

## Abdominal Pain with Severe Sepsis in a Young Woman

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A 18-year-old Thai woman was admitted to Vichaiyut Hospital on February 7, 1995 (H.N. 163808; A.N. 663) because of fever, abdominal pain and jaundice for 7 days.

She had been well until 7 days before admission, when an abdominal pain, developed at epigastrium. Initially the pain was localized and intermittent, then continuous and expanded to around umbilicus. She had nausea and vomiting, but did not lose appetite. She went to a clinic and was treated for peptic disease but the clinical condition did not improve. Two days later, she developed fever and jaundice and was admitted to a private hospital in Bangkok. Physical examination revealed fever with jaundice and tenderness at the upper part of abdomen. Laboratory examination on the first day of that admission revealed Hb 11.6 gm/dl, Hct 35%, total bilirubin 5.5 mg/dl (normal range : 0.5-1.5) direct bilirubin 3.7 mg/dl (normal range : 0.0-0.5), SGOT 516 U/L (<40), SGPT 290 U/L (<40), alkaline phosphatase 1,078 U/L (<48). Plain abdomen and ultrasound of the upper abdomen were reported as unremarkable. The clinical diagnosis was acute viral hepatitis and she was treated symptomatically. However her condition became worse. She developed high fever with chills, anemia, deep jaundice and abdominal pain. Laboratory examination on the 4<sup>th</sup> day of admission showed Hb 9.5 gm/dl, Hct 27%, total bilirubin 8.5 mg/dl, direct bilirubin 5.2 mg/dl, SGOT 76 U/L, SGPT 144 U/L, and alkaline phosphatase 913 U/L. Plain abdomen and ultrasound of the upper abdomen were repeated which showed marked hepatosplenomegaly with diffuse parenchymal disease of liver. The diagnosis of sepsis with

an undefined source was then made and cefazolin and gentamicin were given, and she was transferred to Vichaiyut Hospital.

She is a student who resides in Bangkok and has never been out of the city within the past 3 months. She has been healthy and has no history of taking any drugs prior to this illness. There is no history of anemia nor jaundice in her family. Her menstrual period is normal and she denies any history of sexual contact.

Physical examination on admission revealed a body temperature of 37.8°C, pulse rate 112/min, blood pressure 100/80 mmHg and respiratory rate 40/min. She was very sick, moderately pale, deep icteric and had orthopnea. The heart was normal. Rales were heard in both lower lungs. Abdomen was definitely distended with generalized tenderness and guarding. Rebound tenderness was detected. The liver was enlarged about 3 cms below the right costal margin with tenderness. The spleen was not palpable. No mass or fluid wave was detected. Bowel sound were markedly decreased. Rectal examination revealed a hard stool. The other examinations were negative. Laboratory tests showed Hb 8 gm/dl, Hct 27.4%, WBC 16,500/mm<sup>3</sup>, neutrophil 92%, band 2%, lymphocyte 4%, monocyte 2%, platelet 38,000/mm<sup>3</sup>, prothrombin time 13.9 sec (control, 12.1), partial thromboplastin time 61.2 sec (control, 31.8), thrombin time 13.3 sec (control, 12.0), nonfasting blood sugar 149 mg/dl, blood urea nitrogen 7 mg/dl, creatinine 0.9 mg/dl, alkaline phosphatase 284 U/L (control, <110), SGOT 43 U/L (control, <40), SGPT 73 U/L (control, <40), total bilirubin 7.1 mg/dl (control, <1.5), direct bilirubin

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6.2 mg/dl (control, <0.5), total protein 5.2 gm/dl, albumin 2.2 gm/dl, amylase 8 U/L (control, <90), Sodium 138 mEq/L, potassium 3.0 mEq/L, chloride 100 mEq/L, bicarbonate 24 mEq/L. The serologic tests for HBsAg, HBcAb, HAVIgM, HCV and HIV antibodies were negative. Urinalysis was normal. Two hemocultures were done.

Chest X-ray showed a prominent heart size with pulmonary congestion and edema (Fig.1). The portable plain abdomen film showed haziness of the upper abdomen which may have been from fluid filled stomach. Minimal fluid in pelvic cavity was suspected. The spleen was prominent. No opaque stone was noted. The bowel gas pattern of small and large bowel was unremarkable. No free air was detected.

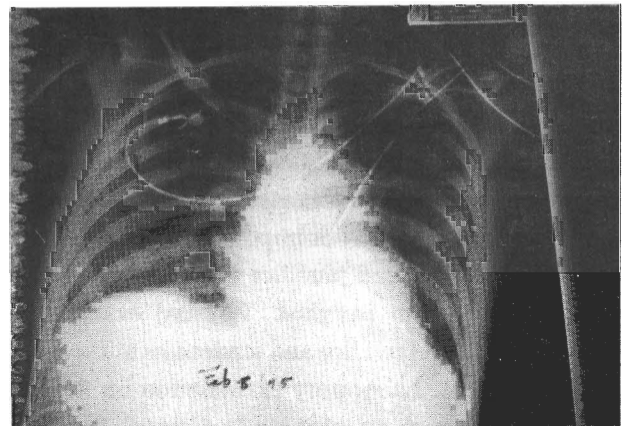
Electrocardiography showed only sinus tachycardia.

Echocardiography revealed good left ventricular function. The ejection fraction was about 60-65%. There was neither chamber enlargement nor pericardial effusion.

Based on the clinical features of sepsis and the rapidly decreased in liver enzymes, the previous diagnosis of acute fulminating hepatitis was disregarded. Since the clinical signs of peritonitis was so definite, there must have been a source of intraperitoneal sepsis. The immediate surgical intervention could not be done because the patient's condition was critical. Hematological evidence suggested disseminated intravascular coagulation associated with severe vasculitis as shown by pulmonary edema and hypoproteinemia. Hypokalemia was also detected. These abnormalities were corrected during the first few hours. A combination of ceftriaxone 2 gm every 12 hours, metronidazole 500 mg every 8 hours, and netilmicin 250 mg once daily was given intravenously. Furosemide and morphine were given for a treatment of pulmonary edema. Packed red cells and fresh frozen plasma were given for replacement therapy. Twelve hours after admission, the patient's general condition was considerably improved. Repeated chest X-rays showed decreased area of pulmonary congestion (Fig.2). Then an exploratory laparotomy was done which revealed ruptured gangrenous appendicitis with localized abscess formation and peritonitis. The liver and spleen were enlarged but there was no other detectable abnormality. Appendectomy with pus drainage and liver biopsy were done. The pus was sent for gram stain and culture. Gram stain revealed mixed organisms and pus culture grew *E. coli* that was sensitive to cephalosporins and aminoglycosides. The

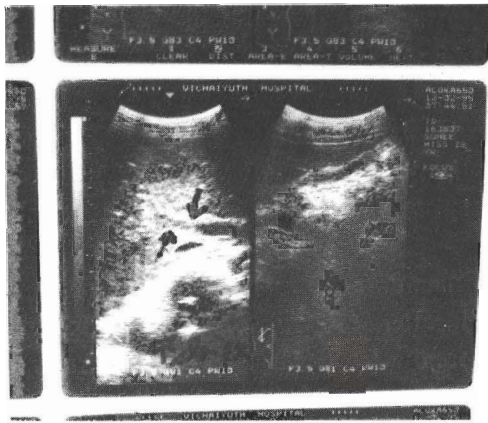


**Fig. 1** Chest X-ray showed prominent heart size with pulmonary congestion and edema.

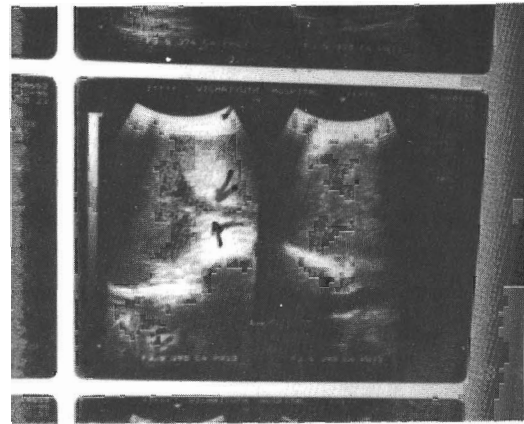


**Fig. 2** The follow-up chest X-ray showed decrease in heart size and pulmonary edema.

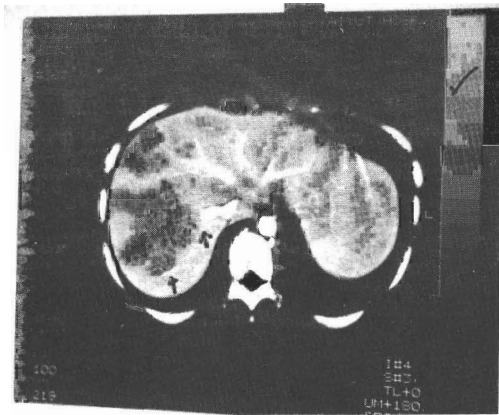
hemocultures done on the first day of admission yielded no growth. Pathology of the liver showed mild fatty change and mild cholestasis. The same antibiotics were continued. The patient's condition improved, and the abdomen was rather soft with some bowel movement. But unexpectedly, she still had high fever and tenderness at the right upper quadrant of abdomen and hepatomegaly. Subdiaphragmatic collection and/or liver abscess were suspected. An ultrasound of the upper abdomen was then performed on the 4th day after surgery which showed hepatosplenomegaly, right portal vein thrombophlebitis with multiple abscesses in the right lobe of the liver, many of which were localized superoposteriorly (Fig. 3). CT scan of the upper abdomen done on the same day confirmed the same diagnosis with evidence of pericholangitis (Fig. 4). Due to the abnormal coagulation a percutaneous liver aspiration was delayed even though the clinical condition did not



**Fig. 3** Sonography of the upper abdomen showed an enlarged liver with multiple illdefined masses of 1.2 up to 6.3 cms. in size in the superior and anterior portion of right lobe of liver. Echogenic shadow in right portal vein was also noted.



**Fig. 5.** The follow-up sonography study of the upper abdomen showed hepatomegaly with decrease in size of abscess in the right lobe. The right portal vein was still dilated and filled with echic thrombus.



**Fig. 4 (A)**CT scan of the upper abdomen showed hepatomegaly with multiple low density lesions in right lobe of liver, more at superoposteriorly. Low density defects in right portal vein and its branches were also seen with enhancing wall.



**Fig. 4 (B)**Pericholangitis was evident.

improve. She was treated with the same antibiotics to cover both aerobic enteric gram-negative bacilli and anaerobes. The temperature was lower and tenderness of the liver was decreased. Her condition improved. Eight days after surgery, the systemic antibiotics were then changed to ofloxacin 200 mg twice daily and metronidazole 200 mg four times a day orally. She was discharged 10 days after surgery and had been followed two weeks after discharge where the clinical condition improved. The follow-up ultrasound of the upper abdomen revealed hepatomegaly with a definite decrease in the extent of low echoic areas in the right lobe. However the right portal vein thrombosis was still evident (Fig. 5). Two and four weeks later she was fully recovered and could return to her normal life. The antibiotics were continued for 8 weeks. The last ultrasound on March 24, 95 revealed a normal liver size with small area of residual liver abscesses. The portal vein was patent and normal in caliber.

## DISCUSSION

This previously healthy 18-year-old woman presented with sudden onset of epigastric pain, followed by fever and jaundice seven days before admission to this hospital. Physical examination revealed signs of peritonitis and laboratory examination revealed anemia, thrombocytopenia, prolonged partial thromboplastin time, hypoalbuminemia and abnormal liver function tests. The chest X-ray showed pulmonary edema. All of these findings suggested that this patient had severe sepsis with multiorgan dysfunction. The most likely source of

sepsis was from intra-abdominal infection. The initial presentation of fever, epigastric pain, jaundice, and abnormal liver function tests especially very high alkaline phosphatase during the first admission in another hospital strongly indicated hepatobiliary tract infection. Biliary tract obstruction with ascending cholangitis and/or liver abscess were the very likely diagnoses, but the recent ultrasound from that hospital was reported as negative. Therefore the sonogram was not repeated. The other diagnostic possibility was acute pancreatitis, as a normal amylase level may be due to the late stage. Rupture of the gastrointestinal tract from a peptic ulcer was less likely because no free air in the plain X-ray of abdomen was detected. The negative history of peptic disease and habitual drugs intake in this young healthy woman made the peptic perforation unlikely. Genitourinary tract infection could be excluded by the history and examination. All of these reasons made rupture appendicitis the probable primary diagnosis. The abnormalities of liver function tests might be from the primary liver involvement or secondary from systemic sepsis.

Since we could not rule out an intra-abdominal surgical condition, the exploratory laparotomy was the most reasonable approach in this patient. Diagnosis of appendicitis is not always easy, the typical historical sequence (poorly localized periumbilical pain followed by nausea and vomiting with subsequent shift of pain to the right lower quadrant) and classical physical findings of cases are presented in only 50 to 60 percent of cases (1). A wide variety of atypical patterns of disease are encountered, especially at the extreme and during pregnancy, which vary with time after the onset of the illness and according to the location of the appendix. It may simulate any diseases which cause abdominal pain. Delay in diagnosis is associated with perforation and an increased morbidity and mortality. The complications of perforated appendicitis are peritonitis, appendiceal abscess and pylephlebitis with or without liver abscess.

Portal vein thrombosis is an uncommon condition associated with a wide variety of conditions including cirrhosis, neoplasms, infection, intra-abdominal inflammatory process, myeloproliferative disorders, etc (2). Infection is an important cause of portal vein thrombosis especially in children, accounting for 43 to 52 percent of all cases (3,4). In adults who have no evidence of cirrhosis or malignant diseases, 10 to 25 percent of cases of portal vein thrombosis are associated with sepsis. Portal pyemia, biliary tract infections, post abdominal

surgery sepsis, amoebic colitis with hepatic abscess, acute necrotizing pancreatitis, diverticulitis and generalised septicemia may lead to portal vein thrombosis. Of these, portal pyemia appears to be the most common and is often secondary to suppurative appendicitis (5,6). On the other hand, acute appendicitis complicated with pylephlebitis is very rare now because of effective antibiotic therapy and surgery. It may occur simultaneously with or follow appendicitis and there have been reports of portal hypertension developing ten years after the initial disease (7,8).

Liver abscess formation is frequently associated with pylephlebitis either as an initial focus leading to infection of the portal system, or more commonly as seeding from the same intraabdominal site that infected the portal vein, which occurred in this patient (9,10). In the past liver abscess associated with pylephlebitis has been recognized as a common complication of intraabdominal infection. In reviewing of studies on pyogenic liver abscess, pylephlebitis was found in 5-10% of cases during the year 1923-1966 (11-14). However it is quite unusual during the past 10-20 years probably because of early diagnosis and immediate appropriate antimicrobial and surgical treatments (15-17). At Vichaiyut Hospital during February 1989-1995, a total of 23 cases of pyogenic liver abscess were documented, and this is the only case of liver abscess secondary to pylephlebitis and appendicitis. The diagnostic work up in a suspicious case of portal vein thrombosis is an ultrasound examination, preferably with color doppler capability and CT scan. MR imaging has recently been introduced for the evaluation of patients with suspected portal vein thrombosis, although the results are preliminary. Portal venography or superior mesenteric arteriography, which has long been used to be a definite diagnosis of portal vein thrombosis, is now replaced by afore-mentioned accurate noninvasive techniques. The recommended management of appendicitis complicated with pylephlebitis and liver abscess is appropriate antibiotics administration combined with surgical therapy, to eradicate sources of infection. Antibiotics must cover all organisms in the gastrointestinal tract, ie gram-positive cocci, gram-negative bacilli and anaerobic bacteria. There is little evidence in the literature that anticoagulant therapy has any beneficial role in portal vein thrombosis. The management of liver abscess secondary to pylephlebitis is the same as the management of a pyogenic liver abscess from the other causes, namely appropriate antibiotics therapy alone

or combined with percutaneous drainage (16-18).

Finally, there is a small subset of patients who present with acute symptoms at the time of thrombosis. It is most often seen in patients who develop portal vein thrombosis secondary to intraabdominal sepsis or suppurative pylephlebitis. It is heralded typically by progressive ascites or signs of intestinal ischemia. Variceal bleeding may occur if varices already exist. This is important because variceal bleeding carries a high mortality, approximately 50 percent in one study (5).

In retrospect, the clinical features of acute liver involvement on the 4th day of the illnesses as demonstrated by transient abnormal liver function tests in this case may be the result of pylephlebitis and early formation of liver abscess. After appendectomy and drainage of abscess, she still had high fever and right upper abdominal pain which resulted from pylephlebitis and multiple liver abscesses. However, after continued appropriate antibiotics, the fever subsided, and her general condition was greatly improved. The long term antibiotics were given to combat intravascular foci as well as anaerobic infection. Hemocultures done on the first day of admission showed no growth which was probably the result of previous antibiotics therapy from the previous hospital. Therefore, the percutaneous liver aspiration was not done with the consideration of not adding more harm to already seriously ill patient. She must be followed up to detect the possible long term complications of portal vein thrombosis such as portal hypertension and variceal bleeding, if the obstruction can not be resolved.

### SUMMARY

We reported a rare complicated case of acute appendicitis in a young Thai woman who presented with acute epigastric pain, fever and jaundice seven days before admission. The diagnosis was delayed until she had peritonitis secondary to ruptured appendicitis and sepsis with multiorgan dysfunction. After treatment with broad spectrum antibiotics and appendectomy, she still had fever and abdominal pain. Repeated ultrasound of the abdomen four days later showed portal vein thrombophlebitis and multiple liver abscesses. The patient was successfully treated with appropriate antibiotics alone without surgery or percutaneous drainage. The antibiotics were continued for eight weeks and she was fully recovered. The last ultrasound examination

of the liver revealed complete disappearance of portal vein thrombosis. However, the subsequent portal hypertension must be observed in a long-term follow-up.

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