Clinical Case Report

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Acute appendicitis complicated with necrotizing fasciitis in a patient with adult-onset Still's disease

A case report

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Abstract

Rationale: Adult-onset Still disease (AOSD) is a rare systemic inflammatory disease of unknown etiology characterized by evanescent salmon-pink rash, spiking fever, arthralgia/ arthritis, and lymphadenopathy. AOSD sometimes was fatal when it is complicated by macrophage activation syndrome (MAS) or hemophagocytic lymphohistiocytosis (HLH). Nonetheless, the literature provides no recommendations for treatment of AOSD patients with severe sepsis.

Patient concerns: A previously healthy 65-year-old man with history of AOSD was referred to our hospital for persistent right lower quadrant abdominal pain for 2 days. One week later, an abdominal wall abscess and hematoma developed by extravasation from the inferior epigastric vessels, complicated by necrotizing fasciitis of the right thigh and groin region. To our best knowledge, this case was the first reported case of a perforated appendix complicated with necrotizing fasciitis in a patient with AOSD.

Diagnoses: The patient was diagnosed as acute appendicitis complicated with necrotizing fasciitis and abdominal wall abscess.

Interventions: This case received intravenous tigecycline injection and daily 10 mg prednisolone initially, and shifted to daily intravenous hydrocortisone 200 mg for suspected MAS or HLH. This patient underwent surgical intervention and debridement for necrotizing fasciitis.

Outcomes: The patient's symptoms progressed worse rapidly. He died from cytomegalovirus viremia and bacterial necrotizing fasciitis complicated by septic shock.

Lessons: (1) The steroid dose was difficult to titrate when AOSD complicated by sepsis. The differential diagnosis from MAS/HLH with bacterial/viral infection related severe sepsis was difficult but critical for decision making from clinicians and rheumatologists. (2) The conservative treatment with antibiotics for perforated appendix is safe but has a higher failure rate in immunocomprised patients such as systemic lupus erythematosus and AOSD. Early surgical intervention might contribute to better outcome. (3) The abdominal wall abscess can be spread from intra-abdominal lesion through the inferior epigastric vessels which were as weak points of abdominal wall. Imaging examinations contribute to acute diagnosis and help surgeons perform surgical interventions to prevent morbidity and mortality.

Abbreviations: AOSD = adult-onset Still disease, CMV = cytomegalovirus, DMARD = disease modifying antirheumatic drug, ER = emergency room, HLH = hemophagocytic lymphohistiocytosis, MAS = macrophage activation syndrome, NSAID = nonsteroid anti-inflammatory drug, WCC = white cell count.

Keywords: abdominal wall abscess, adult onset still's disease, appendicitis, necrotizing fasciitis, steroid

Editor: Bernhard Schaller.

Authorship: All authors had access to the data and a role in writing this manuscript

The authors have no funding and no conflicts of interest to disclose.

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Medicine (2018) 97:5(e9794)

Received: 2 August 2017 / Received in final form: 4 December 2017 / Accepted: 9 January 2018

http://dx.doi.org/10.1097/MD.0000000000009794

1. Introduction

Adult-onset Still's disease (AOSD) is a rare multisystemic inflammatory disease characterized by spiking fever, arthralgia, salmon-like rash, sore throat, and abnormal liver function. The etiologic factors and pathogenesis of AOSD are still largely blurry. The clinical research has been limited to case reports and small retrospective series.[1] There is no currently any specific serological markers for AOSD,[2] so the evaluation of the severity of AOSD is also difficult.

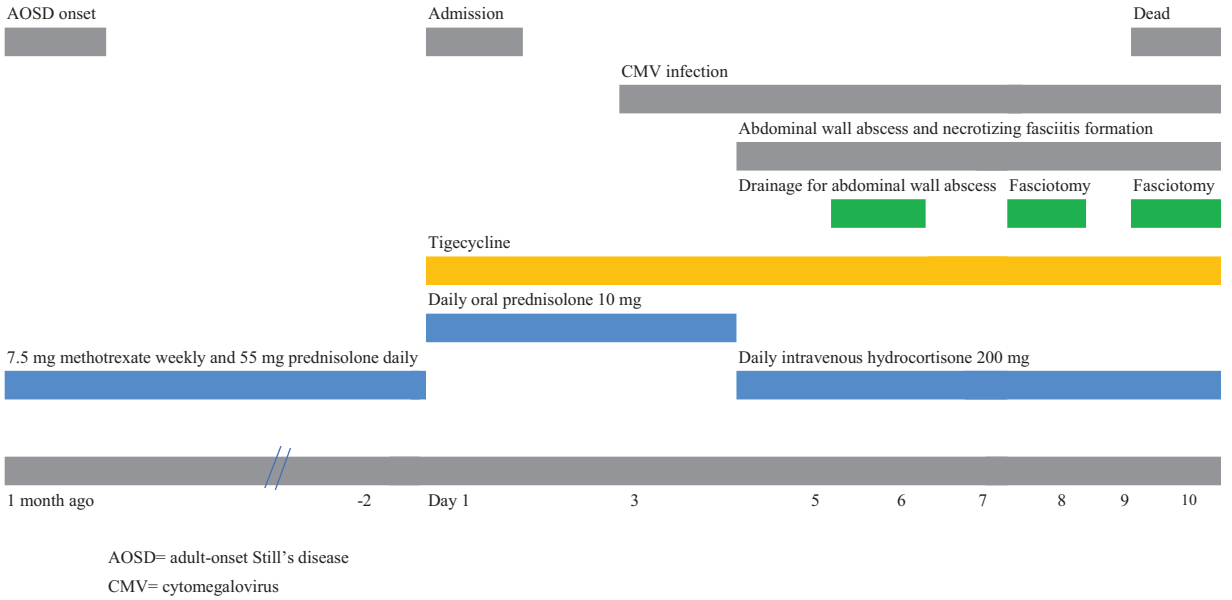
Perforated appendix complicated with necrotizing fasciitis of the abdominal wall or thigh is rare[3,4] and has a high mortality rate of 30%. Conservative treatment with antibiotics for perforated appendix is safe but has a failure rate of about 7%,[5] higher in immunocompromised patients such as steroid using for autoimmune disease. The aggressive treatment must be arranged rather than conservative treatment when AOSD is complicated by infectious episode such as appendicitis.

2. Case presentation

A 65-year-old man, retired Taiwanese, was diagnosed with AOSD 1 month before admission based on Yamaguchi's criteria

Table 1

Timetable of disease events and antibiotics usage.



AOSD= adult-onset Still's disease

CMV= cytomegalovirus

of spiking fever, arthralgia, salmon-like rash, leukocytosis, sore throat, abnormal liver function, and the absence of serum antinuclear antibody and rheumatoid factor (Table 1). He had no history of foreign travel and familial problems. He received 7.5 mg methotrexate weekly and 55 mg prednisolone daily, plus isoniazid because of latent tuberculosis. Tocilizumab treatment had been scheduled to commence after 1 month's treatment with isoniazid. Right lower quadrant abdominal pain developed and continued for 2 days before vising emergency room (ER). The physical finding revealed tenderness and rebounding tenderness over right lower abdomen. Abdominal computed tomography showed a ruptured appendix complicated by localized intra-abdominal peritonitis, but the lesion was capsuled by peritoneum. Patient denied operation at ER, and we decided conservative treatment for the localized limited ruptured appendix. Initial laboratory examinations at ER revealed a white cell count (WCC) 5040/μL with 47.6% neutrophils, C reactive protein 18.56 mg/L, hemoglobin 13.0 g/dL, platelet count 422,000/μL, aspartate aminotransferase 10 U/L, ferritin 985.2 ng/mL, E.S.R. 44 mm/h, and procalcitonin 2.88 ng/dL. After admission, his treatment included fasting, intravenous flumarin 1.0 g per 8 hours injection and daily 10 mg oral prednisolone, which all led to the clinical improvement of his peritonitis. Five days after treatment, pancytopenia developed, with WCC 2320/μL, hemoglobin 10.5 g/dL and a platelet count 117,000/μL. He received daily intravenous 200 mg hydrocortisone for suspected macrophage activation syndrome (MAS) or hemophagocytic lymphohistiocytosis (HLH). One week after admission, an abdominal wall abscess and hematoma developed by extravasation from the inferior epigastric vessels (Figs. 1 and 2), complicated by necrotizing fasciitis of the right thigh and groin region. He was treated with fasciotomy and debridement, which revealed a turbid milk-coffee-like abscess (Fig. 3). The cultures showed *Klebsiella pneumoniae*, *Streptococcus viridans*, and *Enterococcus avium*. We shifted antibiotic from flumarin to intravenous tigecycline 50 mg per 12 hours injection in the second week. He developed cytomegalovirus (CMV) infection complicated by bone marrow suppression with WCC 1260/μL, hemoglobin 10.1 g/dL, and platelets 6000/μL in the last days. He died from bacterial necrotizing fasciitis complicated by septic shock. At autopsy, no evidence of MAS or HLH was seen in liver, spleen or bone marrow.

3. Discussion

Here we reported the first case of a perforated appendix complicated with necrotizing fasciitis in a patient with AOSD.

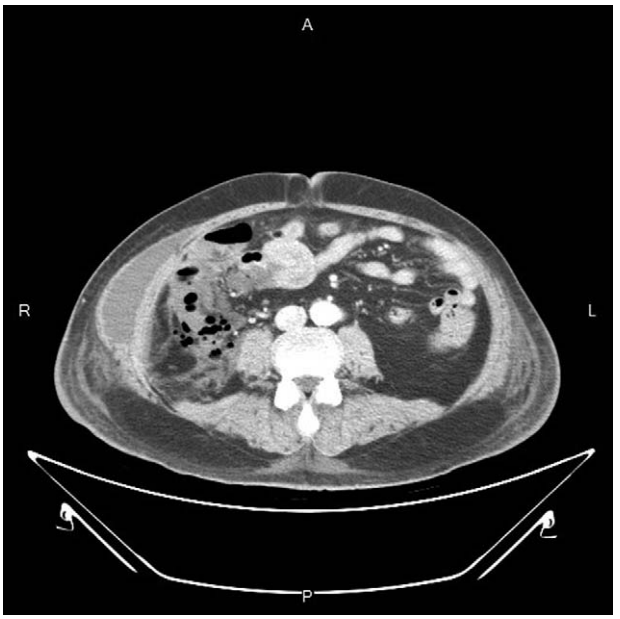


Figure 1. The horizontal view of abdominal computed tomography showed abdominal wall abscess and hematoma developed by extravasation from the inferior epigastric vessels.

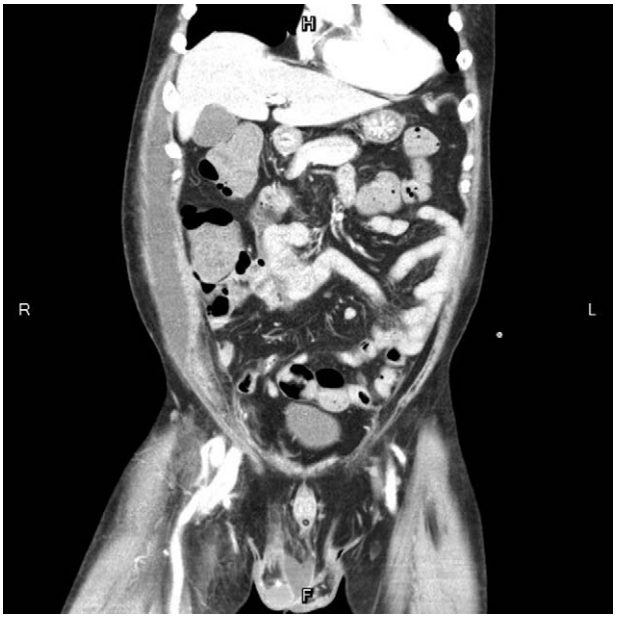


Figure 2. The coronal view of abdominal computed tomography showed abdominal wall abscess and hematoma developed by extravasation from the inferior epigastric vessels.

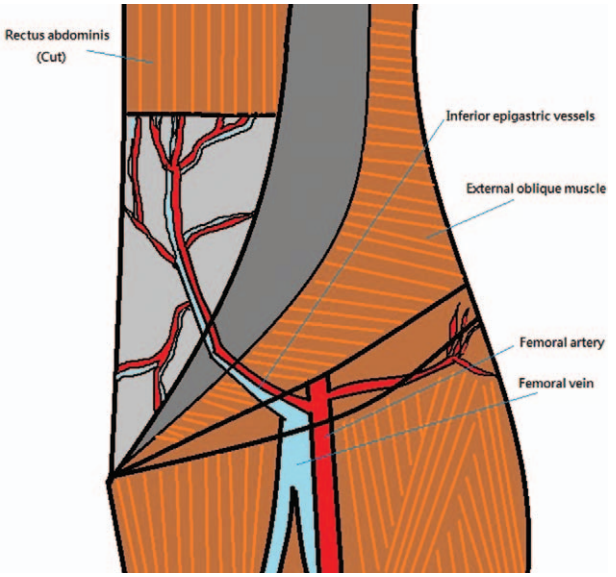


Figure 4. Anatomy of the inferior epigastric vessels identified a weak point between the intra-abdominal space and the abdominal wall.

Perforated appendix complicated with necrotizing fasciitis of the abdominal wall or thigh is rare[3,4] and has a high mortality rate of 30%. Steroid is a standard treatment for AOSD but can mask the toxic signs of appendicitis, and we should pay more attention to differential diagnosis in these complicated and easily missed diagnosis cases at ER. Conservative treatment with antibiotics for perforated appendix is safe but has 7% to 8% failure rate about, higher in immunocompromised patients such as steroid using for autoimmune disease.[5] Emergency surgery must be considered for these patients. This patient was diagnosed with a ruptured appendix complicated by localized peritonitis. A bacterial abscess disseminated through the rectus abdominis muscle and influenced the inferior epigastric vessels, which caused extravasation of hemorrhage-like pus seen on the imaging examinations. The anatomy of the inferior epigastric vessels identified a weak point between the intra-abdominal space and the abdominal wall (Fig. 4). The literature reported rare cases of acute appendicitis with necrotizing fasciitis of unknown association. Based on the anatomical structure and tomographic images, we clearly illustrated a case of ruptured appendix complicated by intestinal pathogens associated with an abdominal wall abscess. The abdominal wall linear hardness, redness, tenderness, and swelling can occurred when abscess formation from intra-abdominal pathogen through inferior epigastric vessels.

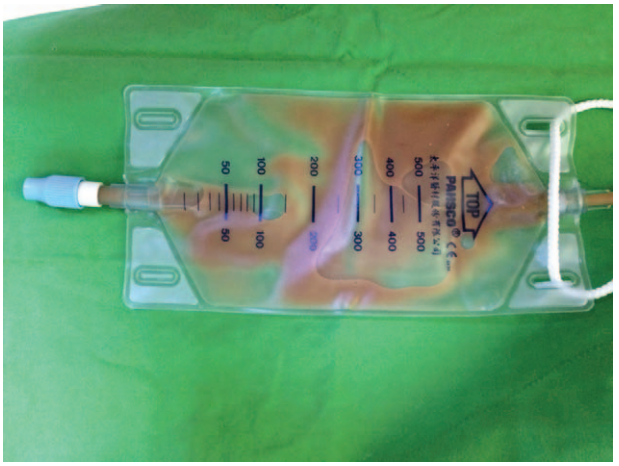


Figure 3. The turbid milk-coffee-like abscess was drained from abdominal wall abscess.

Patients with AOSD receive a titrated dose of steroids after an initial 4 to 6 weeks treatment. Nonetheless, the literature provides no recommendations for treatment of AOSD patients with severe sepsis. MAS and HLH are critical and fatal complications that can occur during the titration of steroid dose. AOSD is a rare systemic inflammatory disorder with unknown pathogenesis.[6] Traditional treatments for AOSD include nonsteroid anti-inflammatory drugs (NSAIDs) and steroids. Patients treated with steroid doses of 0.8 to 1 mg/kg/day achieve faster remissions and have fewer relapses than those who receive lower doses of steroids.[7] Unfortunately, 40% to 45% of patients with AOSD develop steroid dependence and its related long-term adverse effects. Septic shock is a major complication during treatment.[8] Conventional and biologic disease modifying antirheumatic drugs (DMARDs) are required for steroid-sparing treatments to avoid adverse effects.[9] Common complications of AOSD include hepatic failure, disseminated intravascular coagulopathy, thrombotic thrombocytopenic purpura, diffuse alveolar hemorrhage, pulmonary arterial hypertension, MAS, and HLH.[1,10] Nonetheless, in the presence of AOSD, it is difficult to distinguish the development of severe sepsis-related bone marrow suppression from MAS or HLH, which leads to challenging decisions about titrating steroid dose. This patient, who presented with a ruptured appendix and localized peritonitis, was not suitable for surgery.[5] Bacterial intra-abdominal infection complicated by septic shock and CMV viremia developed, followed by severe bone marrow suppression that mimicked MAC or HLH. Here we report a challenging clinical dilemma for accurate diagnosis at ER and adequate treatment for clinicians by presenting a case of

acute appendicitis complicated with necrotizing fasciitis, severe sepsis and bone marrow suppression in an AOSD patient.

4. Conclusion

The mortality rate was higher when perforated appendix complicated with necrotizing fasciitis. The opinion of operation was safer than conservative treatment from patients of AOSD when they suffered from ruptured appendix with localized peritonitis. High-dose steroid and nonsteroid anti-inflammatory drugs are standard treatments for patients with adult-onset Still's disease, and steroid can mask the toxic signs of acute appendicitis. We should pay more attention to patients presented with acute abdomen or abdominal pain and fever in the presence of treatment with high dose steroid at emergency room to make accurate diagnosis and prescribe adequate treatment.

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