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Mimickers of Acute Appendicitis

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Abstract

Acute appendicitis (AA) is a common surgical diagnosis in patients presenting to the Emergency Department with acute abdominal pain. A wide variety of other clinical conditions can present with a very similar presentation to acute appendicitis and therefore it can be occasionally challenging to make the correct diagnosis. In this review paper, the focus is to shed some light on the differential diagnosis of acute appendicitis which includes a variety of gastrointestinal, vascular, urological, and gynaecological conditions. In the emergency setting there are three main imaging modalities to evaluate patients presenting with abdominal pain, this includes computed tomography (CT), ultrasound (US) and magnetic resonance imaging (MRI). The choice of imaging modality for each clinical condition is variable and as such being familiar with those differential diagnoses is vital in deciding what is the best imaging modality for every patient presenting with abdominal pain.

Keywords: acute appendicitis, appendicitis mimics, emergency department, Alvarado score, aortic abdominal aneurysm, inflammatory bowel disease, infectious enterocolitis, diverticulitis, radiation enteritis, neutropenic colitis, Meckel's diverticulitis, mesenteric ischemia, urolithiasis, pyelonephritis, ectopic pregnancy, ovarian torsion, haemorrhagic ovarian cyst, pelvic inflammatory disease, Mittelschmerz

1. Introduction

Although acute appendicitis is one of the most common causes for acute surgical abdomen accounting for 250,000 appendectomies in the United States every year, a large number of other clinical conditions can mimic the presentation of this acute surgical emergency [1]. Those conditions include a variety of gastrointestinal, vascular, genitourinary and gynaecological diseases. It is very important to consider those mimics when assessing patients presenting to the emergency department (ED) with acute right-sided abdominal pain.

The use of imaging modalities such as abdominal and pelvic ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) can be crucial in assessing those equivocal cases with vague nonspecific symptoms. The use of imaging in those circumstances not only aids in ruling in the diagnosis of acute appendicitis but also helps in differentiating other forms of pathology contributing to patient's symptoms.

The most common imaging modality used in patients with right-sided abdominal pain is abdominal and pelvic CT, which has a sensitivity of 97% and a specificity of 98% [2, 3].

Classical features suggestive of appendicitis on CT include concentric and thickened appendiceal wall, the presence of an appendicolith, fat stranding, mesenteric lymphadenopathy and the presence of surrounding fluid. The presence of other features such as appendiceal wall defect, extraluminal air or localised abscess is more suggestive of a perforated appendix.

Ultrasound abdomen and pelvis is the second most common imaging modality used in patients presenting with acute abdominal pain in whom there is a degree of clinical uncertainty. Ultrasound has a sensitivity of 78% and a specificity of 83% [4]. It is the most preferred imaging modality in pregnancy and paediatric age group due to the inherent risk of radiation associated with computed tomography. Features suggestive of appendicitis on ultrasound include dilated (>6 mm outer diameter) non-compressible appendiceal wall, hyperechoic appendicolith with posterior acoustic shadowing, peri appendiceal fluid collection and mural hyperaemia on colour flow Doppler mode. Although it is the preferred imaging modality in pregnancy, it can be extremely challenging to interpret the images given the distorted abdominal and pelvic viscera especially in the third trimester of pregnancy.

When it comes to the elderly population presenting with acute abdominal pain, choosing the best Imaging modality can be extremely challenging due to the high mortality risk associated with false-negative imaging. The incidence of acute appendicitis in patients older than 50 years of age is only 15% when compared to younger patients where the incidence doubles to 30% [5]. Despite the declining incidence of acute appendicitis with advancing age, there is an increase in mortality rate from 1% in young patients to almost 8% in patients over 65 years of age [5]. This high mortality rate in the elderly age group can be explained by the increased incidences of appendicitis complications such as the development of appendicular abscess and perforation. There is also a considerable decline in the imaging diagnostic accuracy with advancing age as studies have shown that the percentage of patients with positive histological evidence of appendicitis drops from 78% to 64% in patients older than 65 years of age [6]. The use of enhanced CT scan for imaging in the elderly population is superior to ultrasound imaging. The low sensitivity, and negative predictive value along with the increased number of false-negative imaging in patients with complicated appendicitis make the ultrasound modality less preferable when it comes to choosing the best imaging modality. Due to the aforementioned reasons, the Jerusalem guidelines recommend the use of CT with IV contrast in patients older than 60 years old with an Alvarado score ≥ 5 and a negative ultrasound study [7]. This recommendation taking into account the risk of radiation where the number of performed CT scans after a negative ultrasound is reduced by 50% [7, 8]. It is also worth mentioning that the use of ultrasound is very important in screening elderly patients presenting to the Emergency Department with abdominal pain for an aortic abdominal aneurysm which a vascular emergency that can mimic appendicitis. The current recommendation by the UK Royal College of Emergency Medicine (RCEM) is for the Emergency Physician to perform an ultrasound scan on any patient older than 50 years presenting with abdominal pain [9].

The use of magnetic resonance imaging (MRI) depends on accessibility as it differs from one hospital to another. The presence of other more readily accessible imaging modalities such as computed tomography and ultrasound makes the use of magnetic resonance less popular. Features suggestive of appendicitis on MRI include the presence of dilated appendix (>7 mm outer diameter), fat stranding and restricted diffusion.

2. Conditions that mimic appendicitis

2.1 Gastrointestinal diseases

2.1.1 Inflammatory bowel disease (IBD)

Terminal ileitis caused by Crohn's disease and Backwash ileitis associated with Ulcerative colitis both can present with right lower abdominal pain mimicking acute appendicitis. Typical age group is from 15 to 30 years and clinical presentation usually include symptoms of diarrhoea and bloody stool. IBD cannot be diagnosed via a blood test, however routine blood tests checking for pro-inflammatory markers such as raised white cell count (WCC), C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) may aid in supporting the diagnosis and monitoring the disease activity later on.

Although colonoscopy remains the investigation of choice for confirming the diagnosis, the use of radiological imaging is warranted when colonoscopy is not accessible.

As per imaging choice, IBD is best evaluated with either CT or MRI enterography and classical findings include bowel wall thickening of more than 3 mm, mucosal hyperenhancement, fat stranding and engorged vasa recta known as "Comb" sign. Management of IBD includes both surgical and non-surgical treatment depending on the severity, the extent of the disease and the presence of complications.

2.1.2 Infectious enterocolitis

This refers to bowel inflammation caused by bacteria, viruses or parasites. Patients commonly present with abdominal pain, tenesmus and diarrhoea. Stools are often purulent and mixed with mucous and blood. Commonly implicated organisms include *Campylobacter jejuni*, *Salmonella*, *Shigella*, *Escherichia coli*, *Yersinia enterocolitica*, *cryptosporidium*, *Norovirus*, *Rotavirus* and *Entamoeba histolytica*. Some infections such as tuberculosis and cryptosporidiosis are very important to consider in immunocompromised patients such as those with HIV infection. Routine blood tests looking for raised inflammatory markers along with stool microscopy and culture may help to support the diagnosis and monitor response to antimicrobial therapy. CT features include bowel long-segment circumferential wall thickening with homogenous enhancement and typically with no adjacent fat stranding. Treatment for infectious enterocolitis depends on the causative organisms.

2.1.3 Radiation enteritis

This is an inflammation of the bowel that occurs after radiotherapy. Symptoms include diarrhoea, nausea, vomiting and abdominal pain. Most cases of radiation enteritis resolve spontaneously a few weeks after treatment ends however for some it can extend for months and years after the termination of treatment. CT and MRI findings include bowel wall thickening with luminal narrowing, small bowel obstruction and sometimes the presence of a fistula between the bowel and the bladder or the vagina.

2.1.4 Neutropenic colitis

Also known as Typhlitis is an acute life-threatening condition that affects immunocompromised patients such as patients with HIV disease or those who are on

immunosuppressive therapy. The aetiology involves mucosal damage secondary to ischemia and secondary bacterial infection with a predilection for the caecum and ascending colon. Patients may present with abdominal pain, diarrhoea, vomiting and fever. Typhlitis is commonly associated with Neutropenia. Early diagnosis and management are crucial to prevent complications such as perforation and sepsis. Classical CT findings include dilated caecum with circumferential wall thickening, peri-colic fluid collection and pneumatosis. Management includes bowel rest and antibiotic therapy.

2.1.5 Diverticular disease and diverticulitis

This is commonly seen in patients over the age of 40, where small bulging pouches also known as diverticula, form at the weakest portion of the bowel. Diverticulitis is the term used when there is associated inflammation of the diverticula. Symptoms include abdominal pain, vomiting and fever. Risk factors include aging, smoking, low fibre diet, obesity and sedentary life. Laboratory blood tests checking for raised inflammatory markers are useful in making the diagnosis of diverticulitis. Classical features of diverticulitis on CT include bowel wall thickening with infiltration of adjacent mesenteric fat. Managing patients with uncomplicated diverticular disease involves the introduction of low-fibre diet and antibiotics. Surgery is reserved for patients with complications such as perforation, diverticular abscess or fistula formation.

2.1.6 Meckel's diverticulitis

This is caused by congenital anomaly characterised by the presence of the vitelline duct which normally connects the yolk sac to the midgut during the fetal development. It occurs in 2–3% of the general population [10]. Inflammation of Meckel's diverticulum usually caused by enterolith and symptoms include abdominal pain, rectal bleeding and vomiting.

CT findings include the identification of a blind-end tubular structure protruding from the antimesenteric side of the distal ileum, wall thickening, hyperenhancement and fat stranding. Management is surgical resection of the diverticulum.

2.2 Vascular diseases

2.2.1 Abdominal aortic aneurysm (AAA)

This is a life-threatening emergency where there is an abnormal dilatation of the abdominal aorta due to vascular wall weakness. This abnormal dilation (1.5 times its normal diameter or greater than 3 cm) of the aorta is commonly seen involving the infrarenal part of the abdominal aorta. AAA is a fatal condition where mortality is about 80% with leaking aneurysm and only half of the patients survive 30 days post emergency repair [11]. AAA is more common in men and the risk factors implicated in the aetiology are the same factors contributing to atherosclerosis such as advancing age, diabetes, hypertension, hypercholesterolemia and smoking history. Clinical presentation of AAA includes a variety of symptoms such as abdominal pain, back pain, groin pain, and a pulsating abdominal mass. Ultrasound aorta remains the gold standard for screening patients for AAA in the emergency setting and the UK Royal College of Emergency Medicine (RCEM) recommends that all emergency physicians are to perform ultrasound aorta in all patients who are over the age of 50 presenting with abdominal pain. Disadvantages

for ultrasound include difficult studies due to the patient's body habitus, or the presence of overlying bowel obscuring the visualisation of the aorta. Another downside to the use of ultrasound is its operator dependability and the inability to exclude any aneurysmal leak. CT aortogram is a highly acute study that can confirm the presence and the size of an aneurysm which aids in planning surgery. Management of AAA involves either open repair or endovascular aneurysm repair (EVAR) depending on the fitness of patients for surgery and the morphology of the aneurysm.

2.2.2 Mesenteric ischemia

This refers to small bowel injury secondary to insufficient blood supply which can be acute or chronic. Patients with mesenteric ischemia can present with diarrhoea, rectal bleeding, abdominal pain, especially after eating, and unintentional weight loss due to the fear of eating and vomiting. Risk factors include atrial fibrillation, heart failure and chronic kidney disease. Early CT findings include mesenteric oedema, bowel dilation and wall thickening, mesenteric stranding and the presence of an adjacent solid organ infarction. Treatment depends on the cause of ischemia and as such can be medical or surgical however if it is a late presentation the only treatment is surgical since there is a risk of necrotic bowel.

2.3 Urological diseases

2.3.1 Urolithiasis

Urolithiasis or kidney stone disease can present with a right lower abdominal pain mimicking acute appendicitis. Careful consideration for the presence of obstructive uropathy is very important to prevent kidney injury. CT Urinary system is the gold standard imaging when assessing patients with suspected urolithiasis. CT findings include the identification of a high attenuation calculus within the urinary system with or without hydroureter and hydronephrosis, ureteral wall thickening and adjacent fat stranding.

Ultrasound can be used in patients with ureteric colic to identify any features of hydronephrosis. The only disadvantage of ultrasound imaging is its operator dependability. Conservative treatment is indicated for patients with stones measuring less than 4 mm.

2.3.2 Pyelonephritis

Pyelonephritis or kidney infection is commonly caused by ascending urinary tract infection with the most commonly implicated organism being *Escherichia coli*. It is a clinical diagnosis where history and clinical examination play a major role. Although imaging such as Computed tomography and Ultrasound can be normal in pyelonephritis, both can be particularly useful in assessment for complications such as abscess formation and identifying emphysematous pyelonephritis, which typically occurs in immunosuppressed patients. Typical features of pyelonephritis on Computed tomography include nephromegaly, delayed nephrogram, perinephric fat stranding and enhancement of the collecting system. Ultrasound features of pyelonephritis include nephromegaly and hydronephrosis with the loss of corticomedullary junction. Treatment includes supportive measures and antibiotics.

2.4 Gynaecological and obstetric diseases

2.4.1 Ectopic pregnancy

This medical emergency occurs when pregnancy happens outside the uterus and needs to be excluded in all women of reproductive age who present with abdominal pain. Blood and urine beta-HCG measurement is crucial in making the diagnosis. The absence of an intrauterine gestational sac on transvaginal ultrasound along with a high beta-HCG, intrapelvic fluid and a delayed period should raise the possibility of an ectopic pregnancy. Ultrasound features include the detection of a yolk sac or a live embryo outside the uterus makes the diagnosis. Other features include the detection of a hyperechoic ring around the adnexal gestation sac also known as the “tubal ring” sign. If detected early, methotrexate can be administered to terminate the ectopic pregnancy. Surgical intervention is indicated in the case of methotrexate contraindication, ruptured ectopic or in patients with hemodynamical instability.

2.4.2 Ovarian torsion

Another medical emergency that should be considered in all women of reproductive age presenting with severe abdominal pain. It is caused by twisting of the ovary around its supporting ligaments cutting the blood supply to the ovary and fallopian tube. Ovarian torsion commonly occurs in patients with ongoing gynaecological pathology such as ovarian cysts, tumours, enlarged corpus luteum or in patients who are undergoing ovarian stimulation for assisted fertilisation. Ultrasound is the first line of imaging and features suggestive of torsion include increased ovarian size more than 4 cm in diameter, heterogeneous appearance due to oedema and haemorrhage, and the detection of a cyst or an ovarian mass. Doppler Arterial and venous flow can be helpful when compared to the other non-affected side. Management includes surgical de-torsion of the ovary and debridement of any necrotic tissue.

2.4.3 Haemorrhagic ovarian cyst

This condition occurs when there is a sudden haemorrhage into an ovarian cyst. Ultrasound findings usually depend on how old the haemorrhage is. Most classical feature on ultrasound is a finely septated fishnet pattern caused by the fibrin bands. Management is usually conservative.

2.4.4 Pelvic inflammatory disease (PID)

This refers to the infection of the female reproductive system caused most commonly as a result of untreated ascending sexually transmitted infections. Most commonly implicated organisms are *Chlamydia trachomatis* and *Neisseria gonorrhoea*. Symptoms can be very subtle such as mild abdominal pain with per vaginal discharge. Rarely infection can spread to the liver and other tissues around the liver what is known as Fitz-Hugh-Curtis syndrome or gonococcal perihepatitis. Transvaginal ultrasound features include enlarged heterogenous ovaries, dilated fallopian tubes and adnexal thickening and pelvic fluid collection. CT features of Pelvic inflammatory disease include enlarged ovaries with abnormal enhancement, fluid-filled dilated fallopian tube, pelvic fat stranding, enhancement of the adjacent peritoneum and the presence of a pelvic abscess in severe cases. Treatment is conservative with antibiotics.

2.4.5 Mittelschmerz

This refers to one-sided abdominal pain that is associated with mid-cycle ovulation. Mittelschmerz means “middle pain” in German. If the pain occurs on the right side of the abdomen, it can mimic acute appendicitis. In most cases, mittelschmerz does not warrant any medical treatment.

3. Conclusion

Although the diagnosis of acute appendicitis is essentially clinical, familiarisation with other causes of acute abdominal pain that can mimic appendicitis is equally important especially in females and those with the extremes of age. Here we present a plethora of gastrointestinal, urological, vascular, infectious, and gynaecological conditions that can be similar in presentation to acute appendicitis. The supplementary use of appropriate laboratory tests and radiological imaging can be pivotal where there is clinical uncertainty, not only aiding in confirming the diagnosis of appendicitis or its associated complications but also in identifying other alternative pathology. Routine blood tests that include a full blood count (FBC) and c-reactive protein (CRP) can aid in the diagnosis of acute appendicitis as evidenced by the presence of raised white cell count and CRP. Although raised inflammatory markers can raise the likelihood for clinically suspected acute appendicitis, it is non-specific and less helpful where the clinical presentation is inconclusive and other differential diagnoses are equivocal. A urinalysis also should be considered in all patients with suspected acute appendicitis as part of their workup since it is an important bedside test when assessing for potential renal or urology pathologies such as the presence of blood in urolithiasis or nitrites and leukocytes in urinary tract infection (UTI).

Special consideration is warranted for female patients presenting with abdominal pain as the presence of an underlying gynaecological pathology can potentially complicate the clinical picture and affect the diagnostic accuracy. In this special category of patients, it is particularly important to check the blood or urine samples for beta Human chorionic gonadotrophin hormone (Beta-hCG) in all female patients of childbearing age presenting to the Emergency Department with acute abdominal pain to exclude ectopic pregnancy. Ultrasound remains the first line of imaging in investigating gynaecological pathology (transvaginal ultrasound) and in the paediatric age group due to the inherent risk of radiation associated with CT imaging.

Another special consideration is given to the elderly population where the incidence of acute appendicitis is less common. In assessing elderly patients, it is of a high priority to exclude time-critical conditions such as ruptured abdominal aortic aneurysm and bowel ischemia. The current recommendation by the Royal College of Emergency Medicine in the UK is for the emergency physician to perform an ultrasound aorta in all patients who are older than 50 years presenting with acute abdominal pain to rule out abdominal aortic aneurysm (AAA). A follow up dedicated CT aortogram may be required if the patient is hemodynamically stable to confirm the diagnosis of abdominal aortic aneurysm and to evaluate for any potential leak. Bowel ischemia is another time-critical emergency where there is a compromise to the bowels blood supply. Risk factors for bowel ischemia include diabetes, hypertension, smoking, hypercholesterolemia and atrial fibrillation (AF). It is important to consider the diagnosis of bowel ischemia in all patients who are older than 50 years presenting with a sudden onset of severe abdominal pain along with a raised serum lactate level reflecting organ hypoperfusion. CT abdomen and pelvis with IV contrast or a dedicated CT angiography remains the best imaging

technique for all hemodynamically stable patients in whom bowel ischemia is suspected.

As discussed above a variety of clinical conditions can mimic acute appendicitis and familiarisation with those alternative conditions is crucial when deciding what imaging modality will best suit the patient assessment thus increasing the diagnostic accuracy and ensuring optimal care to all patients.

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Dedication

I dedicate this work to my beloved wife and parents who have both supported me throughout my career in emergency medicine. I will always appreciate their love, affection, patience and encouragement.

Abbreviations


AA	Acute appendicitis
AAA	Abdominal aortic aneurysm
US	Ultrasound
CT	Computed tomography
MRI	Magnetic resonance imaging
WCC	White cell count
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate

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