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Association between infections and appendicitis

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بسم الله الرحمن الرحيم

(أَقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ * خَلَقَ الْإِنْسَانَ مِنْ عَلَقٍ * اقْرَأْ وَرَبُّكَ الْأَكْرَمُ * الَّذِي عَلَّمَ بِالْقَلَمِ * عَلَّمَ الْإِنْسَانَ مَا لَمْ يَعْلَمْ)

من سورة العلق الأيات 1-5

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Abstract

Appendicitis a serious medical condition in which the appendix — a small, finger-shaped organ attached to the large intestine — becomes swollen and inflamed**.** Signs and symptoms of appendicitis may include: Sudden pain that begins on the right side of the lower abdomen, sudden pain that begins around the umbilicus and often shifts to the lower right abdomen, vomiting, nausea etc. there was hypotheses about the possible infectious association with appendicitis and there are some contradictions in literature about that. The pathologic spectrum of the inflamed appendix encompasses a wide range of infectious entities, some with specific histologic findings, and others with nonspecific findings that may require an extensive diagnostic evaluation. This review discusses the pathologic features of bacterial, viral, fungal, and parasitic infections affecting the appendix.

Introduction

Appendicitis a serious medical condition in which the appendix — a small, finger-shaped organ attached to the large intestine — becomes swollen and inflamed. It's not always clear what causes appendicitis. Often, appendicitis is probably the result of an obstruction of the area inside the appendix called the appendiceal lumen (the interior of the tube of the appendix), or appendix lumen (Figure 1) (1).

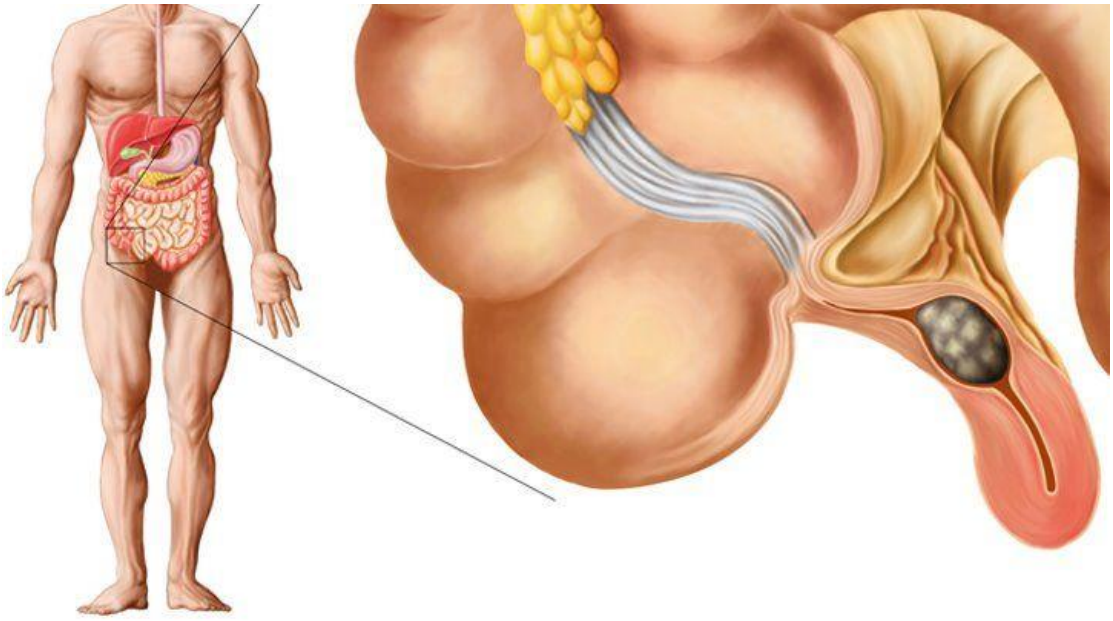

Figure 1: Appendicitis is often the result of an obstruction in the area inside the appendix called the appendiceal lumen.

There are numerous issues that can cause appendix luminal blockage, including:

- Appendicoliths or fecaliths, which are calcified fecal deposits, also known as "appendix stones" (this is more common in children than adults) (2)
- Intestinal worms or parasites, including pinworm (*Enterobius vermicularis*)
- Irritation and ulcers in the gastrointestinal (GI) tract resulting from long-lasting disorders, such as Crohn's disease or ulcerative colitis
- Abdominal injury or trauma
- Enlarged lymph tissue of the wall of the appendix, which is typically the result of infections in the GI tract
- Benign or malignant tumors
- Various foreign objects, such as stones, bullets, air gun pellets, and pins (3).

Clinical features

Signs and symptoms of appendicitis may include:

- Sudden pain that begins on the right side of the lower abdomen
- Sudden pain that begins around the umbilicus and often shifts to the lower right abdomen
- Pain that worsens during cough, walk or make other jarring movements
- Nausea and vomiting
- Loss of appetite
- Low-grade fever that may worsen as the illness progresses
- Constipation or diarrhea
- Abdominal bloating
- Flatulence

The site of the pain may vary, depending on the age and the position of the appendix. When the patient is pregnant, the pain may seem to come from the upper abdomen because the appendix is higher during pregnancy (4).

Association with infections

1-Many viral disorders are associated with lymph node enlargement, which, in turn, can obstruct the appendiceal lumen. Viral infections could cause mucosal ulcerations that could result in subsequent bacterial infection of the appendix. Appendicitis has been associated with a viral prodrome compatible with a viral illness preceding the first symptoms of appendicitis. Early epidemiologic investigations found that appendicitis was more frequent during months when respiratory infections were present (5).

Previous analysis of appendicitis time trends demonstrated that the increasing appendicitis rates observed after 1995 paralleled the rise, and could possibly be related to, increased use of computed tomographic

scanning and laparoscopic surgery. However, the year-to-year variation in the nonperforating appendicitis incidence and apparent disease outbreaks suggested that appendicitis is caused by an infectious agent (6).

Appendicitis shared no common pattern with intestinal infections or with documented rotavirus infections. These findings suggest that nonperforating appendicitis may be caused by an infectious agent or other process related to influenza virus infection; however, since influenza has a winter peak that is not observed with nonperforating appendicitis, it is unlikely to be a proximate cause. These findings also suggest that our previously observed parallel rise in nonperforating appendicitis after 1995 and in use of laparoscopic appendectomy and/or computed tomographic scanning might be coincidental and not causative (5).

Further evidence for the likelihood that appendicitis is caused by an infectious disease is the observation that the disease occurs in clusters. Several well-defined disease outbreaks have been identified. Seasonal changes in appendicitis have also been described. Although there was a tendency for appendicitis to be more common in the summer months, the seasonal variation was modest, consistent with previous reports (7).

Viral illness has been implicated by some researchers as the cause for appendicitis. Viral infection of the appendix could cause mucosal ulceration followed by secondary bacterial infection of the appendix. Alternatively, viral disease could result in lymphoid hyperplasia of the appendix with resultant obstruction and mucosal injury followed by bacterial infection. Several viral agents have been hypothesized to cause appendicitis. Coxsackievirus has been associated with cecal inflammation and periappendiceal lymphoid hyperplasia. Animal studies have shown that coxsackievirus infection can result in an appendicitis-like syndrome (8).

Lymph nodes and sera obtained from patients with appendicitis have shown evidence for simultaneous adenovirus infection. Measles virus and cytomegalovirus have also been associated with appendicitis (9).

2- Bacterial infection with pathogens (10), such as:

a- *E. coli*, which are bacteria found in the environment, foods, and intestines of animals. Most strains of *E. coli* are harmless, but others can cause illness. (5)

b-Pseudomonas bacteria, which are found in soil and water and moist areas such as sinks and toilets (6)

c-Bacteroides, bacteria that already inhabit the digestive tract of humans (7)

d-*Salmonella,* a foodborne bacteria that typically causes gastrointestinal upset (diarrhea, nausea, and vomiting) but can have serious complications

e-Shigella bacteria, germs that are very contagious and typically result in diarrheal illness that usually lasts no more than a week. (9)

3-The fungal infections mucormycosis (a rare but serious mold infection caused by environmental molds) (11) and histoplasmosis; most people who breathe in these spores won't get sick or will have mild symptoms, but infection can become severe in people with weakened immune systems (11).

Risk factors

There's no way to predict who will get appendicitis, but scientists have uncovered several risk factors for the condition. These include:

- Being a teenager or in r twenties; most cases of appendicitis occur in this age group
- Having a long-lasting inflammatory bowel disease, such as Crohn's disease or ulcerative colitis

- Studies have suggested that family history plays a role; a study published in 2014 in the *Western Journal of Emergency Medicine* found that among adults at an emergency room who presented with appendicitis, those with a known family history were more likely to have the condition (11)

And a study published in 2001 in the *Journal of Pediatric Surgery* found that "heredity is a significant factor" in children who have appendicitis.

There's also a link between air pollution — in particular, high levels of ozone — and appendicitis. Scientists aren't sure why air pollution is associated with an increased risk of appendicitis, but it may be that high levels of ozone increase intestinal inflammation or increase susceptibility to bacterial and viral infections. (12)

Studies suggest that people get appendicitis more during the summer than at other times of the year. It's not clear why, but a review of over 40 years of research, published in February 2014 in *Annals of Medical and Health Sciences Research*, concludes that it's likely due to a combination of increased exposure to air pollution and more GI infections during summer months (13).

Diagnosis

Physical exam findings are often subtle, especially in early appendicitis. As inflammation progresses, signs of peritoneal inflammation develop. Signs include:

- Right lower quadrant guarding and rebound tenderness over McBurney's point (1.5 to 2 inches from the anterior superior iliac spine (ASIS) on a straight line from the ASIS to the umbilicus)
- Rovsing's sign (right lower quadrant pain elicited by palpation of the left lower quadrant)
- Dunphy's sign (increased abdominal pain with coughing)

Other associated signs such as the psoas sign (pain on external rotation or passive extension of the right hip suggesting retrocecal appendicitis) or obturator sign (pain on internal rotation of the right hip suggesting pelvic appendicitis) are rare. The time course of symptoms is variable but typically progresses from early appendicitis at 12 to 24 hours to perforation at greater than 48 hours. Seventy-five percent of patients present within 24 hours of the onset of symptoms. The risk of rupture is variable but is about 2% at 36 hours and increases about 5% every 12 hours after that.

Several practical scores have been defined to facilitate the prompt diagnosis of acute appendicitis, mainly based on the history and physical examination, accompanied by laboratory tests and imaging measures, including abdominal ultrasonography. Accordingly, evaluation of patients with suspicious signs and symptoms suggestive of acute appendicitis has been widely undertaken with Alvarado criteria since 1986. The highest score among Alvarado criteria is allocated to the tenderness in the right iliac fossa, leukocytosis, and each of the other predicted symptoms, including migratory right iliac fossa pain, nausea, and or vomiting, and anorexia, hold one score. Moreover, positive findings in the remaining indexes of physical examination, including fever and rebound tenderness in the right iliac fossa, would hold a similar score of one (14).

Laboratory measurements, including total leucocyte count, neutrophil percentage, and C-reactive protein (CRP) concentration, are requested to proceed with diagnostic steps in patients with suspected acute appendicitis. Elevated white blood cells count (WBC) with or without a left shift or bandemia is classically present, but up to one-third of patients with acute appendicitis will present with a normal WBC count. There are usually ketones found in the urine, and the C-reactive protein may be elevated. A combination of normal WBC and CRP results has a specificity of 98% for the exclusion of acute appendicitis. Moreover, the WBC and

CRP results have a positive predictive value to differentiate uninflamed, uncomplicated, and complicated appendicitis. Both increasing levels of CRP and WBC correlate with a significant increase in the likelihood of complicated appendicitis. The possibility of a patient having appendicitis with both normal values of WBC and CRP level is extremely low. The WBC count of 10,000 cells/mm^3 is highly predictable in patients with acute appendicitis; however, the level would increase in patients with complicated appendicitis. Accordingly, the WBC count of equal and or above 17,000 cells/mm^3 is associated with complications of acute appendicitis, including perforated and gangrenous appendicitis (15).

Management

While in the emergency department, the patient must be kept NPO and hydrated intravenously with crystalloid. Antibiotics should be administered intravenously as per the surgeon. The responsibility for the consent falls on the surgeon. The gold-standard treatment for acute appendicitis is to perform an appendectomy. Laparoscopic appendectomy is preferred over the open approach. Most uncomplicated appendectomies are performed laparoscopically. Several studies have compared the outcomes with the laparoscopic appendectomy group and patients who underwent open appendectomy. The results were suggestive of lower incidence of wound infection, decreased level of postoperative analgesic requirement, and shorter postoperative hospital stays in the former group. The main disadvantage of laparoscopic appendectomy is the longer operative time (16).

While laparoscopic appendectomy has been widely used as the preferred approach for the surgical management of acute appendicitis in many centers, still open appendectomy might be selected as the practical choice, specifically in the management of complicated appendicitis with phlegmon and in the patients who are subjected to the conversion from the

laparoscopic approach mainly due to the potential issues related to poor visibility. Several other alternative surgical approaches, including Natural Orifice Transluminal Endoscopic Surgery (NOTES) and Single-incision Laparoscopic Surgery (SILS), have been introduced recently. The idea of utilizing a flexible endoscope to enter the gastrointestinal or vaginal tract and consequently traversing the mentioned organ to enter the peritoneal cavity is an interesting alternative for patients who are considerate about the cosmetic aspects of the procedures. It has been later tested with successful performing of trans-gastric appendectomy in a group of ten Indian patients. The major potential advantages of appendectomy with NOTES are avoiding scars and limiting postoperative pain. Regarding the limited number of patients who have been under NOTES appendectomy, the detailed comparison of postoperative outcomes is still impossible. Hence, the major drawback with performing this technique is the demand to hybrid with the laparoscopic approach is to provide adequate retraction during the procedure and to confirm closure of the entry site (17).

Complications

Postoperative abscesses, hematomas, and wound complications are all complications that can be seen after appendectomies. If the wound does get infected, one may grow Bacteroides. "Recurrent" or "stump" appendicitis can occur if too much of the appendiceal stump is left after an appendectomy. This acts just like an appendix and can become occluded and infected just as with the initial episode. Therefore, it is important to ensure that there be very minimal and preferably less than 0.5 cm appendiceal stumps after an appendectomy. If left untreated, appendicitis can lead to abscess formation with the development of an enterocutaneous

fistula. Diffuse peritonitis and sepsis can also develop, which may progress to significant morbidity and possible death (17).

Conclusion

Appendicitis is serious and surgical emergency that need to be treated immediately. It was found that there is a high chance that the infections, including virus, bacteria, and fungi play an essential a role in the infection. Therefore, it is important to prevent and treat the infections immediately that may cause appendicitis.

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