Occult Colon Cancer in a Patient with Diabetes and Recurrent *Klebsiella pneumoniae* Liver Abscess

Wen-Hung Hsu,[1] Fang-Jung Yu,[1] Chien-Han Chuang,[2] Chin-Fan Chen,[3] Chien-Ting Lee,[4] and Chien-Yu Lu[1,5]

[1]Division of Gastroenterology, Department of Internal Medicine, and [5]Faculty of Medicine, College of Medicine, Kaohsiung Medical University, [2]Division of Gastrointestinal and General Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung, and Departments of [3]Surgery and [4]Internal Medicine, Pingtung Hospital, Department of Health, Pingtung, Taiwan.

Klebsiella pneumoniae (*Kp*) is a well-known leading cause of liver abscess in patients with diabetes, but recurrent *Kp* liver abscess in such patients within a period of time is seldom seen. Here, we report a patient with diabetes who experienced three episodes of *Kp* liver abscess within 1 year. The patient was subsequently diagnosed to have an occult sigmoid cancer. The liver abscess did not recur after resection of the colonic tumor. Occult sigmoid colonic cancer may have played an important role in the recurrent *Kp* liver abscess in our case. Therefore, further investigation of gastrointestinal malignancies, particularly of the colonic tract, is necessary in patients with diabetes and *Kp* liver abscess.

Key Words: colonic cancer, diabetes mellitus, *Klebsiella pneumoniae*, liver abscess
(*Kaohsiung J Med Sci* 2009;25:98–103)

Liver abscess is a common intra-abdominal infection that has many possible causative pathogens including bacterial, fungal or parasitic organisms. In the 1990s, *Klebsiella pneumonia* (*Kp*) liver abscess was first described as an emerging disease in Taiwan, and *Kp* was found to be the leading cause of liver abscess in patients with diabetes [1–4]. *Kp* is a colonizer of the human gastrointestinal tract and is rarely associated with disease in the normal host. Various diseases have been associated with liver abscess, including biliary tract malignancies, appendicitis, diverticulitis and enteritis [5]. Patients with diabetes mellitus were also found to be more susceptible to *Kp*-associated liver abscess and bacteremia. It is well-known that *Streptococcus bovis* (*Sb*) bacteremia offers a diagnostic marker for the presence of occult colon carcinoma. The ulcerated surface of neoplastic lesions forms a pathway for the microorganism to enter the bloodstream [6]. In addition to *Sb*, other kinds of colon-colonizing bacteria may enter the blood stream via a similar pathway. Here, we report a case of a patient with diabetes with recurrent *Kp* liver abscess who was later confirmed to have an occult sigmoid colonic tumor.

Case Presentation

The case was an 82-year-old female with type 2 diabetes mellitus and hypertension, which were controlled by regular oral medications for more than 20 years. The first time she was admitted to our hospital was on July 10, 2006 for general malaise and fluctuation of self-monitored blood sugar at home.

Received: Jul 18, 2008 Accepted: Sep 8, 2008
Address correspondence and reprint requests to: Dr Chien-Yu Lu, Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Medical University Hospital, 100 Tzyou 1st Road, Kaohsiung 807, Taiwan.
E-mail: dr820188@pchome.com.tw

Laboratory examination showed leukocytosis and elevated C-reactive protein. Accordingly, abdominal ultrasonography (US) was done to identify the focus of infection and a mixed echoic space-occupying lesion was found over the anterior superior segment of the right hepatic lobe (S8), and which showed as a hypodense lesion on routine abdominal computed tomography (CT) (Figure 1). The liver abscess was confirmed by fine needle aspiration with black-red pus from a hepatic-occupying lesion. Blood and aspirated (drained) abscess cultures showed wild-type *Kp*. She was treated with percutaneous transhepatic abscess drainage and parenteral antibiotic during hospitalization. After discharge, an oral antibiotic was prescribed for a total 6 weeks of treatment. Follow-up abdominal US showed the liver abscess was resolved into a residual cystic lesion (Figure 2C).

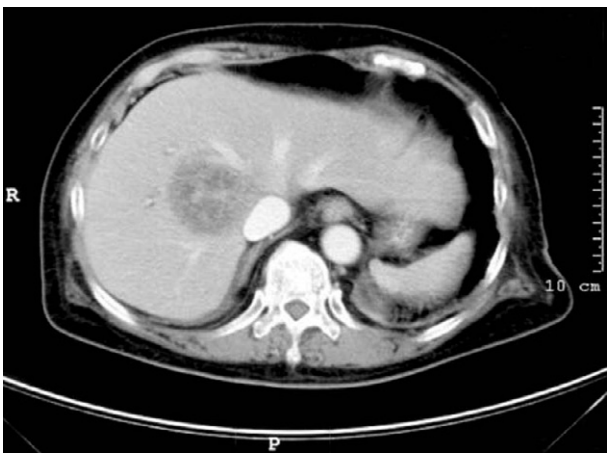

Figure 1. *Abdominal computed tomography at the first admission shows a hypodense space-occupying lesion over the S8 area.*

Unfortunately, this patient developed another two episodes of *Kp* liver abscess in the following year. In May, 2007, she suffered from intermittent fever with chills for 1 week. Complete blood counts showed leukocytosis and mild anemia, but negative stool occult blood test. Abdominal US showed a mixed echoic space-occupying lesion over the posterior superior segment of the right hepatic lobe (S7), which was different from the first episode. Liver abscess was diagnosed by fine needle aspiration of the S7 lesion. Blood and aspirated pus cultures again showed wild-type *Kp*. A similar therapeutic procedure and complete course of antibiotics were also given. Unexpectedly, 3 months later, the third episode of *Kp* liver abscess occurred with the presentation of general malaise and intermittent fever over 1 week. This time, abdominal US disclosed a mixed echoic space-occupying lesion over

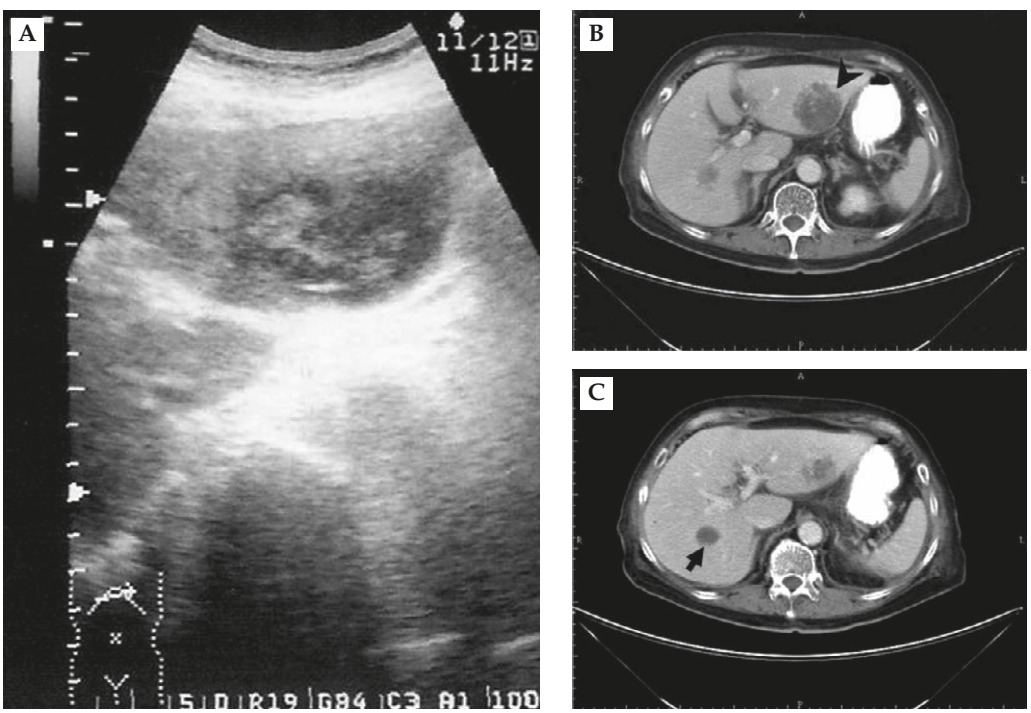

Figure 2. *(A) A heterogeneous space-occupying lesion in the S2 area was found by abdominal ultrasonography. (B) Abdominal computed tomography shows a hypodense lesion over the S2 area (arrowhead). (C) Abdominal computed tomography reveals trace remnants of a previous S8 liver abscess (arrow).*

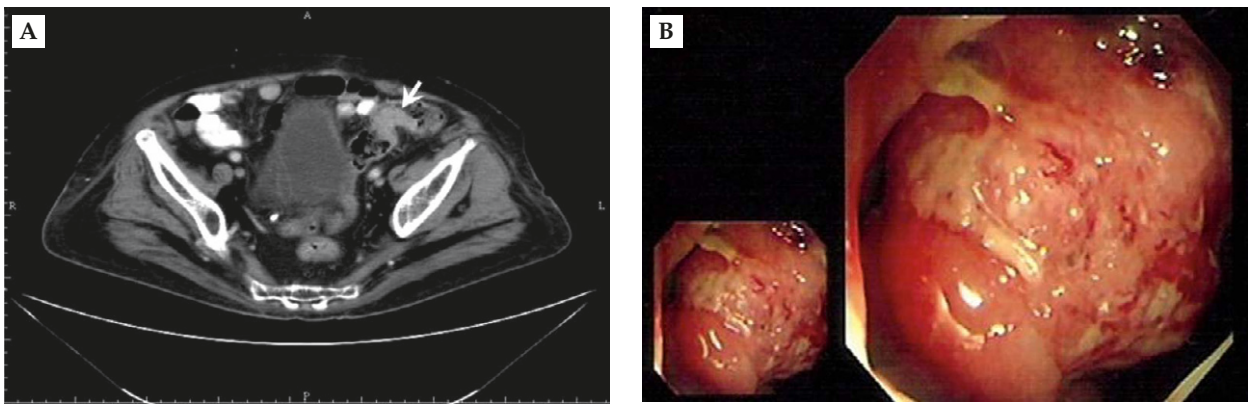

Figure 3. *(A) Abdominal computed tomography extended to the pelvic area shows segmental wall thickness over the sigmoid colon (arrow). (B) An ulcerated tumor mass was detected by colonoscopy and pathologic biopsy verified adenocarcinoma.*

Table. Presentation, location, laboratory data, and treatment of three episodes of liver abscess in our patient

	Time of diagnosis		
	July 2006	May 2007	August 2007
HbA1C (%)	8.8	6.8	6.6
Presentations	General malaise, unstable blood sugar	Intermittent fever with chills	General malaise, intermittent fever
Location of liver abscess	Segment 8	Segment 7	Segment 2
Blood culture	*Kp*	*Kp*	No growth
Abscess culture	*Kp*	*Kp*	*Kp*
Hemoglobin (g/dL)	12.6	10.2	9.5
Stool occult blood	Not checked	Negative	Positive
CEA (ng/mL)	Not checked	Not checked	2.31
Treatment	Abscess drainage, cephalosporin*	Abscess aspiration, cephalosporin*	Abscess aspiration, surgical drainage, cephalosporin*

*Empirical antibiotic with cefotaxime initially, then shifting to cephradine according to culture result and drug sensitivity test. *Kp* = *Klebsiella pneumoniae*; CEA = carcinoembryonic antigen.

the lateral superior segment of the left hepatic lobe (S2), which was surprisingly different from the previous two episodes (Figure 2). Fine needle aspiration of the S2 liver abscess was performed again, and the aspirated pus culture again showed *Kp* bacteria. A progressive decline in her hemoglobin level and positive stool occult blood test were found during this admission.

Colonoscopy was advised, but the patient refused. Again, abdominal CT with enhancement was arranged, and the scan was extended to the pelvic area to completely evaluate the gastrointestinal tract. Segmental wall thickness over the sigmoid colon was noted on the CT scan (Figure 3). Colonoscopy was strongly advised and colonic adenocarcinoma was confirmed by pathologic biopsy. After controlling the infection, surgical intervention was performed to resect the sigmoid tumor. During the operation, periabscess liver tissue was collected for pathologic examination to rule out metastatic lesions, and surgical drainage was done incidentally. Postoperative pathology showed stage IIa ($T_3N_0M_0$) and the tumor had invaded the serosa; however, lymph nodes were not involved.

Discussion

The clinical course of our patient is summarized in the Table. Diabetes mellitus was well controlled in the last two hospitalizations, as documented by HbA1C levels less than 7%. At the first admission, the patient's diagnosis was thought to be primary *Kp* liver abscess because the abdominal CT did not show any other biliary tract or intra-abdominal sources of infection.

The patient did not complain of any abdominal symptoms except for a mild right upper quadrant tenderness due to the liver abscess. The patient did not report any bowel habit change, tenesmus or bloody stool. The misdiagnosis of sigmoid cancer in the first admission could be attributed to the "routine" abdominal CT scan, which does not normally include the pelvic area.

The two subsequent episodes of *Kp* liver abscess occurred in different hepatic segments within 1 year, which implied that these different episodes may arise from the same portal venous seeding of colon colonization [7]. The other findings implicating colonic lesion were that the test of stool occult blood became positive and a decline in hemoglobin levels was noted in the follow-up laboratory data. After resection of sigmoid cancer, no more liver abscess was noted until now.

The association between *Sb* bacteremia with colonic carcinoma is well known. Several possible mechanisms have been proposed to account for this association. Increased *Sb* colonization along with disruption of the colonic mucosa may favor *Sb* bacteremia [6]. Moreover, *Sb* and *Kp* are both colonizers in the human gastrointestinal tract. *Kp*-pathogenic liver abscess is a well-known infectious complication in patients with diabetes [1–4]. Indeed, patients with diabetes are known to show defects in neutrophil chemotaxis and phagocytosis, which are thought to be the most important predisposing factors for *Kp*-pathogenic liver abscess [8]. Most of these cases were thought to be primary *Kp* liver abscess because they were free of biliary disease or other intra-abdominal infection. Patients with diabetes who recovered from primary *Kp* liver abscess after adequate antibiotic treatment have rarely relapsed [2].

Pyogenic liver abscess secondary to malignancy has been reported by Yeh et al [9]. Six patients (11.5%) had colorectal cancers among their 52 studied cases with underlying malignancy. They concluded that pyogenic liver abscess can be a presentation of underlying hepatopancreatobiliary malignant disease before the terminal stage, but carried a poor prognosis compared with non-hepatopancreatobiliary malignant patients [9]. Our patient was a non-hepatopancreatobiliary malignant case and received a good prognosis after surgical resection of sigmoid cancer.

Hiraoka et al reported three cases of *Kp* liver abscess associated with colon cancer and reviewed 41 pyogenic liver abscess cases in their hospital [10]. Malignant disease occurred in 12 of a total of 41 patients (29.3%) including three cases of colonic cancers. In their 41 cases, diabetes mellitus was found to be the most commonly associated disease for liver abscess (14/41, 34.1%), and was also the major medical disease in our patient. Thirty-two of these 41 patients received liver abscess drainage and 71.9% (23/32) patients were positive for bacteria, with *Kp* being the most frequent (13/32, 40.6%), followed by *Escherichia coli* (6/32, 18.8%). Our patient also had positive *Kp* cultures from blood and aspirated pus.

Few reports have described *Kp* liver abscess associated with diabetic and colonic malignancy [10,11]. *Kp* liver abscess could be a complication of *Kp* bacteremia, because this organism enters the portal circulation from the erosive surface of colonic cancer [12]. Diabetes and colonic malignancies may have synergistic effects on the occurrence of *Kp* liver abscess. To our knowledge, *Kp* liver abscess associated with colonic neoplasm have been rarely reported [11]. In our case, the characteristic recurrent episodes of liver abscess prompted us to further investigate if there was any underlying predisposing factor.

Kp liver abscess is a common intra-abdominal infection in patients with diabetes. The real incidence of colonic neoplasms in such cases may be overlooked. Our case with recurrent *Kp* liver abscess reminded us that colonic cancer may also be present without specific symptoms or laboratory findings. *Kp* liver abscess could be the only initial presentation of colonic cancer, and CT of the whole abdomen, including the pelvic area, provides an opportunity to detect possible occult colonic lesions.

Many risk factors have been identified for colorectal cancer including aging, high-fat diet, obesity, familial polyposis syndrome and inflammatory bowel disease. Recent evidence indicates metabolic abnormalities such as impaired glucose tolerance and diabetes mellitus are also associated with increased incidence of colonic adenoma and cancer [13,14]. Insulin resistance and hyperinsulinemia may also play critical roles, but the detailed mechanisms are still being investigated. Accordingly, diabetes mellitus can be thought of as a risk factor for colorectal cancer. In our case, old age and diabetes mellitus were additional prompts to consider further evaluation of colon lesions.

Therefore, we recommend that, when a liver abscess is diagnosed, aggressive evaluation of colonic

occult malignancy is essential, particularly in patients with diabetes.

References

1. Chang SC, Fang CT, Hsueh PR, et al. *Klebsiella pneumoniae* isolates causing liver abscess in Taiwan. *Diagn Microbiol Infect Dis* 2000;37:279–84.
2. Wang JH, Liu YC, Lee SS, et al. Primary liver abscess due to *Klebsiella pneumoniae* in Taiwan. *Clin Infect Dis* 1998;26:1434–8.
3. Lee KT, Wong SR, Sheen PC. Pyogenic liver abscess: an audit of 10 years' experience and analysis of risk factors. *Dig Surg* 2001;18:459–66.
4. Yang CC, Chen CY, Lin XZ, et al. Pyogenic liver abscess in Taiwan: emphasis on gas-forming liver abscess in diabetics. *Am J Gastroenterol* 1993;88:1911–5.
5. Wallack MK, Brown AS, Austrian R, et al. Pyogenic liver abscess secondary to asymptomatic sigmoid diverticulitis. *Ann Surg* 1976;184:241–3.
6. Klein RS, Recco RA, Catalano MT, et al. Association of *Streptococcus bovis* with carcinoma of the colon. *N Engl J Med* 1977;297:800–2.
7. Lai HC, Chan CY, Peng CY, et al. Pyogenic liver abscess associated with large colonic tubulovillous adenoma. *World J Gastroenterol* 2006;12:990–2.
8. Delamaire M, Maugendre D, Moreno M, et al. Impaired leucocyte functions in diabetic patients. *Diabet Med* 1997; 14:29–34.
9. Yeh TS, Jan YY, Jeng LB, et al. Pyogenic liver abscesses in patients with malignant disease: a report of 52 cases treated at a single institution. *Arch Surg* 1998;133: 242–5.
10. Hiraoka A, Yamashita Y, Uesugi K, et al. Three cases of liver abscesses complicated with colon cancer without liver metastasis: importance of screening for digestive disease. *Intern Med* 2007;46:2013–7.
11. Weng SW, Liu JW, Chen WJ, et al. Recurrent *Klebsiella pneumoniae* liver abscess in a diabetic patient followed by *Streptococcus bovis* endocarditis—occult colon tumor plays an important role. *Jpn J Infect Dis* 2005;58: 70–2.
12. Teitz S, Guidetti-Sharon A, Manor H, et al. Pyogenic liver abscess: warning indicator of silent colonic cancer. Report of a case and review of the literature. *Dis Colon Rectum* 1995;38:1220–3.
13. Nilsen TI, Vatten LJ. Prospective study of colorectal cancer risk and physical activity, diabetes, blood glucose and BMI: exploring the hyperinsulinaemia hypothesis. *Br J Cancer* 2001;84:417–22.
14. Giovannucci E, Michaud D. The role of obesity and related metabolic disturbances in cancers of the colon, prostate, and pancreas. *Gastroenterology* 2007; 132:2208–25.

潛藏性大腸癌併發糖尿病患反覆性克雷白氏菌肝膿瘍

許文鴻[1] 余方榮[1] 莊捷翰[2] 陳欽凡[3] 李建廷[4] 盧建宇[1,5]

高雄醫學大學 [1]胃腸內科 [5]醫學院醫學系

[2]高雄醫學大學附設醫院 胃腸外科

署立屏東醫院 [3]外科 [4]內科

克雷白氏菌是糖尿病患者罹患肝膿瘍時常見的致病菌種，但短期內反覆性克雷白氏菌肝膿瘍於糖尿病患者並不常見。在此，我們報告一位女性第二型糖尿病患者，一年之中歷經三次不同位置的肝膿瘍，三次肝膿瘍抽吸培養報告皆為克雷白氏菌，大腸鏡檢查發現乙狀結腸腫瘤，病理切片證實為惡性腺細胞癌。施行腫瘤切除手術後，肝膿瘍未再復發。在此病例，我們認為潛藏性大腸癌對於反覆發作的克雷白氏菌肝膿瘍扮演著重要的角色。因此，對於克雷白氏菌肝膿瘍的糖尿病患者，積極查察腸胃道、尤其是大腸，乃是必要的。

關鍵詞：大腸癌，糖尿病，克雷白氏菌，肝膿瘍

(高雄醫誌 2009;25:98–103)

收文日期：**97** 年 **7** 月 **18** 日

接受刊載：**97** 年 **9** 月 **8** 日

通訊作者：盧建宇醫師

高雄醫學大學附設醫院胃腸內科

高雄市三民區自由一路 **100** 號