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Case Report

Pediatric appendicular actinomycosis: a case report and literature review

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ABSTRACT

Background. Actinomycosis (ACM) is a rare infectious granulomatous disease caused by Actinomyces, a Gram-positive, filamentous, saprophytic bacteria. There are several types of pediatric ACM, such as orocervicofacial (55%) and other less common forms: abdominopelvic and thoracic. We report a case of a 16-year-old who presented with abdominal ACM in the setting of acute appendicitis. After the case report, we provide a short literature review of pediatric appendicular ACM cases published.

Case. A 16-year-old boy presented with nausea, vomiting, pain in the upper part of the abdomen and fever (37.5°C) lasting for 24 hours. On physical examination, the patient's epigastrium and lower right abdominal quadrant were tender. White cell count and C-reactive protein (CRP) were elevated at 16,300/μL and 48.6mg/L respectively. Ultrasonography (US) showed appendicolith and edema of the appendiceal wall, focally with stratification as well as periappendiceal inflammation. The patient underwent a classic appendectomy, and the postoperative course was without complications. Histopathological analysis showed diffuse transmural neutrophilic infiltration of the appendix, focally with areas of necrosis and abscesses. There were numerous brightly eosinophilic colonies made of filamentous bacteria, located predominantly in submucosa. Special stains Grocott-Gomori's Methenamine Silver and Gram were positive and a diagnosis of ACM was made.

Conclusions. Although appendicitis is very common in the general population, appendicitis associated with ACM is very rare, accounting for 0.02% - 0.06%, especially in the pediatric population. Diagnosis can be very challenging because they usually present with non-specific symptoms, and can form masses that mimic malignancies. Although rare, clinicians and pathologists should be aware of this entity. Satisfactory results and complete cure are achieved with adequate antibiotic therapy and surgery. In most cases, if there are no associated diseases, early and accurate diagnosis ensure an excellent prognosis.

Key words: appendix, actinomycosis, children.

Actinomycosis (ACM) is a rare infectious granulomatous disease, with an incidence between 1/300,000 and 1/1,000,000. ACM in the pediatric population is very rare, accounting for 3% of all ACM cases. It is caused by Actinomyces, a Gram-positive, filamentous, saprophytic bacteria. The most common cause of ACM in the human population is Actinomyces israelii.[1-3] There are several types of pediatric ACM such as orocervicofacial (55%) and other less common forms: abdominopelvic (20%) and thoracic (15%).[1]

In this paper, we report the case of a 16-year-old who presented with abdominal ACM in the setting of acute appendicitis. We also provide a short literature review of pediatric appendicular ACM cases published. We used MEDLINE database literature, and the search was performed using the PubMed service.

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Search terms: actinomycosis, appendix, children and pediatric were used in various combinations. Pediatric (0-18 years) cases with confirmed appendicular ACM were included.

Case Report

A 16-year-old boy presented with nausea, vomiting, pain in the upper part of the abdomen and fever (37.5°C) lasting for 24 hours. On physical examination, the patient's epigastrium and lower right abdominal quadrant were tender. There were no predisposing factors or associated illnesses that could be linked to the current condition. White cell count and C-reactive protein (CRP) were elevated at 16,300/μL (12,300/μL granulocytes, 2,900/μL lymphocytes) and 48.6 mg/L respectively. A blood sample was obtained for blood culture, but it yielded negative results. Ultrasonography (US) showed appendicolith and edema of the appendiceal wall, focally with stratification as well as periappendiceal inflammation. Mesenteric lymph nodes of ileocecal region were enlarged, up to 16 mm. After preoperative preparations, according to the protocol, the patient underwent a classic appendectomy. Initial drug treatment consisted of the intravenous administration of antibiotics (amikacin and ceftriaxone) and analgesics. The postoperative course was without complications and the wound healed well. Control laboratory analyzes were within the reference range. Histopathological analysis of the appendix showed diffuse transmural neutrophilic infiltration, focally with areas of necrosis and abscesses (Fig. 1, Fig. 2). There were numerous brightly eosinophilic colonies made of filamentous bacteria, located predominantly in the submucosa (Fig. 3). Special stains Grocott-Gomori's methenamine silver and Gram were positive and a diagnosis of ACM was made (Fig. 4, Fig. 5). Amoxicillin was continued to be administered to the patient for the following six months after the diagnosis of ACM. The follow-up period lasted for one year, and no

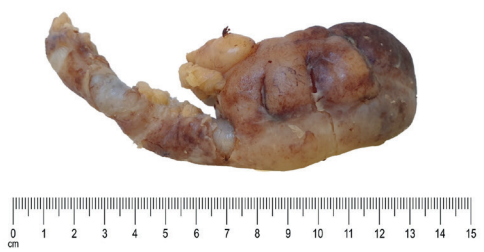

Fig. 1. Enlarged, inflamed appendix with fibrinous depositions on the serosal surface.

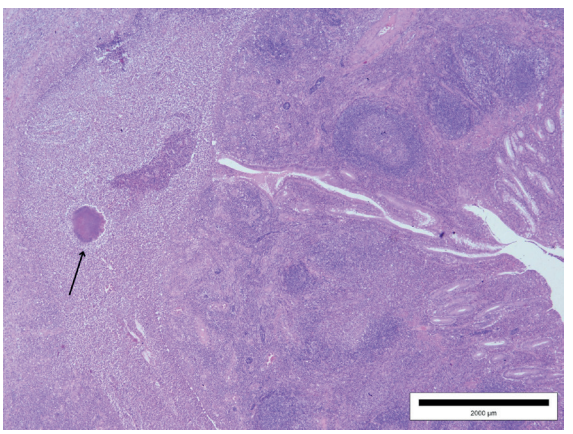

Fig. 2. Appendiceal wall with diffuse polymorphonuclear inflammatory infiltrate. Arrow pointing to oval eosinophilic mass in the submucosa (Actinomyces colony). (H&E, x40)

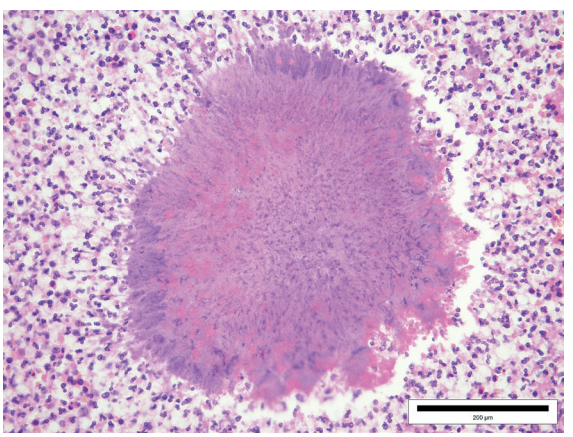

Fig. 3. Colony of Actinomyces rimmed by eosinophilic proteinaceous material (Splendore-Hoeppli). (H&E, x400)

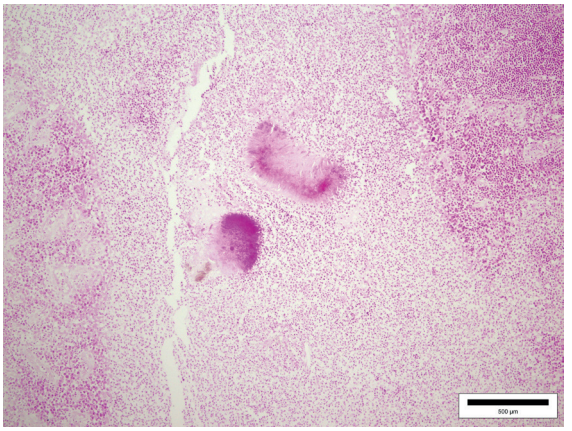

Fig. 4. Two colonies of actinomyces admixed with polymorphonuclear inflammatory infiltrate (Gramm stain, x100).

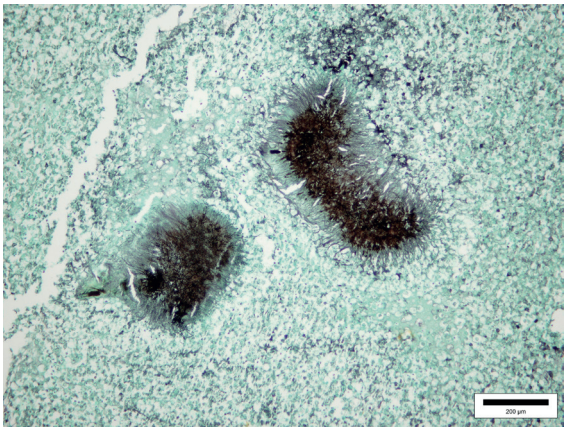

Fig. 5. Grocott-Gomori's Methenamine Silver stain depicts filamentous bacteria (Actinomyces). (x200)

complications were recorded. Informed consent for publication of this case report was obtained from the patient's family.

Discussion

Actinomyces are obligatory anaerobic, commensal bacteria of the oral, gastrointestinal and urogenital mucosa.[4] In most cases, actinomyces enter the tissues through small mucosal defects, usually during pathologic processes that disrupt the integrity of the mucosa such as appendicitis in our case.[4] Abdominopelvic ACM can be associated with diverticulitis, other intestinal diseases such as Crohn's disease or ulcerative colitis, trauma, recent surgery and intrauterine contraceptive devices. Factors predisposing the development of infection are alcoholism, diabetes, immunosuppression etc.[1,5] Despite all the aforementioned, according to a systematic review conducted by Manterola et al.[4], no contributing factor was identified in 57.9% of articles associated with ACM, which is consistent with our findings.

Of patients with abdominopelvic ACM, 66% have ileocecal region involvement.[6] Although very common in the general population, appendicitis associated with ACM is very rare accounting for 0.02% - 0.06% of the cases, especially in the pediatric population.[7] Diagnosis of these infections can be very challenging. They usually present with non-specific symptoms lasting for several months such as abdominal pain, fever, weight loss etc. The most common symptoms of abdominal ACM in the pediatric population are pain and a palpable lump.[1] Also, ACM can form masses mimicking malignancies, often with suppurative granulomatous inflammation which results in fistula formation.[5] There are plenty of complications related to ACM such as abscess formation with draining fistulas, osteomyelitis, meningitis, brain abscess, endocarditis and disseminated ACM.[4]

ACM is usually underdiagnosed due to the empirical application of antibiotics and specific anaerobic conditions needed for cultivation (only 17.9% of ACM cultures are positive).[4] Preoperative diagnosis of ACM is only 10%.[6] Computerized tomography (CT) and magnetic resonance imaging (MRI) are useful methods for determining the exact location of the inflammation. Those methods can also depict sinus and fistula tracts often associated with ACM, but they are not specific enough. Fine needle aspiration (FNA) or core biopsy are still useful diagnostic procedures for the confirmation of CT and MRI suspected lesions.[8] Laboratory findings are non-specific, they may indicate anemia, leukocytosis with elevated neutrophils and elevated values of

inflammatory parameters such as CRP, as in our case.[5] Colonoscopy findings are also non-specific, showing normal, thickened or ulcerated mucosa, appendicular inversion or nodular button like lesion.[9]

There are a wide variety of differential diagnoses for ACM. Due to its infiltrative pattern, ACM usually mimics neoplasms and Crohn's disease of the ileocecal region.[9-12] In the majority of cases, the correct diagnosis was determined postoperatively, following histopathological analysis. On standard hematoxylin and eosin staining ACM is characterized by sulfur granules made of densely packed filamentous bacteria outlined by eosinophilic material made of immunoglobulins called the Splendore-Hoeppli phenomenon.[13]

ACM is usually treated with high doses of antibiotics such as beta lactams (penicillin) often for a long period, between 6 and 12 months. Also, ACM is sensitive to erythromycin, minocycline, doxycycline and clindamycin, which is very important in cases of allergic reactions to beta lactams.[5,14]

Table I summarizes the published pediatric cases with confirmed appendicular ACM.[13-19] One of the most prominent differences between our case and other cases listed in Table I were the duration of the symptoms and the formation of a pseudotumorous mass. Unlike the other cases listed in the table, where a macroscopically visible pseudotumorous mass or phlegmonous inflammation of the appendix involving surrounding organs was observed in six out of seven cases, such findings were not present in our case. We presume that such findings are due to the short duration of the illness in our case, only 24 hours, and the pseudotumorous mass did not have time to develop in contrast to most cases listed in Table I where symptoms of the disease appeared several weeks or even months prior to surgery.

Appendicular ACM often presents a diagnostic challenge as it can mimic the appearance of a tumor or other noneoplastic conditions in the ileo-cecal region across different age groups. It is crucial to differentiate between conventional appendicitis and appendicular ACM, as the treatment approach and duration differ significantly, with ACM requiring a much longer course of therapy.[20,21] Furthermore, it should be noted that not every case of ACM presents with the formation of a mass or follows a long course of the disease, as demonstrated in our case. Although rare, it is important for clinicians and pathologists to be aware of this condition. In a majority of cases, when there are no associated diseases, an early and accurate diagnosis, followed by appropriate treatment, ensures an excellent prognosis.

Ethical approval

Informed consent was obtained from the patient's family for publication of this case report and accompanying images.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: MM, RJ, MĐ, LjS, NP, JJ; data collection: MM, RJ, MĐ, LjS, NP, JJ; analysis of results: MM, RJ, MĐ, LjS, NP, JJ; draft manuscript preparation: MM, RJ, MĐ, LjS, NP, JJ. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

Table I. Appendicular actinomycosis in the pediatric population.

Case author, year, reference no.	Sex, age (years)	Signs and symptoms	Symptom duration	WBC (/μL); CRP (mg/L)	Imaging methods and findings	Diagnosis HP; culture	Surgery	Medication
Schmidt P, et al. 1999. (15)	F, 15	pain nausea mass	2 days	11,200; 98	US: traget sign, RLQ	+ ; -	appendix and cecum resection	tetracyclines (penicillin alergy)
Campo JM, et al. 2001. (16)	M, 11	fever pain mass	3 months	NA; 108	CT: RLQ mass, hydronephrosis	+ ; -	appendix and mass resection	IV PG, OP (12M in total)
Sumer Y, et al. 2004. (17)	F, 17	pain fever mass	2 months	12,700; NA	US, CT: RLQ mass, hydronephrosis	+; NA	*en bloc* excision of the mass	IV PG 4W, amoxicillin 6M
Yiğiter M, et al. 2007. (14)	M, 13	pain nausea mass	4 weeks	RR	US, CT: RLQ mass	+; NA	appendectomy	IV PG 2W, OP 6M
Liu V, et al. 2010. (1)	F, 13	pain nausea fever constipation mass	3 weeks	14,700; NA	CT: RLQ mass	+; NA	appendectomy	IV PG 3W, OP 10W
Karakuş E, et al. 2014. (1)	M, 14	pain vomiting	NA	10,400; 35,6	US: appendicitis	+; NA	appendectomy	NA
Completo S, et al. 2022. (13)	M, 9	pain mass	5 months	17,800; 65	US: appendicitis	+; NA	appendectomy	IV PG 1M, amoxicillin 12M

CRP: C-reactive protein, CT: computerized tomography, F: female, HP: histopathology, IV PG: intravenous penicillin G, M: male, M: months, NA: not available, OP: oral penicillins, RLQ: right lower abdominal quadrant, RR: within the reference range, US: ultrasound, W: weeks, WBC: white blood cells.

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