



Fever in a Patient with Liver Cirrhosis: Tuberculous Peritonitis with Cytomegalovirus Co-infection

Ying-Chuan Wang¹, Chun-Hsiang Chiu², Yu-Chieh Lin³, Hueng-yuan Shen⁴,
Ya-Sung Yang², and Ning-Chi Wang^{2*}

¹Department of Family Medicine; ²Division of Infectious Diseases and Tropical Medicine,
Department of Internal Medicine; ³Department of Pathology; ⁴Department of Nuclear Medicine,
Tri-Service General Hospital, National Defense Medical Center, Taipei,
Taiwan, Republic of China

Tuberculous peritonitis is an insidious disease without clearly indicative clinical, laboratory, or radiologic findings. Therefore, the diagnosis of this disease is difficult. We present a liver cirrhosis patient who had simultaneous tuberculous peritonitis and reactivation of cytomegalovirus (CMV) infection. The diagnosis of tuberculous peritonitis could have been missed due to concurrent cytomegalovirus viremia and lymphadenitis and because lymphadenopathy was initially believed to be caused by malignancy. Positron emission tomography and computed tomography (PET/CT) scans revealed an increased uptake of the dye over the lymph nodes of the right supraclavicular region, left subclavicular region, and the right-side of the pelvis. These findings were initially considered to be indicative of malignancy related lymphadenopathy. The diagnosis of tuberculous peritonitis was confirmed by paracentesis and Mycobacterium culture of the ascetic fluid. Diagnostic paracentesis with Mycobacterium culture of the ascetic fluid, and endoscopy with biopsy may provide conclusive evidence for the diagnosis of peritoneal tuberculosis.

Key words: liver cirrhosis, tuberculous peritonitis, cytomegalovirus, fever

INTRODUCTION

The incidence of tuberculosis has resurged worldwide during the last 10 years because of the epidemic of human immunodeficiency virus, the rapid spread of multidrug-resistant strains of *Mycobacterium tuberculosis*, and the migration of communities to different parts of the world.¹ Tuberculous peritonitis is one of the most prevalent forms of extrapulmonary tuberculosis.¹ It has an insidious and subtle course without any specific clinical, laboratory, and radiological findings. Therefore, the clinical diagnosis of this disease is extremely difficult. We present a patient with liver cirrhosis with concurrent tuberculous peritonitis and cytomegalovirus (CMV) lymph-

adenitis woman. The initial symptoms of the patient were fever and abdominal distension. The tuberculous peritonitis was not diagnosed because of the presence of concurrent liver cirrhosis and CMV lymphadenitis. This case aims at increasing the awareness among physicians regarding the concurrent occurrence of diseases.

CASE REPORT

A 70-year-old woman had hypertension with congestive heart failure NYHA Fc III for 5 years. She presented distended abdomen and fever for one week. No other symptoms such as chills, nausea, vomiting, diarrhea, and weight loss were found.

A physical exam revealed body temperature 38.3°C and heart rate 110 beats per minute. The abdomen was diffusely distended without tenderness or rebound pain. The patient had lymphadenopathy over right subclavicular region without tenderness.

Laboratory work included white blood cell count of 7700/ μ L without a left shift; hemoglobin of 12.2 g/dL; hematocrit of 35.1%, and CRP 3.19 mg/dL. Chest X ray did not reveal abnormality. A contrast enhanced computed tomography of the abdomen (Fig.1) demonstrated massive ascites, irregular surface of liver, and splenomegaly

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*Corresponding author: Ning-Chi Wang, Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Tri-Service General Hospital, National Defense Medical Center, 3F, No. 325, Sec. 2, Cheng-gong Road, Taipei 114, Taiwan, Republic of China. Tel: +886-2-87927257; Fax: +886-2-87927258; E-mail: Wangmax49@gmail.com

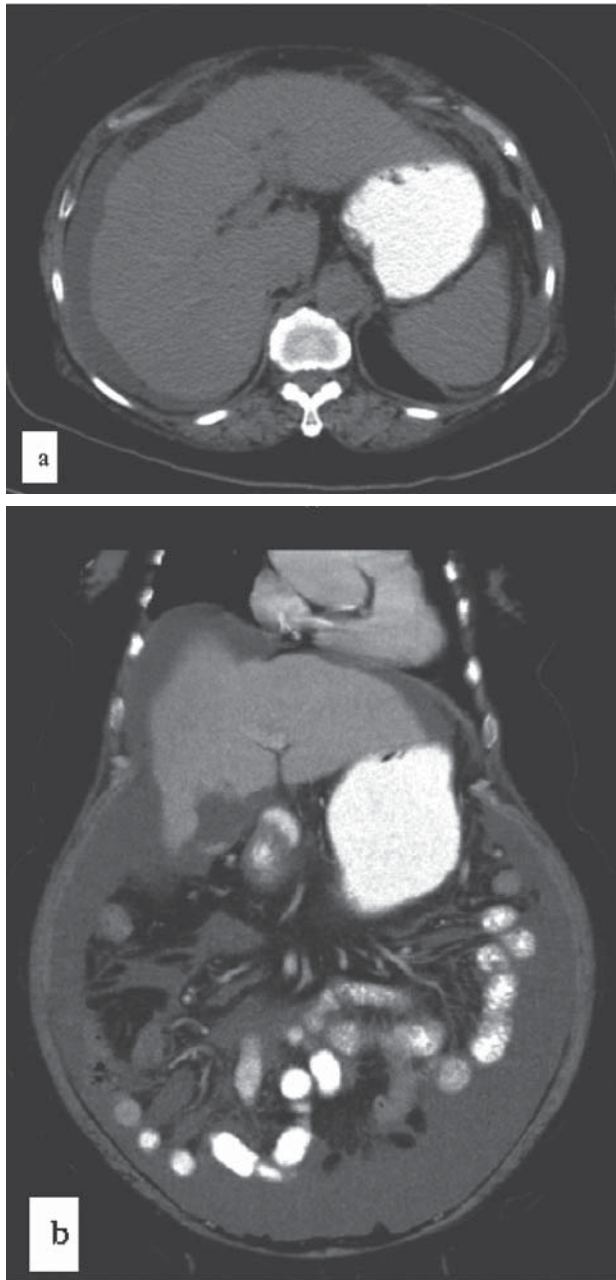


Fig. 1 The contrast enhanced CT of abdomen demonstrated massive ascites, irregular surface of liver, and splenomegaly. (a: axial view and b: coronal view)

with 13cm in length. The patient underwent liver biopsy and the pathology report showed cirrhosis without evidence of malignancy. Diagnostic paracentesis was performed and the data were as followings: WBC: 4000 cells/mm³, Neutrophils 1%, Lymphocyte: 88%, RBC: 21000 cells/mm³, and the serum-ascites albumin gap (SAAG):1.5. It revealed polymorphous lymphoid cells



Fig. 2 F-18-fluorodeoxyglucose (FDG) PET revealed several lesions with FDG accumulation including: lymph nodes at right lower neck, right supraclavicular region, left subclavicular region and right inguinal region and also nodules at spleen.

without malignant cells. Acid fast stain and polymerase chain reaction (PCR) for tuberculosis of ascites fluid were negative. The serum CA-125 showed obvious elevated level of 730.8 unit/ML. Negative results of hepatitis B surface antigen (HBs Ag) and Anti-HCV antibody were noted. Autoimmune diseases markers such as anti-nuclear antibody, anti-mitochondrion antibody, rheumatoid factor, C3, C4 were all within normal range.

Due to high level of CA-125, unknown origin fever, and cervical lymphadenopathy, F-18-fluorodeoxyglucose (FDG) PET was performed using Biograph system (Siemens Inc, German) consisting of integrated PET with two-slice computed tomography (CT). It revealed several lesions with FDG accumulation (Fig.2) including: lymph nodes at right lower neck, right supraclavicular region, left subclavicular region and right inguinal region and also nodules at spleen. Among which, FDG avidity are more intense at the ones of spleen and right lower neck lymph node with standardized uptake values approximate 5.9 and 3.9, respectively. Thus lympho-proliferative disorders are impressed and the differential diagnoses include lymphomas, chronic inflammatory process and opportunistic infection, especially when patient is in immunocompromised condition. Excisional biopsy of right supraclavicular lymph node was performed and the pathology report disclosed histiocytes and atypical transformed lymphoid cell hyperplasia and intranuclear inclusion bodies in interfollicular area by Haematoxylin and Eosin (H&E) staining and immunohistochemical stain of CMV (Fig.3). Positive serum CMV polymerase chain re-

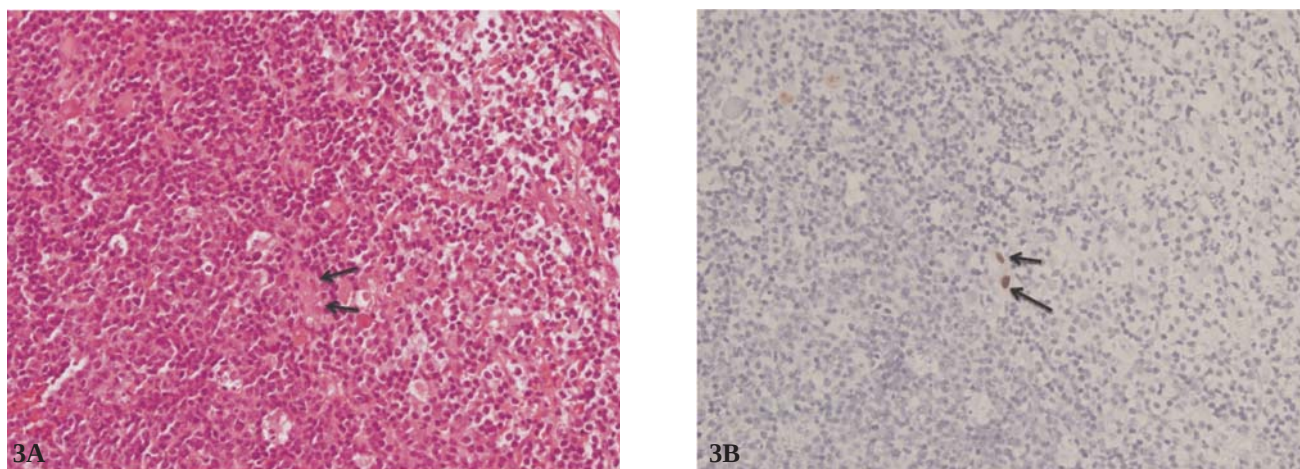


Fig. 3 (a): H&E: some atypical cell with distinct nuclear and ill-defined cytoplasmic inclusions. (b): Immunohistochemical stain of CMV: The atypical cells show positive for immunohistochemical stain of the CMV.

action was also detected. Acute CMV lymphadenitis with atypical lymphoid hyperplasia was diagnosed. Ganciclovir was prescribed for CMV infection.

Fever and ascites persisted despite ganciclovir therapy. Positive tuberculosis culture of ascites fluid was announced 50 days after diagnostic paracentesis. Anti-tuberculous medications were prescribed and fever subsided 2 weeks later when her white blood cell count showed 7600/ μ L without a left shift; and CRP 1.05 mg/dL. The patient was well at a following 3 months later.

DISCUSSION

Liver cirrhosis is the most common underlying disease associated with tuberculous peritonitis.^{2,3} Nonspecific clinical features, laboratory tests, and radiological findings of abdominal tuberculosis made the diagnosis difficult. Because of the simultaneous occurrence of cytomegalovirus lymphadenitis, tuberculous peritonitis could have remained undiagnosed. Although the sensitivity of various methods for the diagnosis of abdominal tuberculosis has already been speculated in previous studies^{3,4}, a definite conclusion has not been drawn.

The clinical presentations of abdominal tuberculosis are nonspecific. The most frequent clinical presentation is abdominal pain followed by fever, weight loss, anorexia, hepatomegaly, ascites, and cervical lymphadenopathy.^{2,4-8} Laboratory investigations of patients with abdominal tuberculosis may reveal anemia (70.4–100%), hypoalbuminemia (48–100%), elevated erythrocyte sedimentation rate (64–100%), leukocytosis (6.4–50%), and elevated levels of serum transaminases (22.4–25%).⁴⁻⁶ The puri-

fied protein derivative skin test (PPD) was positive in 19.2–71% patients.^{4-5,7} In our case, only hypoalbuminemia (3.4 g/dL) was detected.

The radiographic presentation of abdominal tuberculosis frequently mimics those of other conditions; and reports have indicated that 27–37% of patients with abdominal tuberculosis demonstrate abnormalities in chest radiographs.^{5,7-8} Abdominal ultrasonography performed on these patients reveals abnormalities such as ascites, hepatomegaly, mesenteric thickening, and mesenteric lymphadenopathy.^{4,9} However, all the findings are non-specific. Abdominal computed tomography (CT) is considered to be the most convenient and consistent diagnostic tool with accuracy as high as 85–94%.^{4,6,7,10} Mesenteric micro- or macronodules, low-density center in the peritoneal masses, calcifications within the macronodules in the mesentery, or enlarged lymph nodes at other sites have been considered to be the characteristic findings of abdominal tuberculosis.¹¹ The abdominal CT findings in our case included only massive ascites, irregular surface of the liver, and splenomegaly.

Ultrasound-guided fine needle aspiration of abdominal ascitic fluid for analysis was also considered as a reliable diagnostic approach.¹² Although this procedure had been performed in our patient, we were unable to determine the cause of the fever and abdominal distension because the results of culture for the tuberculosis cannot be obtained immediately.

Although the combination of positron emission tomography (PET) and CT have a high negative predictive value (100%) for assessment of fever of unknown origin (FUO)¹³, these modalities can fail to diagnose tubercu-

lous peritonitis. While the abdominal tuberculosis may be highly suspected clinically, further invasive procedures such as laparoscopy and colonoscopy should be considered to obtain the tissue for further mycobacterial and cytological studies, even if the findings of PET/CT are negative.

CONCLUSION

Since the symptoms, laboratory findings, radiologic presentation of tuberculous peritonitis are obscure and nonspecific, delayed diagnosis of this disease is common. For patients presenting with ascites and fever, tuberculous peritonitis can not be excluded even when the PET/CT findings are negative. Abdominal CT scan and further invasive procedures such as laparoscopy with biopsy or diagnostic paracentesis may be required for the diagnosis of this situation.

DISCLOSURE

The author declares that this study has no conflict of interest.

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