Ovarian carcinoma in two patients with chronic liver disease

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Abstract

Ascites is a common and debilitating complication of cirrhosis. However, patients with chronic liver disease are not spared from other causes of ascites and physicians should be careful not to miss an underlying malignancy. Ovarian cancer is an insidious disease, which is difficult to diagnose and it ranks first in mortality among all gynecological cancers. Here, we present two cases of patients with chronic liver disease that developed ascites not simply because of cirrhosis but as a manifestation of ovarian cancer. We would like to emphasize that the causes of ascites, other than the liver itself, should not be overlooked in patients with chronic liver disease.

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Key words: Ovarian carcinoma; Ascites; Chronic liver disease

Isildak M, Guven GS, Kekilli M, Beyazit Y, Erman M. Ovarian carcinoma in two patients with chronic liver disease. World J Gastroenterol 2005; 11(28): 4445-4446

http://www.wjgnet.com/1007-9327/11/4445.asp

INTRODUCTION

Ascites is the most common complication of viral, alcoholic or metabolic liver cirrhosis. Approximately half of the cirrhotic patients are expected to develop ascites within 10 years after the diagnosis[1]. Development of ascites is an important prognostic sign in the usual course of chronic liver disease since it shortens the 5-year survival rate of a cirrhotic patient[2-4].

Ascites may develop in 75% of all patients with liver disease. The remaining 25% is due to malignancy (10%), cardiac failure (3%), pancreatitis (1%), tuberculosis (2%) and other uncommon causes[5]. However, it is important to comprehend that cirrhotic patients are not spared from these non-cirrhotic causes. Herein we present two patients with chronic liver disease who were diagnosed to have ovarian cancer after a thorough investigation of their ascites.

CASE REPORT

Case 1

A 45-year-old woman with chronic liver disease was seen at the outpatient clinic, because of her recent complaints. She complained of abdominal swelling, in the previous 2 mo. She had abdominal pain radiating to her back, which was aggravated after meals. Famotidine was of no use in relieving the pain. She also complained of weight loss as much as 5 kg in 20 d. The patient had been followed up for chronic hepatitis B infection for 8 years. The diagnosis was confirmed with a liver biopsy, which showed cirrhosis at developmental stage. She underwent esophageal variceal band ligation and transjugular intrahepatic portosystemic shunt (TIPSS) for the management of chronic ascites before 5 years. TIPSS was performed once again before 3 years. She received medical treatment while awaiting liver transplantation. She had no evident family history.

Physical examination revealed that she had massive ascites and was admitted to our hospital for further investigation. Ultrasonographic examination of the abdomen had no remarkable finding except ascites and parenchymal changes in the liver. Hepatic and portal venous systems were normal since the portosystemic shunt functioned well. Diagnostic paracentesis was performed and biochemical analysis was as follows: LDH: 318 U/L (concomitant serum LDH was 337 U/L), albumin: 2.4 g/dL (serum albumin: 2.9 g/dL). Cytological investigation of the ascites showed malignant cells. Abdominal computed tomography (CT) revealed peritoneal carcinomatosis and solid mass lesions of both the ovaries. CT of the thorax showed metastatic nodules on the pleural surface. Serum CA 125 level was 9 853 U/mL.

The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and pelvic–paraortic lymph node dissection. Tumor debulking surgery and histopathological examination of the specimens reported that she had ovarian serous papillary adenocarcinoma (stage III). Paclitaxel–carboplatin therapy was started. Unfortunately, during the first course of chemotherapy she developed acute pneumonia and empyema, which rapidly progressed to septic shock leading to her death.

Case 2

A 40-year-old woman was admitted to hospital because of ascites. She was also suffering from loss of weight and appetite...
in the last 10 d. She was known to have had chronic hepatitis B and D. She received interferon treatment for 6 mo, followed by another course of pegylated interferon 2 years later. She had no significant complication of chronic liver disease.

Biochemical analysis of ascites showed an LDH level of 564 U/L and serum-ascites albumin gradient was 0.7. Computed tomography of the abdomen showed massive ascites, omental cake sign and mass lesions of 4-5 cm in both adnexal regions. Serum CA 125 level was 3 028 U/mL. She underwent total abdominal hysterectomy, bilateral oophorectomy, lymph node dissection and tumor debulking surgery. Pathological diagnosis of the tumor was poorly differentiated adenocarcinoma, which was positive for CA 125 and CK7, thus confirming an ovarian origin. Serum CA 125 value of the patient decreased to 25.9 U/mL after the operation.

**DISCUSSION**

Ovarian carcinoma is difficult to diagnose and it is usually discovered only in its advanced stages. It therefore has the highest mortality among all gynecological malignancies. Cachexia with pelvic mass, ascites and elevated CA125 levels generally lead to its correct diagnosis, but usually there are no pathognomonic radiological or laboratory findings. Therefore, a laparatomy is usually necessary for its final diagnosis.

In the majority of ovarian cancer cases, the etiology is unknown. A small percentage of cases may be attributed to hereditary disorders. Close follow-up with annual transvaginal ultrasound examination and measurement of CA125 levels is advocated for patients with high at genetic risk. Prophylactic oophorectomy after completion of fertility may be a reasonable option for BRCA mutation carriers and might be effective in preventing both ovarian or breast cancers. However, such an approach has not been evaluated[6]. Multiple pregnancies or the use of oral contraceptives might have a protective effect as they can reduce ovulation and related hormonal effect[7].

The 5-year survival rate for advanced disease is about 30%. In a study reviewing the general practice records of patients with epithelial ovarian cancer, the most frequent symptoms are abdominal pain, change in bowel habits, abdominal swelling, vaginal bleeding, weight loss, and backache[8]. The same study revealed that the most significant independent variable for survival is the stage of the disease at surgery[8].

Ascites is an important clinical finding in ovarian cancer. Any patient who presents with ascites should undergo a thorough investigation of ascites influencing cytological analysis and measurement of amylase level. Though an elevated CA125 level should raise a suspicion of ovarian cancer, its interpretation in patients with any serosal involvement may not be easy, since any type of pleural, peritoneal or pericardial irritation can lead to elevated serum level of this high molecular weight glycoprotein[9].

CA125 level greater than 35 U/mL has been reported in 35-75% of cirrhotic patients, most commonly in those with ascites. Studies have shown that cirrhotic patients with ascites have different mean serum CA125 levels of 291 and 572 U/mL, respectively[10-12]. All these data show that CA125 is not a strong diagnostic tool for ovarian cancer in patients with preexisting cirrhotic ascites.

Though it is not possible to define a strict dividing line between “expected” and “alarming” ascites during the course of chronic liver disease, some clues may help physicians to find other underlying causes. We believe that the two cases in our study contribute to this. The first patient had a rapid development of ascites despite a functional TIPSS. The other patient did not have overt signs of cirrhotic changes of the liver, the reason why ascites occurred is not clear. In both cases, the presence of an exudative rather than transudative peritoneal fluid is another underlying cause other than cirrhosis[13]. As mentioned above, an elevated CA125 level is not a specific diagnostic marker for ovarian cancer as it may be elevated in a cirrhotic patient, due to peritoneal irritation. Thus, extremely high CA125 levels merit further investigation.

We conclude that the development of ascites in patients with chronic liver disease should never be considered as “normal” and a search for other causes should be considered. Prompt diagnosis and surgical intervention may be life-saving in such cases.

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Science Editor Wang Xl  Language Editor Elsevier HK