9)
Percussive tenderness	1.9 (1.2, 2.9)

Atypical equivalents of each feature would represent the reciprocal; for example, 1/6.6 would be the adjusted odds ratio for WBC of <10,000 per mm^3.
WBC = white blood cell count; ANC = absolute neutrophil count.

for progression of symptoms, radiologic imaging followed by observation or operative care, and direct transfer to the surgical suite for an open or laparoscopic procedure. Many of the pathways result in an increase in the time from the initial evaluation until the diagnosis is made. Although no one knows the exact time from presentation to appendix rupture, it is believed by many authorities to be anywhere from 12 to 24 hours in younger children[1] and to be more than 24 hours in older children.[4] Regardless of the exact time frame, perforation correlates strongly with delay in diagnosis.[6] Because of the difficulty of making this diagnosis in children, numerous investigators have attempted to develop scoring systems,[18,20,21] and others have attempted to define the role of radiologic advances.[10–16] In addition to prolonging the time period from presentation to diagnosis, there is also concern that a CT scan exposes patients to the risk of ionizing radiation.[24] Our study aimed to investigate the influence of specific findings, typical and atypical, on the risk of appendicitis.

We found that 44% of patients ultimately diagnosed with appendicitis presented with six or more atypical features. In addition, we determined that there are several atypical features that are the greatest negative predictors (Table 4). Logistic regression was used to evaluate the independent value of each of the predictors, and all were independently valuable, with adjusted ORs ranging from 1.9 (percussive tenderness and guarding) to 6.6 for WBC of $\geq$10,000 per cubic millimeter. Not surprising, the more atypical findings for any given patient, the lower the likelihood of appendicitis. However, we were also able to show that the majority of patients with appendicitis have some atypical features.

In contrast to our findings regarding WBC and ANC, reports published elsewhere suggest that laboratory studies are not useful.[5,25] One reason that we considered for this finding was that our population included only patients suspected to have appendicitis by an attending pediatric EP, whereas other studies included broader groups of patients with undifferentiated abdominal pain. An added benefit of laboratory testing is its objectivity, in contrast to variability of examination findings between multiple examiners. Recently, investigators have begun looking at other laboratory markers, such as C-reactive protein and procalcitonin, for the diagnosis of appendicitis.[26–28] In the future, the evaluation of patients with possible appendicitis may incorporate more specific laboratory studies, in addition to a comprehensive history and examination.

LIMITATIONS

Our study has several strengths. Data regarding history and physical examination were collected prospectively, and before knowing the final diagnosis, from a relatively senior group of emergency medicine subspecialists. In comparison to prior studies, we were able to complete follow-up on patients who did not have operative care to properly assign final diagnoses. However, there is an inherent limitation to such data; despite the prospective collection and a coded questionnaire, there will always be variability in the declaration of specific examination findings by different clinicians. We did not study the interrater agreement for specific historical elements or examination findings, which probably has exaggerated importance in studying young children. Despite the large study population, our findings would not be applicable to a different population (such as patients with nonspecific abdominal pain). Likewise, given referral patterns and regionalized care, it is possible that our patients present relatively early in their course; accordingly, the presence and severity of symptoms might be less and thereby may potentially increase the proportion of atypical findings. Finally, we used stepwise logistic regression, which may not be a reliable technique for identifying a unique set of independent predictors.

In the past, it has been reported that one third of children with appendicitis present with atypical clinical findings. In reviewing the literature, it is interesting to note that this often-quoted statistic was the result of a small study that was performed to look at the usefulness of US in the diagnosis of pediatric appendicitis[17]; 38% of patients with appendicitis were initially stratified to a low or intermediate clinical risk of disease, which led the investigators to consider them atypical presentations. To the best of our knowledge, our study is the first to look at atypical features in a large prospective cohort of pediatric patients. Our findings show that many more than one third of patients with appendicitis present with atypical findings and that 25% of patients with appendicitis have more atypical than typical findings.

CONCLUSIONS

In summary, the majority of children with appendicitis present with some atypical clinical findings. Certain atypical features stand out as strong negative predictors of appendicitis; these are a WBC of <10,000 per cubic millimeter and an ANC of <7,500 per cubic millimeter. Patients with a mixture of atypical and typical signs and symptoms are candidates for further diagnostic testing. A high level of clinical suspicion, combined with the knowledge of the significance of certain atypical features, will aid the clinician in establishing the correct diagnosis.

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