

CASE REPORT

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An FUO patient diagnosed as appendicitis: a case report

Shupeng Song¹, Jinqiu Zhao¹, Yingzi Tang² and Yongguo Li^{1*}

Abstract

Background The diagnosis and management of fever of unknown origin pose significant challenges in the field of infectious diseases, as it is influenced by various factors. Infectious diseases have long been recognized as the primary etiology of fever of unknown origin. However, not all infectious diseases can definitively identify the causative pathogen and infection sites.

Case presentation we present a case report of an individual with fever, nausea, and anorexia but did not report any abdominal pain. Physical examination revealed no signs of abdominal tenderness. Repeated imaging studies including enhanced CT and color US of the appendix, only one color US suggested the possibility of appendicitis. Despite effective anti-infective treatment, the patient continued to experience low-grade fever, leading to the decision for laparoscopic exploration and subsequent appendectomy. Pathological findings confirmed the presence of appendicitis. After the surgical procedure, the patient's temperature and infectious markers returned to within normal range, ultimately leading to a diagnosis of appendicitis.

Conclusions The atypical symptoms and signs, along with the negative imaging results, contribute to the under diagnosis of appendicitis and the progression of fever of unknown origin, thereby exacerbating the physical, mental, and economic burden on patients. Consequently, there are valuable insights to be gained regarding the management of both appendicitis and fever of unknown origin.

Keywords FUO, Appendicitis, Color US, CT scan, Surgical resection

Background

Infectious diseases have long been recognized as the primary etiology of fever of unknown origin (FUO). However, not all infectious diseases can definitively identify the causative pathogen and infection sites. Focal occult infections, such as intraperitoneal abscesses, pelvic abscesses, and bacterial endocarditis, are often

overlooked due to nonspecific symptoms and missed diagnoses on imaging modalities. The delayed diagnosis in the present case of FUO pending examination was attributed to the absence of typical clinical manifestations and negative test results. Fortunately, our persistent focus on infectious fever prompted us to conduct multiple repeated examinations, one of which revealed a suggestive finding of appendicitis through color US. Ultimately, laparoscopic exploration and surgery confirmed the diagnosis. The fever lasting for over 1 month was ultimately resolved. Through this case, we further discussed the diagnosis and treatment of appendicitis.

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Case presentation

The 43-year-old male patient had no history of underlying disease, surgical procedures, traumatic incidents, allergies, recent travel, or exposure to animals or insects. Two weeks prior, he presented with an unprovoked fever peaking at 39.8 °C, accompanied by chills, nausea, anorexia, and fatigue. There was no abdominal pain or diarrhea, no cough or phlegm, and no urinary frequency, urgency, or pain. After self-administering ibuprofen for 3 days without improvement, he sought treatment at a district hospital where physical examination revealed no abnormal findings. The vital signs remained stable, and laboratory tests revealed leukocytosis with a predominance of neutrophils, along with an elevated concentration of procalcitonin (PCT) (Table 1), indicating the presence of an infectious fever. However, no evidence of infection was detected on lung computed tomography (CT), color ultrasound (US) of the appendix and heart, enhanced CT scan of the entire abdomen, and magnetic resonance imaging of the head; Additionally, all laboratory tests including urine test, stool test, EBV-IgM, CMV-IgM, viral hepatitis antibodies, HIV antibodies, syphilis antibodies, G+GM test, thyroid function evaluation, autoimmune antibody screening panel analysis, tumor marker assessment as well as blood and stool culture exhibited no aberrations. After receiving three days of cefoxitin and eight days of cefoperazone/sulbactam sodium treatment, which resulted in a decrease in white blood cell (WBC) count and procalcitonin (PCT) levels but without a significant reduction in body temperature, the patient was referred to our hospital for further evaluation. He presented a normal general build and was currently alert and coherent. A thorough physical examination revealed no abnormal findings across all systems. His vital signs were stable, with a temperature of 37.3 °C, a heart rate of 113 beats per minute, a respiratory rate of 21 breaths per minute, and a blood pressure of 130/88 mmHg. Comprehensive physical examination revealed no significant findings across all systems. Specifically, there were negative results for tenderness at McBurney's point indicating appendicitis or peritonitis, absence of Rovsing's sign suggestive of acute appendicitis, lack of psoas sign indicative of retrocecal appendicitis, and no presence of obturator sign suggesting pelvic appendix inflammation. The laboratory findings revealed a normal white blood cell count with an increased proportion of neutrophils and concentration of PCT (Table 1).

The potential for resistance to cefoperazone/sulbactam cannot be disregarded. Simultaneously, in order to minimize the risk of drug-induced fever, we opted for a more secure and efficacious alternative treatment with meropenem, resulting in gradual resolution of nausea and anorexia while low-grade fever persisted following two weeks. Considering the patient's response to anti-infection treatment, we still suspected infectious fever with the digestive system as the most probable infection focus. Therefore, a repeat color US examination of the appendix and enhanced CT scan of the abdomen were performed. The repeated color US revealed a maximum diameter of 5 mm with slight mucosal thickening measuring approximately 2.2 mm on the appendix wall along with visible blood flow signals and continuous submucosal echo suggestive of inflammatory changes (Fig. 1A, B). However, enhanced CT did not reveal any abnormalities including the appendix (Fig. 1C, D). Subsequently, another sonographer performed a repeat appendiceal color ultrasound examination after three days which showed a slightly thickened appendix base and presence of few fecaliths within its cavity. The atypical clinical presentation and divergent imaging findings between CT scan and color ultrasound may pose challenges in diagnosing appendicitis particularly when considering their impact on accuracy. However, we firmly believed that based on presentations indicative of an infectious disease exhibited by the patient with only appendiceal color US suggesting possible infection in the appendix; laparoscopic exploration followed by appendectomy was opted for facilitating further diagnosis and treatment. The post-operative histopathological examination revealed interrupted and discontinuous mucosa, presence of fecalith in the lumen, as well as neutrophil infiltration in both the mucosa and submucosa, consistent with pathological manifestations indicative of acute appendicitis (Fig. 1E, F, G, H). Subsequent follow-up after surgery demonstrated normalization of body temperature, neutrophil proportion, PCT, and C-reactive protein (CRP) levels (Table 1). The diagnosis of appendicitis was ultimately confirmed through pathological examination along with restoration of normal body temperature and inflammatory markers.

Discussion and conclusions

Acute appendicitis typically presents with abdominal pain originating from the peripheral umbilicus and progressing towards the right lower abdomen as

Table 1 Changes of laboratory indicators

variable	reference range	prior to admission	at admission	Two weeks after admission	postoperation
WBC	$(3.6-9.5)\times 10^9/L$	$11.39\times 10^9/L$	$7.14\times 10^9/L$	$8.56\times 10^9/L$	$9.44\times 10^9/L$
NEUT%	(40-75)%	87.76%	75.8%	79.6%	67.4%
PCT	(0-0.1)ng/ml	4.15	0.55	0.46	0.07
CRP	(0-10)mg/L	>200	121	56	<10

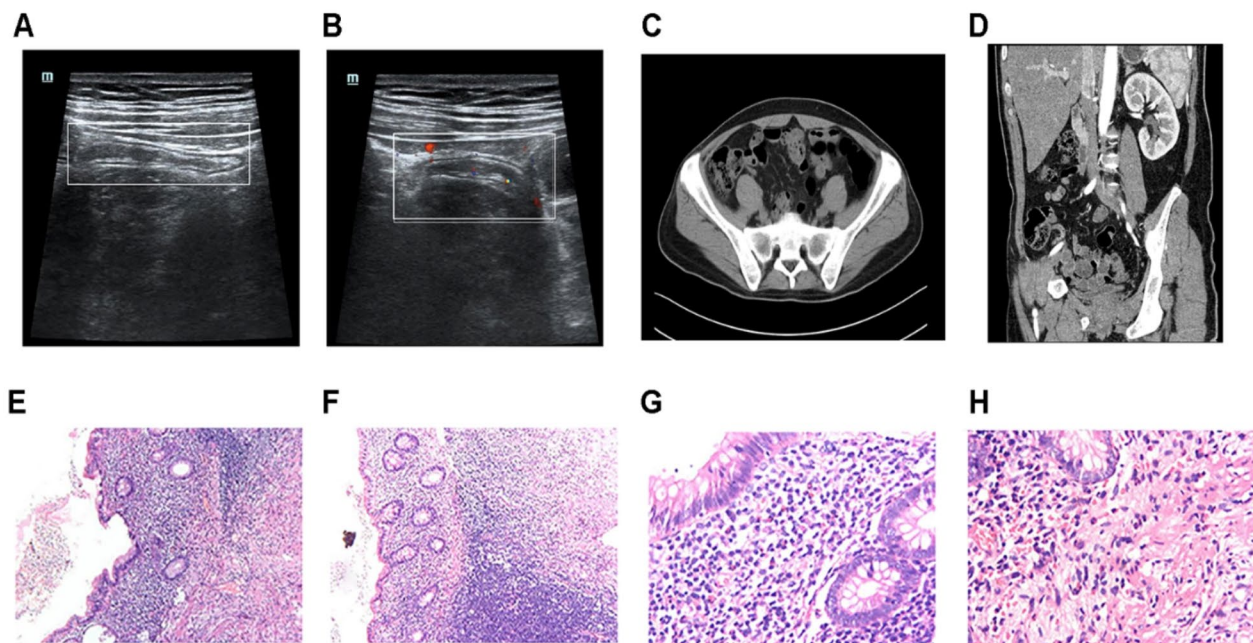


Fig. 1 Results of imaging and pathological examination of the patients. **(A)** The appendix exhibited slightly swollen, with a cavity diameter of 5 mm and mild mucosal thickening measuring approximately 2.2 mm. No echogenicity was observed within the cavity. **(B)** Few blood flow signals were detected in the appendiceal wall; **C & D.** The enhanced CT scan of the abdomen revealed that the fat space surrounding the ileal-cecal region appeared normal, with no significant thickening of the appendix; **E.** Inflammatory cells exudate from the lumen and the mucosal surface was discontinuous (H&E stain,100X). **F.** Fecaliths were observed within the cavity of the appendix (H&E stain,100X). **G & H.** Mucosa and submucosa were filled with acute inflammatory cells (H&E stain,400X)

inflammation develops. Although metastatic abdominal pain is considered a characteristic symptom, it only manifests in 50–60% of patients with appendicitis [1]. Early signs and symptoms of appendicitis are often subtle or atypical; therefore, their significance may be underestimated by both patients and clinicians, leading to missed early diagnosis. This case of acute appendicitis underwent a complex diagnostic and treatment process involving atypical clinical manifestations, incongruent findings between CT scan and color US examination, as well as incomplete antibiotic therapy.

Imaging is used mainly to increase the specificity of the diagnostic evaluation for appendicitis and to decrease the negative appendectomy rate. Numerous studies have consistently demonstrated that CT exhibits superior sensitivity and specificity compared to color US in the imaging assessment of suspected appendicitis in adults, particularly when enhanced. In terms of diagnosing appendicitis, CT and color US exhibit sensitivities and specificities of 95%, 96% versus 86.7%, 90.9% [2, 3]. Consequently, CT is widely regarded as the ‘gold standard’ for imaging diagnosis in clinical practice. Nevertheless, color US possesses distinct advantages in several aspects: early or mild appendicitis detection based on submucosal echo [4], identification of blood flow signals within

the appendix wall [5], tenderness evaluation using an ultrasound probe, changes observed in appendix cavity diameter after graded compression [6], especially fecalith discovery. For this patient, misdiagnosis occurred at the early stage due to atypical clinical presentations despite both color US and CT being performed. During the course of the disease, the patient’s clinical symptoms and infection indicators improved; however, complete cure was not achieved after antibiotic treatment. Therefore, repeat color US and enhanced CT were conducted. Color US revealed blood flow signals on the appendix wall as well as a fecalith within its cavity while CT did not show any signs of appendicitis. We speculate that inflammation was alleviated after approximately one month of antibiotic treatment which led to a misdiagnosis by enhanced CT scan. However, color US has more advantages in diagnosing mild inflammation and detecting fecaliths despite CT being considered more important for diagnosing appendicitis.

About the treatment of appendicitis, The recent systematic reviews and meta-analyses of randomized controlled trials have concluded that the antibiotic-priority method is a suitable treatment for most patients with uncomplicated acute appendicitis [7, 8]. Critical factors for successful antibiotic treatment include a low body

temperature, Alvarado score (<4), small appendix diameter [9], C-reactive protein (CRP) <60 g/L, WBC <12 K/ μ L, and age <60 years [10]. However, Harnoss et al.'s meta-analysis data showed that approximately 8% of patients experienced initial treatment failure, while another 20% relapsed within one year [11]. The presence of fecalith can contribute to the failure of antibiotic treatment. A randomized controlled trial demonstrated that about half of the patients with fecalith had poor antibiotic efficacy and it was an independent risk factor for treatment failure [12]. Therefore, we hypothesized that in this case, the presence of fecalith along with persistent inflammatory stimulation resulted in the failure of antibiotic treatment. Furthermore, the lack of typical early-stage symptoms and signs that may go unnoticed, prompt administration of antibiotics, and limited diagnostic and therapeutic capabilities may contribute to the absence of diagnoses in the former hospital. Upon admission to our hospital, there were no appendicitis-related signs probably due to prolonged antibiotic use for two weeks. Fortunately, we were able to maintain the possibility of infectious fever by improving clinical symptoms and infection indicators through antibiotic treatment, as well as conducting repeated screenings for infection foci. Despite inconsistent results from color US and CT scans, we still considered appendicitis as a potential diagnosis and ultimately resolved the patient's condition through exploratory laparotomy. It is crucial to consider the possibility of appendicitis when an infectious disease is identified but its precise location cannot be determined. The diagnosis of appendicitis and fever of unknown origin can be equally challenging.

Abbreviations

FUO	Fever of unknown origin
WBC	White blood cells
NEUT%	Neutrophil proportion
PCT	Procalcitonin
CT	Computed tomography
US	Color ultrasound
CRP	C-reactive protein

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-024-09851-7>.

Supplementary Material 1

Author contributions

All authors contributed to the study's conception and design. Shupeng Song and Yongguo Li were responsible for material preparation, data collection, and analysis. Yingzi Tang conducted the pathological examination and confirmation. Jinqiu Zhao and Yongguo Li were responsible for the revision of the manuscript. All authors read and approved the final manuscript.

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

Ethics and informed consent waiver applications were approved by the Ethics Committee of The First Affiliated Hospital University of Chongqing Medical University (K2023-302).

Consent for publication

Written informed consent was obtained from the patient for publication of this report and any accompanying images.

Competing interests

The authors declare no competing interests.

Conflict of interest

The authors reported no conflicts of interest.

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