Incidence and outcomes of unexpected pathology findings after appendectomy

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ABSTRACT

Purpose: Pathologic evaluation of the appendix after appendectomy is routine and can identify unexpected findings. We evaluated our experience in children undergoing appendectomy to review the clinical course of patients with unexpected appendiceal pathology.

Methods: After IRB approval, a retrospective review was conducted on patients who underwent appendectomy from January 1, 1995 to March 1, 2011. Patient demographics, diagnosis, pathological findings, disease outcomes, and treatment were collected only on patients with abnormal pathology.

Results: 3602 patients underwent appendectomy, 113 patients had normal appendices, and 86 patients had unexpected findings, including carcinoid tumor (n = 9), pinworm (n = 34), granuloma (n = 14), eosinophilic infiltrates (n = 18), and other (n = 11). All cases of carcinoid tumor were completely resected, with no recurrence or need for reoperation. Of the 34 patients with pinworm infestation, 41.2% underwent antimicrobial therapy, and none had post-operative symptoms. One patient (7%) with an appendiceal granuloma developed Crohn’s disease. Three patients (16.7%) with eosinophilia developed symptomatic intestinal eosinophilia.

Conclusions: Pediatric appendiceal carcinoid is an incidental finding; in this series, none required further intervention. Appendiceal granulomas are not commonly associated with developing Crohn’s disease in the short term. Routine antibiotics for the treatment of pinworms are adequate. Patients with appendiceal eosinophilia may develop symptomatic intestinal eosinophilia.

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Acute appendicitis is the most common condition necessitating abdominal surgery and is one of the most common causes of abdominal pain in children [1–8]. The etiology of acute appendicitis is hypothesized as being secondary to obstruction of the appendiceal lumen resulting in ischemic mucosal damage and secondary bacterial invasion [3,4,8,9]. The most common causes of appendiceal obstruction are fecal stasis and/or fecaliths that result in bacterial overgrowth [8], however other luminal processes may result in appendicitis or even mimic appendicitis [3,4,9–11]. Therefore, the histopathological examination may be relevant. We audited our experience with appendectomies to define the incidence of unexpected pathological findings and outline the clinical course created by these findings.

1. Methods

After Institutional Review Board approval (#11 09-158E), we conducted a retrospective review on all patients who underwent an appendectomy at our institution from January 1, 1995 to March 1, 2011. Patient medical records were reviewed and clinical data were collected. Data recorded included demographics, diagnosis, pathological findings, disease outcomes, and treatment for all patients identified with abnormal pathology. Only patients with abnormal pathology were included in the study.

2. Results

3602 appendectomies were performed during the study period. A normal appendix was documented by the pathologist in 113 cases (3.1%). Overall, 86 patients (2.4%) had unexpected pathological findings. Unusual pathology was suspected in only 4 patients (4.7%) after gross review by the surgeon and pathologist; all other patients were suspected to have either acute appendicitis or a normal appendix. Demographics are listed in Table 1. Abnormal pathological findings were carcinoid (n = 9), pinworm (n = 34), granuloma (n = 14), eosinophilic infiltrates (n = 18), and other (n = 11). Table 2 lists the clinical signs and symptoms at presentation for all patients.

Carcinoid tumor of the appendix was an incidental finding in all 9 patients. All patients in this group had a preoperative computed tomography (CT) scan and acute appendicitis was the most common finding (n = 7), with 2 patients having CT findings suggestive of appendiceal perforation. The remaining 2 patients had preoperative CT findings of intussusception and bowel obstruction. All surgical margins were negative, no recurrences occurred, and no subsequent treatments were needed in any of the patients. Additionally, there
were no postoperative abscesses or wound infections. Table 3 describes the location and size of each carcinoid tumor.

Although never diagnosed preoperatively, pinworm infestation was identified histologically in 34 patients; 39% of patients with unexpected pathological findings. Fourteen of the patients (41%) were treated with antimicrobials and none developed postoperative symptoms or disease sequela.

Appendiceal granuloma was diagnosed in 14 patients. Nine patients (60%) underwent drainage of an abscess identified on preoperative CT scan by interventional radiology. Preoperative abscess drainage resulted in interval appendectomy in 7 of 9 patients, while 2 patients required appendectomy during their hospital admission. One patient developed a postoperative abscess and was subsequently found to have Crohn’s disease.

Appendiceal eosinophilia was encountered in 18 patients, none of whom carried a previous diagnosis of eosinophilia. Three patients (16.7%) subsequently developed recurrent severe abdominal pain, and were diagnosed with eosinophilic enteritis.

Table 4 outlines those patients diagnosed with other unexpected pathology (n = 11). All patients who presented with an infectious etiology were treated and recurrence of infection was not seen. None of these patients developed a postoperative wound infection or abscess.

3. Discussion

Acute appendicitis is a common surgical disease in children [1,2,9,12,13]. Histopathologic examination is routinely performed and findings other than appendicitis are often noted, though not identified on gross examination [12]. Various studies have reported on unexpected pathology [3,9,12]. Incidental findings in this study included carcinoid, pinworm, granuloma, eosinophilia, lymphoid hyperplasia, other infectious etiologies, melanosis coli, serosal inflammation, and xanthomatous changes.

Carcinoids are the most common appendiceal tumor; in children appendiceal carcinoids are the most common malignant tumors found in the gastrointestinal tract [11,14–17]. Carcinoid tumors are derived from the enterochromaffin cells of the gastrointestinal and bronchopulmonary systems and are slow growing neuroendocrine tumors [16]. The reported incidence of appendiceal carcinoid in children and adolescents is 1 in every 100,000, and the overall incidence of carcinoid in children is reported to be between 0.085% and 0.3% [15–19]. The incidence in our study, which is narrowed down to the appendectomy population, was 0.25%. Some may argue this result supports the need for continued routine histological examination; however, no patients developed disease manifestation in our study, or required reoperation or further intervention [11,20,21]. Typically, appendiceal carcinoids are asymptomatic, difficult to diagnose, and are incidentally found on histopathological examination [11,14,15]. According to the literature appendiceal carcinoid tumors are more commonly found in females [16], contrary to our results where 78% of carcinoid tumors were in males.

The present study is concordant with others who have documented that patients with appendiceal carcinoid typically do not develop carcinoid syndrome, recurrence, and metastasis [15–17,19]. Generally, appendectomy alone is the only treatment necessary [16]. Prognosis typically depends on tumor size, with tumors less than 1 cm carrying the best prognosis, and rarely metastasizing [14,16,17,19]. Treatment for tumors measuring between 1 and 2 cm remains controversial given unknown frequency of metastasis [14,16,17], though the current recommendation for tumors between 1 and 2 cm in pediatric patients with positive lymph nodes is to perform a right hemicolectomy due to concerns of recurrence [14]. Tumors greater than 2 cm carry a higher risk of metastasis and right hemicolectomy or ileocecal resection is required [11,14,16,17,19,22]. Further surgical intervention is also warranted if tumor involves the base of the appendix with positive margins, if the cecum is involved, for high grade malignant tumors, or for tumors of intermediate type with mucus producing cells [16,19,22]. In our study only one patient presented with tumor size greater than 1 cm. This patient was followed closely with serial CTs, octreotide scans, monitoring of serum serotonin and chromogranin, and urine 5 hydroxyindoleacetic acid levels, all of which were negative for recurrence or metastasis after 3 years.

Enteroctobius vermicularis (pinworm) is the most common helminth infection worldwide and a rare cause of appendicitis [8,10,23]. The natural host of pinworms is humans and infection is via fecal–oral transmission. Eggs may remain viable for up to 3 weeks on clothing, fingernails, and bedding [10,24]. After the eggs are ingested, they hatch in the stomach and develop into larvae. The larvae then migrate to the cecum and grow to become adult pinworms. Female pinworms travel at night to the perianal area depositing eggs [24]. The majority of patients infected with E. vermicularis are asymptomatic. However, when symptoms develop, the most common symptom is anal pruritus [10,24]. Pinworm infection of the appendix often times mimics acute appendicitis, with reported incidence of pinworm infection in patients presenting with clinical symptoms of appendicitis between 0.2% and 41.8%, similar to our incidence of 0.8% [11,24]. It is suggested that parasitic infestation causes an obstruction of the appendiceal lumen or secondary inflammation leading to appendicitis [8]. Patients

### Table 1

Demographics of patients who had unexpected pathologic findings after appendectomy.

<table>
<thead>
<tr>
<th>Gender (M:F)</th>
<th>Carcinoid (n = 9)</th>
<th>Pinworm (n = 34)</th>
<th>Granuloma (n = 14)</th>
<th>Eosinophilic Infiltrate (n = 18)</th>
<th>Other (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>10.9</td>
<td>8.6</td>
<td>10.1</td>
<td>9.9</td>
<td>10.9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>50.4</td>
<td>36.9</td>
<td>38.7</td>
<td>40.2</td>
<td>50.4</td>
</tr>
<tr>
<td>BMI</td>
<td>20.8</td>
<td>18.9</td>
<td>19.3</td>
<td>16.7</td>
<td>20.8</td>
</tr>
</tbody>
</table>

### Table 2

Admission signs and symptoms in patients with unexpected pathologic findings after appendectomy.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>RLQ pain</th>
<th>Anorexia</th>
<th>Emetic</th>
<th>Diarrhea</th>
<th>Constipation</th>
<th>Symptoms (Days)</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoid</td>
<td>7 (77.7%)</td>
<td>6 (66%)</td>
<td>6 (66%)</td>
<td>2 (22.2%)</td>
<td>0 (0%)</td>
<td>3.5</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td>Pinworm</td>
<td>24 (72.3%)</td>
<td>23 (70%)</td>
<td>17 (52%)</td>
<td>1 (3%)</td>
<td>1 (2.9%)</td>
<td>3.1</td>
<td>5 (14.7%)</td>
</tr>
<tr>
<td>Granuloma</td>
<td>12 (85.7%)</td>
<td>14 (100%)</td>
<td>13 (92.9%)</td>
<td>3 (21.4%)</td>
<td>2 (14.2%)</td>
<td>3.4</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Eosinophilic Infiltrate</td>
<td>16 (88.9%)</td>
<td>16 (88.9%)</td>
<td>12 (66.7%)</td>
<td>3 (16.7%)</td>
<td>0 (0%)</td>
<td>3.2</td>
<td>3 (16.7%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (55%)</td>
<td>10 (91%)</td>
<td>6 (55%)</td>
<td>3 (27.3%)</td>
<td>1 (9.1%)</td>
<td>8.4</td>
<td>4 (36.4%)</td>
</tr>
</tbody>
</table>

RLQ, right lower quadrant.
may also present with ileocolitis, enterocutaneous fistula, urinary tract infection, mesenteric abscesses, and salpingitis [10,23]. Pinworm infection is more common in girls and patients usually present between the ages of 5 and 14 years old [23–25], which are similar to the data found in our study with 50% of the patients being female and a mean age of 8.6 years old (range 2.5–15 years).

Some authors have also reported the presence of appendiceal pinworm infestation to be associated with granulomas, eosinophilia, and lymphoid hyperplasia [7,10,23–26], and in this study pinworm infestation with lymphoid hyperplasia was seen in 5 patients (15.2%). According to the current literature, the recommendation for treatment of parasitic infestation after final histological diagnosis is anti-helminthic treatment [7,10,11,24]. In this study only 41.2% (n = 14) were treated after diagnosis. However, no patients were readmitted or developed recurrence. Furthermore, 15% (n = 5) of patients had perforated appendicitis, but no increased postoperative wound infection. Perforation of an appendix with pinworm infestation does not appear to carry increased risk compared to those without pinworm infections.

Granulomatous disease of the appendix is uncommon, and isolated granulomatous disease of the appendix is even more rare [27,28]. Granulomatous disease is commonly associated with the gastrointestinal tract and has been reported in cases of Crohn’s disease, sarcoidosis, foreign body reaction, and infectious processes including Mycobacterium tuberculosis, Yersinia pseudotuberculosis, schistosomiasis, parasites, and fungi [11,22,27–29]. The reported incidence of granulomatous appendicitis is less than 2% [26,31,34]. It has been reported that 5% to 10% of patients with idiopathic granulomatous appendicitis will eventually develop Crohn’s disease [27], similar to our finding of 7%, although other authors have reported that granulomatous appendicitis is an incidental finding unrelated to Crohn’s disease [29,31]. Additionally, the majority of patients that are later diagnosed with Crohn’s disease are not suspected at the time of the initial surgery [29]. In our series the overall incidence of granulomatous disease was 0.39%, similar to the reported incidence of 0.14%–0.3% [28,30]. Our results demonstrate a low incidence for subsequent development of Crohn’s disease in this population.

Acute eosinophilic appendicitis is a rare diagnosis and is often mistaken for acute appendicitis [32,33]. The etiology of eosinophilic appendicitis is uncertain, but many postulate that it is the result of an allergic response [33,34]. Eosinophilic enteritis may present as gastric antrum or intestinal disease with chronic gastrointestinal complaints, anemia, or polyoid lesions causing obstruction, intussusception, or gastrointestinal hemorrhage [33]. In our series 18 patients were diagnosed with eosinophilic appendicitis with 3 of those patients (16.7%) subsequently developing complicated eosinophilic enteritis with findings of chronic abdominal pain with duodenitis and colonic eosinophilia. Our results demonstrate that follow-up with gastroenterology may be warranted in a minority of patients with eosinophilic appendicitis who develop recurrent abdominal pain given the possibility of long-term morbidity.

Additional rare findings in our study are listed in Table 4. No recurrence was seen in any patients. Four patients presented with infection with Mycobacterium tuberculosis, Aspergillus, Actinomycyes, and beta hemolytic Streptococcus; all underwent treatment with improvement. Xanthogranulomatous change, an incidental finding described as marked histiocytes with xanthoma-like cells thought to be secondary to untreated appendicitis, was seen in one patient who presented with perforation [35]. Lymphoid hyperplasia often described as mimicking subacute or chronic recurrent appendicitis was identified in 1 patient with Crohn’s disease [36]. Two patients were diagnosed with melanosis coli who presented with abdominal pain greater than 7 days. In one adult study, authors report melanosis colis as related to changes in bowel activity, constipation, or abuse with anthracene cathartic resulting in pigmentation changes in the appendix with the proximal portion affected the most [37]. In our study no patients had a previous history of known colonic disease or usage of anthracene. Lipomatous hypertrophy is usually associated with a rare cardiac tumor composed of fatty tissue deposits [38], and was identified in 1 patient.

Routine pathologic examination of tissue in general has been argued to be useful to confirm diagnoses in uncertain clinical presentations, particularly if it will change the management and clinical course of the patient, and to identify unexpected pathology that may not be obvious on gross examination [12]. In our study, unusual pathology was only suspected in 5% of patients based on gross exam by the surgeon or pathologist (which included sectioning the appendix). However, only 2 patients had a change in management secondary to the pathology result: one patient with carcinoid tumor greater than 1 cm in size that required close follow up though no further intervention and one patient with a fungal infection requiring specific anti-fungal antibiotics. In our institution, in the year 2013, the charge for pathological examination of the appendix is $250. The overall cost of pathological analysis for 3602 patients can be estimated to be close to $1 million, equating to an approximate cost of $500,000 to find one patient that may require altered treatment or closer follow up. Gross examination alone does not appear to be a good indicator of an unexpected finding on microscopic exam; however the cost of routine microscopic examination needs to be balanced with the small number of patients in whom findings change their clinical course or management.

A recent review of conservative treatment of acute appendicitis indicates that many studies on the matter have been performed and conservative management is gaining favor in some places [39]. The findings in our study raise the question of whether a wider acceptance of conservative management for acute appendicitis may lead to missed diagnoses or further complications in patients with unexpected pathology.

4. Conclusion

Carcinoid is a rare incidental finding in children and the majority of patients do not require further intervention. Pinworms may be the cause of appendicitis and no further intervention is needed besides routine antibiotics for treatment of pinworms. The majority of patients with granulomatous disease are idiopathic and not related to Crohn’s disease. Eosinophilic appendicitis is less frequently encountered, but may later manifest as eosinophilic enteritis in a minority of patients and gastroenterology follow-up may be necessary. Other unusual findings in appendicitis such as melanosis coli, lymphoid hyperplasia, infectious processes, xanthomatous changes, lipomatous hypertrophy, and serosal inflammation are rare entities
and seldom cause complications. Gross examination alone does not appear to be a good indicator of an unexpected finding on microscopic exam; however the cost of routine microscopic examination needs to be balanced with the potential avoidance of complications in the small number of patients that may require alternate treatment or follow up.

References