



An unusual increase of D-dimer level—pylephlebitis caused by acute appendicitis: a case report

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Abstract: Acute appendicitis (AA) patients who present with a significantly increased level of D-dimer is not common. We speculated that the increase of D-dimer level was a result of pylephlebitis complication in the appendicitis patient. A 34-year-old man presented to the emergency department with sudden onset of lower quadrant abdomen pain. He was diagnosed with AA and scheduled for a laparoscopic appendectomy. He had a blood pressure of 80–90/30–40 mmHg, heart rate of 120–130/min, and his temperature was 38.3 °C. Routine blood test demonstrated a significantly elevated D-dimer (14,037 µg/L) with a negative blood gas test, normal ultrasound of the lower limbs, and normal pulmonary and abdominal computer tomography angiography (CTA) scans. Further tests showed a two-fold increase in D-dimer and abnormal hepatic function, indicating pylephlebitis, a rare but serious complication of AA. The patient was subjected to laparoscopic appendectomy, removing the cause of pylephlebitis, and received intravenous broad-spectrum antibiotics for an additional 1 week. The patient had clinical improvement with almost complete normalization of his D-dimer, white blood cell (WBC), alanine aminotransferase (ALT), aspartate aminotransferase (AST), fibrin degradation product (FDP) and platelet (PLT) levels. The patient was fully recovered and discharged from the hospital without any complications. Pylephlebitis secondary to AA is rare and can be easily missed. The unusual increase of D-dimer level provided critical value for pylephlebitis diagnosis.

Keywords: Acute appendicitis (AA); D-dimer; pylephlebitis; case report

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Introduction

Acute appendicitis (AA) is one of the most common disease in the department of general surgery that requires emergency appendectomy (1). The overall risk of appendectomy is 8.6% and 6.7% for male and female, respectively (2). Appendicitis generally has excellent prognosis with proper management. Nonetheless, AA can be life-threatening without timely treatment. The highlight of treatment for AA is to control inflammation and minimize complications. Antibiotics were commonly provided with AA patients, but timely appendectomy, either open or laparoscopically is recommend. The most common

complication is infection, such as postoperative abscess. Pylephlebitis, a serious infect is rarely seen complication in clinic.

Pylephlebitis, also called pyelophlebitis, is defined as an infective suppurative thrombosis of the portal vein or any of its branches that is caused by intra-abdominal infection. Previous report has shown that pylephlebitis is a rare but fatal complication of appendicitis, accounting for about 2% of all cases of pylephlebitis (3). Pylephlebitis commonly presents with nonspecific symptoms, making it a difficult diagnosis.

D-dimer is a soluble fibrin released from cross-linked fibrin (4) which has been used as a nonspecific index of

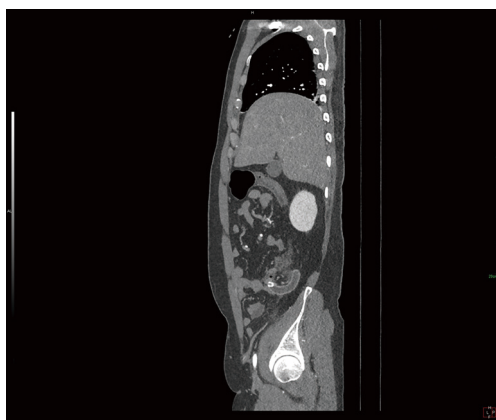


Figure 1 A 34-year-old man presented to the emergency department with sudden onset of lower quadrant abdomen pain. A sagittal CT scan shows a long strip-like dense lesion in the opening of the appendix, and the distant end of the appendix was distended with fluid. CT, computed tomography.

inflammation and coagulation (5). D-dimer level is used most often for exclusion of thrombotic diseases. Recent research showed that elevated D-dimer level is also present in severe inflammation (6). Here, we report a male patient of AA with an unusual increase of D-dimer level. After an overall analysis of clinical manifestations and diagnostic examinations, we diagnosed the patient with pylephlebitis.

We present the following case in accordance with the CARE reporting checklist (available at <http://dx.doi.org/10.21037/apm-19-554>).

Case presentation

A 34-year-old Asian male patient with a chief complaint of lower right abdomen pain for 2 days was admitted to the hospital at 12:50 PM on 4th September 2018. Earlier that day at 1 AM, the patient had upper abdomen colicky pain followed by nausea and vomiting. The patient did not have fever nor diarrhea. When the patient awoke in the morning, the pain had traveled and intensified, localizing at the right lower abdomen. His only significant medical history was a herniorrhaphy at 33 years ago.

The patient came to the Emergency Room, where his complete blood count (CBC) revealed white blood cell (WBC) count of $2.45 \times 10^9/\text{L}$ and his neutrophil percentage (NE%) was 83.6%. Taking his computed tomography (CT) scan (Figure 1) into consideration, the patient was admitted to the hospital with a diagnosis of AA.

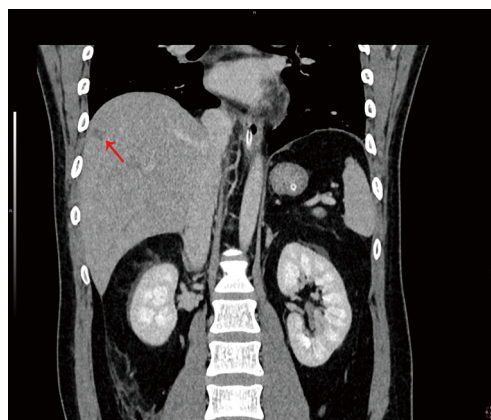


Figure 2 Contrast-enhanced CT scan of the liver in a 34-year-old man with a diagnosis of AA. The low-density lesions in the liver (arrow). CT, computed tomography; AA, acute appendicitis.

At the time of admission, the patient had a blood pressure of 80–90/30–40 mmHg, heart rate of 120–130/min, and his temperature was 38.3 °C. There wasn't any focal symptoms. Physical examination revealed that his abdomen was soft with tenderness and rebound tenderness at the right lower quadrant. Intravenous (IV) injection fluids and antibiotic (ertapenem, 1 g, qd) were given for systemic treatment.

Pre-surgery routine tests were carried out including electrolytes and coagulation, chest X-ray, electrocardiograph, and others. The patient's D-dimer level was increased to 14,037 (normal range: 0–500) µg/L and his WBC count showed a trend of increase at $10.12 \times 10^9/\text{L}$. The patient was given antibiotics and other symptomatic treatment, and was sent for urgent tests including ultrasound of the lower limbs, CTA of the pulmonary and abdominal artery, all of which were negative for thrombosis. However, the CT scan revealed suspicious low-density lesions in the liver (Figure 2). The patient's blood workup revealed the following: alanine aminotransferase (ALT) 636.4 IU/L, aspartate aminotransferase (AST) 1,049.0 IU/L, total bilirubin in serum (TBIL) 20.9 µmol/L, PT 19.0 seconds, fibrin degradation product (FDP) 235.7 mg/L, WBC $23.50 \times 10^9/\text{L}$, NE 93.3%, platelet (PLT) $35 \times 10^9/\text{L}$. A repeat test of D-dimer level was 26,166 µg/L. Sonography revealed that his portal vein had a diameter of 1.1 cm. Based on the patient's history, symptoms including pain and tenderness of the abdomen, along with findings of elevated D-dimer, AST, ALT, PLT and WBC, we considered that the patient might have deep vein thrombosis, diverticulitis, aortic dissection and gastrointestinal perforation.

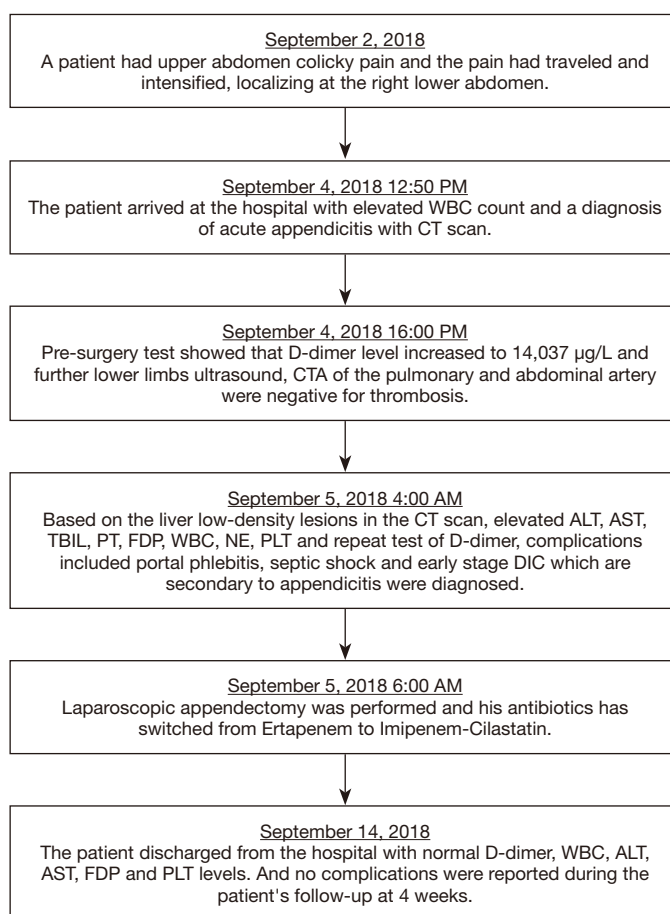


Figure 3 Timeline of major events during hospitalization. WBC, white blood cell; CT, computed tomography; CTA, computer tomography angiography; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin in serum; PT, prothrombin time; FDP, fibrin degradation product; NE, neutrophil; PLT, platelet; DIC, disseminated intravascular coagulation.

With his clinical signs and CT scan, the diagnosis of appendicitis was obvious. Other diagnosis included portal phlebitis, septic shock and early stage disseminated intravascular coagulation (DIC) are secondary to appendicitis. After completion of all above tests, surgery was successfully held under general anesthesia the following day with no complications. We changed his antibiotics from ertapenem to imipenem-cilastatin for 1 week (1 g, q8h, IV) because of negative blood culture, but did not prescribe any anticoagulant therapy.

The pathology report from surgery revealed acute suppurative appendicitis with inflammation of the surrounding. The patient recovered well post-surgery, and had clinical improvement with almost complete normalization of his D-dimer, WBC, ALT, AST, FDP and PLT levels. The patient was discharged from the hospital

at 8 days after surgery with oral antibiotics (cefdinir, 0.1 g, tid) for up to 1 week. No complications were reported during the patient's follow-up at 4 weeks. The timeline of major events during hospitalization as *Figure 3*. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient.

Discussion

AA is one of the most common cause of acute abdomen. Although non-operative management of AA is feasible, appendectomy remains the gold standard of treatment (7). Unlike in elderly patients, diagnosing AA in younger

patients is easier and the accuracy is of high level. As younger patients often present with typical symptoms. AA patients who present with a significantly increased level of D-dimer is not common.

D-dimer is a degradation product of cross-linked fibrin produced by plasmin hydrolysis. Elevation of D-dimer occurs when thrombosis is activated and fibrinolytic activity occurs in blood vessels. Elevation of D-dimer is commonly seen in hospitalized patients who are elderly, have malignant tumors, or who have recently undergone surgical procedures. The main applications of D-dimer measurement are: (I) venous thromboembolism (VTE) screening: used to exclude VTE diagnosis, (II) DIC: D-dimer reflects prothrombin and plasmin activity, >0.5 mg/L is considered a high predictive value for high-risk patients, (III) monitoring of thrombolytic therapy: D-dimer can be used as a specific monitoring indicator for thrombolytic therapy. Although lacking in specificity, there are studies indicated that D-dimer could be used as an indicator of severity for appendicitis (8). Furthermore, in patients with a perforated appendix with D-dimer levels equal to or greater than 1,000 ng/mL, there is a positive correlation between the clinical severity of appendicitis and the D-dimer level (8). On the other hand, there are studies indicated that D-dimer levels are not always correlated with the pathological severity. Indeed, we only observed inflammation in the appendix without signs of perforation, phlegmonous or gangrenous transformation (9). We speculated that the increase of D-dimer level was a result of pylephlebitis complication in the appendicitis patient.

Pylephlebitis is often a complication of intra-abdominal sepsis with high morbidity and mortality, at least partially, due to non-specific symptom and lack of available diagnostic modalities. The common nonspecific symptoms of pylephlebitis include fatigue, fever, abdominal pain, nausea, vomiting, diarrhea, anorexia, and advanced signs that include hepatomegaly and jaundice (10). Pylephlebitis is difficult to diagnose in the early stages and usually diagnosed when abnormal hepatic function is present. The pathogenesis of pylephlebitis be thought of related to the anatomic elements. The portal vein is formed by the union of the superior mesenteric vein with the splenic veins. The portal system drains blood from the abdominal section of the gastrointestinal tract, with the exception of the lower part of the rectum. Pylephlebitis begins with thrombophlebitis of small veins draining an area of infection (11). Extension of the thrombophlebitis into larger veins leads to septic thrombophlebitis of the portal

vein, which can involve the mesenteric veins, the splenic vein and intrahepatic branches of the portal vein. An associated hypercoagulable state is found of pylephlebitis (3,10,11). In this case report, the patient first presented with a decreased WBC count followed by steady increased WBC with markedly elevated D-dimer levels. There was a case reported a pylephlebitis patient with an unexplained WBC transient decrease (12). In addition, we found that the patient had abnormal ALT and AST levels and clinical signs of early stage DIC. Sonography revealed that the patient's portal vein was dilated and his CT scan did not rule out suspicious portal thrombosis. Low density lesion was observed in the live. Combined with the abnormal hepatic function, we predicted that patient had severe infection, portal phlebitis, and early stage DIC.

The patient was undergone appendectomy with antibiotic therapy. As the patients normally present with negative blood cultures, broad-spectrum antibiotics are usually used. With regards to anti-coagulant treatment, there is ongoing debate about the effectiveness of such treatment and therefore no standard protocol (3). The patient was treated with intravenous broad-spectrum antibiotics for 2 weeks after surgery followed by 2-week oral antibiotics. The patient's D-dimer, ALT and AST levels gradually returned to normal. All other laboratory tests were improved with normal blood cell count. No anti-coagulant treatment was prescribed for the patient. Neither liver abscess nor intestinal mesenteric thrombosis was observed in the follow-up CT examination.

Pylephlebitis secondary to AA is rare and can be easily missed. In our case, the unusual increase of D-dimer level provided critical value for diagnosis. This case report highlights the importance of D-dimer measurement for pylephlebitis diagnosis in AA patients.

The strengths of this study including: (I) broad assessment of AA as well as its complications via CT scan, lower limbs ultrasound, CTA of the pulmonary and abdominal artery. (II) A 4 weeks follow-up period after patient has discharged. However, one limitation should be noticed, with a view to the cost of hospitalization, no further CT scan, lower limbs ultrasound, CTA of the pulmonary and abdominal artery were performed after surgery.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <http://dx.doi.org/10.21037/apm-19-554>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/apm-19-554>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient.

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References

1. Ferris M, Quan S, Kaplan BS, et al. The global incidence of appendicitis: a systematic review of population-based studies. *Ann Surg* 2017;266:237-41.

2. Snyder MJ, Guthrie M, Cagle S. Acute appendicitis: efficient diagnosis and management. *Am Fam Physician* 2018;98:25-33.
3. Choudhry AJ, Baghdadi YM, Amr MA, et al. Pylephlebitis: a review of 95 cases. *J Gastrointest Surg* 2016;20:656-61.
4. Weitz JI, Fredenburgh JC, Eikelboom JW. A test in context: D-dimer. *J Am Coll Cardiol* 2017;70:2411-20.
5. Patel P, Walborn A, Rondina M, et al. Markers of inflammation and infection in sepsis and disseminated intravascular coagulation. *Clin Appl Thromb Hemost* 2019;25:1076029619843338.
6. Schutte T, Thijs A, Smulders YM. Never ignore extremely elevated D-dimer levels: they are specific for serious illness. *Neth J Med* 2016;74:443-8.
7. Poon SHT, Lee JWY, Ng KM, et al. The current management of acute uncomplicated appendicitis: should there be a change in paradigm? A systematic review of the literatures and analysis of treatment performance. *World J Emerg Surg* 2017;12:46.
8. Kaya B, Sana B, Eris C, et al. The diagnostic value of D-dimer, procalcitonin and CRP in acute appendicitis. *Int J Med Sci* 2012;9:909-15.
9. Abu Foul S, Egozi E, Assalia A, et al. Is early appendectomy in adults diagnosed with acute appendicitis mandatory? A prospective study. *World J Emerg Surg* 2019;14:2.
10. Kanellopoulou T, Alexopoulou A, Theodossiades G, et al. Pylephlebitis: an overview of non-cirrhotic cases and factors related to outcome. *Scand J Infect Dis* 2010;42:804-11.
11. Abdallah M, Gohar A, Naryana Gowda S, et al. Pylephlebitis associated with inferior mesenteric vein thrombosis treated successfully with anticoagulation and antibiotics in a 37-year-old male. *Case Rep Gastrointest Med* 2020;2020:3918080.
12. Li ZF, Chen JX, Sun JJ, et al. A case report of pylephlebitis and toxic shock secondary to acute appendicitis: a review. *Journal of Nantong University* 2016;36:237-8.

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