



Acute eosinophilic appendicitis: a radiologic-pathologic correlation

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ABSTRACT

Inflammation of the appendix is one of the most common conditions requiring emergent surgical intervention. Computed tomography commonly demonstrates a dilated appendix with adjacent inflammation. Traditionally, luminal obstruction of the appendix has been thought to be the primary etiology of appendicitis. However, current evidence suggests that etiology of appendicitis is multifactorial and can involve a number of different pathogenic pathways. Here we present a case of acute eosinophilic appendicitis with radiologic-pathologic correlation from a hypersensitivity reaction pathway. Acute eosinophilic appendicitis may represent an early precursor to conventional acute suppurative (phlegmonous) appendicitis, or a variant form of acute appendicitis.

1. Introduction

Inflammation of the vermiform appendix is one of the most common conditions requiring emergent surgical intervention in the world with a lifetime risk estimated to be 7–8% [1]. Computed tomography (CT) has become commonplace in the management of the acute abdomen, with a sensitivity and specificity for the detection of appendicitis ranging from 88%–100% and 91%–99%, respectively [2]. Acute appendicitis has its peak incidence in the 2nd or 3rd decade of life and is less commonly seen at the extremes of age [1]. The most specific sign for appendicitis on CT has been visualization of a dilated fluid-filled appendix over 6 mm [3]. Other signs on CT include increased enhancement of the appendix after intravenous contrast administration, appendiceal wall thickening greater than or equal to 3 mm, mural stratification of the wall, appendicolith, intramural gas and periappendiceal inflammation/fat stranding (the radiology correlate to gross pathology findings of edema and/or purulent exudate) [2, 3]. However, a subset of patients presents with clinical symptomatology for acute appendicitis with non-specific CT findings. Here we present the first radiologic-pathologic correlation for a case of acute eosinophilic appendicitis.

2. Case report

A 40-year-old Latino male presented to our institution with two days of diffuse abdominal pain. He had an uncomplicated, elective hemorrhoidopexy and polypectomy one month prior to admission. His past medical history is significant for stage 2 chronic kidney disease, coronary artery disease with prior bypass grafting, deep vein

thrombosis on treatment with factor-Xa inhibitors and allergies to levofloxacin and medical tape. Abdominal examination on admission was benign. He was afebrile and had low-normal blood pressure.

His initial laboratory workup demonstrated a white blood cell (WBC) count of 20.66×10^3 cells/mL (normal ranges 4×10^3 cells/mL– 10.9×10^3 cells/mL) with manual differential showing elevation of his neutrophils of 17.6×10^3 cells/mL (normal 1.9×10^3 cells/mL– 8.6×10^3 cells/mL). The manual eosinophil count was 190 cells/mL (normal 0–870 cell/mL). Stable elevation of his creatinine of 1.19 mg/dL (normal 0.67 mg/dL–1.17 mg/dL) was also noted. Initial workup including influenza swab, urinalysis, electrocardiogram, troponin levels and transthoracic echocardiogram was unremarkable.

A contrast-enhanced CT scan of the abdomen and pelvis was then performed to work up his abdominal pain and evaluate for any post-operative complication related to his recent hemorrhoidopexy and polypectomy. There were no organized fluid collections in the region of recent operative procedures. Of note, the retrocecal appendix was thickened (Figs. 1–3), measuring up to 1.3 cm in maximal diameter (outer to outer diameter) with subtle wall hyperemia as well as thickening of the appendiceal wall up to 5 mm. There were no significant inflammatory changes of the mesoappendix. Given the elevation in white blood cell count and abdominal pain, appendicitis was mentioned by the radiologist as a potential source of his pain.

The patient was treated with intravenous ceftriaxone and metronidazole with improvement in his white blood cell count overnight to 7.66×10^3 cells/mL (normal ranges 4×10^3 cells/mL– 10.9×10^3 cells/mL). Given the patient's comorbidities and improving clinical status, the general surgery team elected to treat his

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Fig. 1. Transverse contrast-enhanced CT image demonstrates a dilated retrocecal appendix (white arrow) with mural thickening, but without signs of periappendiceal inflammation.

appendicitis non-operatively, and the patient was discharged on amoxicillin. Two days later, the patient had severe worsening right lower quadrant pain and again presented to our institution. A follow-up contrast-enhanced CT did not demonstrate any interval changes. A laparoscopic appendectomy was then performed due to failed non-operative management of the patient's uncomplicated appendicitis.

Gross pathologic analysis showed an appendix 1 cm in maximal diameter with scattered regions of punctuate hemorrhage. A pinpoint lumen was found with no luminal obstruction or appendicolith. No gross perforation was seen. The lumen contained some hemorrhagic content and was occluded in the distal aspect. The appendiceal wall measured 3 mm. Microscopic examination showed infiltration of eosinophils throughout the mucosa, submucosa and muscularis propria. No neutrophils were identified in the muscularis propria. Clusters of eosinophilic microabscesses were identified (Fig. 4). There was no evidence of parasites, ova or granulomas in the appendix. The findings were consistent with acute eosinophilic appendicitis.

Following surgery, there were no complications, and the patient had complete resolution of his abdominal pain. He was discharged in stable condition.

3. Discussion

Traditionally, luminal obstruction of the vermiform appendix by lymphoid hyperplasia, appendicolith, stool, or less commonly neoplasm has been thought to be the primary etiology of appendicitis. Obstruction of the lumen causes distention and increased pressure within the lumen, resulting in ischemic changes in the appendiceal mucosa and subsequent invasion by bacteria [4]. However, luminal



Fig. 2. Coronal contrast-enhanced CT image demonstrates a dilated retrocecal appendix with mural thickening (white arrow).

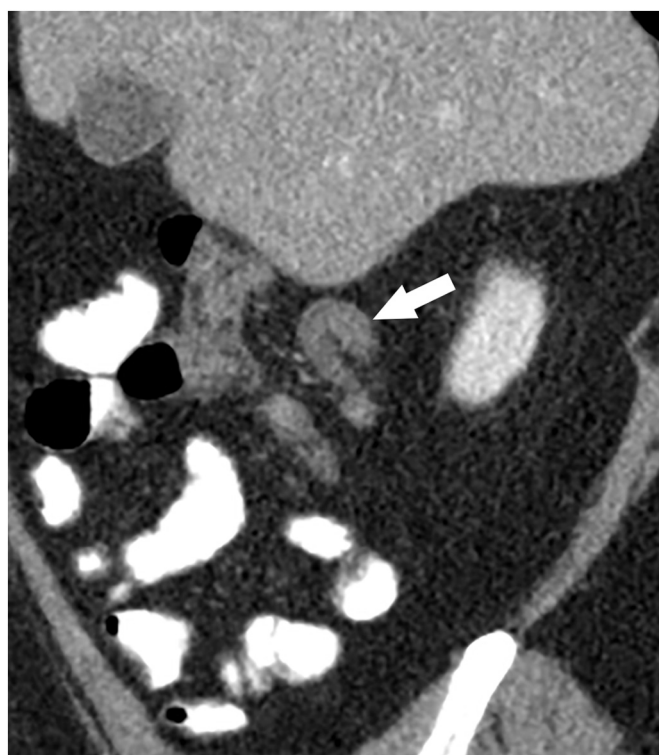


Fig. 3. Sagittal contrast-enhanced CT image demonstrates a dilated retrocecal appendix (white arrow) with mural thickening.

obstruction theory appears to be the exception rather than the rule [1]. Current evidence suggests the etiology of appendicitis is multifactorial and can follow a number of different pathogenic pathways [1, 4]. Etiologies could include environmental factors, geographical

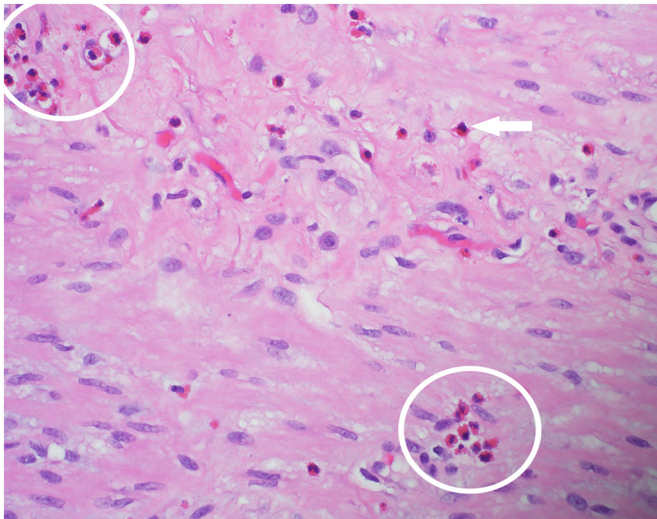


Fig. 4. Appendiceal muscularis propria. Muscularis propria is infiltrated by eosinophils (white arrow). Clusters of eosinophils (eosinophilic microabscesses) [white circle] are identified. There are no neutrophils. Hematoxylin and eosin stain. Magnification 400 $\times$.

differences, dietary factors, genetic predispositions, hypersensitivity reactions and infections [1, 4]. Specific infections including tuberculosis [5], human immunodeficiency syndrome [6] and enteroviruses [4] have been implicated as the causative agent in appendicitis. Parasitic infections involving *Strongyloides stercoralis* [7, 8] have resulted in cases of acute eosinophilic appendicitis with pathological specimens demonstrating transmural infiltration with eosinophils. Eosinophils are normal constituents of the appendiceal lamina propria and submucosa but not seen in the muscularis normally [9].

Not all cases of eosinophilic infiltration of the appendix are due to parasitic infection. One case series of 120 consecutive appendectomies found that eosinophils were more widely distributed in the appendiceal wall than neutrophils, and that eosinophils were more frequent in cases of clinically acute appendicitis compared to incidental appendectomies but those cases could not be diagnosed as acute suppurative (phlegmonous) appendicitis due to lack of neutrophils in the muscularis propria [4, 10]. Eosinophilic infiltration of the muscularis propria has been hypothesized to be an early event universally seen in acute appendicitis, possibly triggered by a type I hypersensitivity reaction [10]. Local allergic reactions in the appendix result in eosinophilic infiltration of the muscularis propria with accompanying edema [9]. Given its small size, the appendix is vulnerable to ischemic changes and damage to the mucosal layer. Entry of microorganisms would follow and cause neutrophilic inflammation and suppurative (phlegmonous) appendicitis. Our case of acute eosinophilic appendicitis may represent a situation where such a cascade of events has led to signs and symptoms of acute appendicitis but has not progressed to suppuration before surgery. Although our patient has had allergic reactions of rash to levofloxacin and medical tape, he does not have a history of atopy. Similarly, none of the cases of acute eosinophilic appendicitis in a case series of 128 emergent appendectomies had a history of atopy either [9]. With respect to parasitic infection, our patient did not have a history of travel or residence in a region where parasitic infections are endemic, and there were no parasites or ova in his appendix. Eosinophilic gastroenteritis, a rare disorder of exclusion, can affect any part of the gastrointestinal tract, but this was excluded due to lack of peripheral eosinophilia. The stomach and duodenum are most commonly involved [11].

Our case of acute eosinophilic appendicitis demonstrated the typical CT findings of acute appendicitis. The appendix was abnormally thickened with the wall measuring greater than 3 mm. However, our

case did not demonstrate significant periappendiceal inflammation. This may be due to the early presentation of the patient. One prospective study evaluating the diagnostic accuracy of multidetector CT for acute appendicitis demonstrated that 22% of cases did not have periappendiceal inflammation [12]. The differential for patients with thickened appendices seen on CT scan includes recurrent/chronic appendicitis, neurogenic appendicopathy, tumors such as mucocoeles or lymphoma, and normal appendices in cystic fibrosis patients. Patients with recurrent appendicitis and chronic appendicitis (pain over 3 weeks duration) may demonstrate CT findings indistinguishable from early appendicitis with mild wall thickening and mural hyperemia with minimal to no periappendiceal fat stranding [2]. Neurogenic appendicopathy, a relatively common condition in children affecting 7.5% of those presenting with signs and symptoms of acute appendicitis, is characterized by proliferation of the sympathetic nerve plexus and neuroma-like growths [13, 14]. CT scans in these patients have shown dilated appendices with wall thickening, but mild or no adjacent fat stranding. Mucocoeles resulting from benign or malignant epithelial tumors typically show mucin-distended appendices with curvilinear mural calcifications (seen in less than 50% of cases) [15]. The mucocoeles result from chronic luminal obstruction but are less likely to manifest with appendicitis compared to other neoplasms. Appendiceal lymphomas, though rare, presents most commonly with acute appendicitis. The shape of the vermiform appearance is maintained, and there is prominent enlargement with mural thickening. Aneurysmal dilation of the lumen can be an associated finding [15]. Appendices in cystic fibrosis (CF) patients, due to intraluminal inspissated secretions, are normally enlarged with a mean diameter of 10.6 mm compared to 6.6 mm in adults without CF and without acute appendicitis [16, 17]. However, appendicitis is less common in CF patients than in non-CF patients, with a prevalence of 1–2% [18]. It has been suggested that the secretions have a protective effect against acute appendicitis.

Our understanding of the etiology and pathogenesis of acute appendicitis has evolved. The commonly held belief of appendiceal luminal obstruction and secondary bacterial invasion is not the only pathogenic mechanism. Many different factors can affect pathogenic pathways resulting in acute appendicitis. In our patient, with the acute clinical presentation of abdominal pain and elevated WBC count and the CT findings of a dilated appendix with wall thickening, acute appendicitis was the primary diagnostic consideration. Pathologic evaluation revealed transmural eosinophilic infiltration with no evidence of neutrophils in the muscularis propria. Without evidence of parasitic infection, our case highlights a hypersensitivity pathway resulting in appendiceal inflammation with signs and symptoms of acute appendicitis. Whether acute eosinophilic appendicitis represents an underestimated early precursor to conventional acute suppurative (phlegmonous) appendicitis, or more simply a variant form of acute appendicitis, remains to be determined.

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Conflict of interests

The authors declare that they have no conflict of interest.

Human and animal rights statement

This article does not contain any studies with animals performed by any of the author(s). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from the individual participant included in the study.

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