

Original Article

Recurrent *Klebsiella pneumoniae* Liver Abscess in a Diabetic Patient Followed by *Streptococcus bovis* Endocarditis – Occult Colon Tumor Plays an Important Role

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SUMMARY: *Klebsiella pneumoniae* is the leading cause of liver abscess in diabetic patients in Taiwan. We report the case of a diabetic patient with a history of four episodes of *K. pneumoniae* liver abscess within 3 years. The patient later developed *Streptococcus bovis* bacteremia originating from a colon tumor with complications of endocarditis, osteomyelitis, and silent splenic abscess. Occult colon tumor may have played an important role in our case, with recurrent infection arising from colonizers of the gastrointestinal tract. As our case shows, the possible association between occult colon tumor and *K. pneumoniae* liver abscess in diabetic patients should be surveyed.

INTRODUCTION

Klebsiella pneumoniae is the leading cause of liver abscess in diabetic patients in Taiwan (1-3). Patients with diabetes mellitus complicated by impaired opsonophagocytosis are much more susceptible to *K. pneumoniae* infection than those without diabetes mellitus (4). However, the pathogenesis has not been completely elucidated. Like *Streptococcus bovis*, *K. pneumoniae* is a colonizer of the human gastrointestinal tract and is rarely associated with disease in the normal host. The association of *S. bovis* endocarditis with carcinoma of the colon is well known. Klein et al. suggested that fecal overgrowth of *S. bovis* in patients with colon carcinoma might disrupt the mucosal barrier and cause *S. bovis* bacteremia (5). In one case report, it was considered that the *K. pneumoniae* liver abscess may also have resulted from *K. pneumoniae* bacteremia after the organism entered into the portal route from the surface of the colon tumor (11). We here report the case of a diabetic patient with repeated *K. pneumoniae* liver abscess who was later confirmed to harbor an occult colon tumor.

PATIENT AND LABORATORY INFORMATION

This 67-year-old male patient was known to have type 2 diabetes mellitus for 20 years with insulin treatment for more than 10 years. He was admitted to our department in November 1997 because of fever, chills, and abdominal pain. He was diagnosed with a *K. pneumoniae* liver abscess and was treated by pigtail drainage and cephalosporin medication. Regular follow-up examinations with abdominal echography showed that the liver abscess was completely resolved. Unfortunately, over the following 2 years, *K. pneumoniae* liver abscesses developed three more times - in February 1998,

October 1998, and February 1999 (Table 1). There was no dyspnea nor heart murmur noted during these three episodes. Cultures of abscess yielded *K. pneumoniae*, but all the blood cultures were negative. A combination treatment of aspiration and intravenous cephalosporin medication was given. A subsequent abdominal ecography also revealed complete resolution.

About 3 years later, in April 2002, the patient presented with a complaint of right shoulder pain and limitation of motion for the previous 7 days and fever and chills for the previous 3 days. Initially, the patient was treated as a case of frozen shoulder before the emergence of fever, since he was right handed and played basketball daily. He had no history of dyspnea, abdominal pain, flank pain, dysuria, nausea, vomiting, drug abuse, or relevant travel.

Physical examination revealed him to be physically fit, well-nourished, and alert, but also fatigued and weak. His blood pressure was 125/75 mmHg, his temperature was 36.8°C, his pulse was 89/min and his respiratory rate was 18/min. His lungs were clear both by percussion and auscultation. A new onset grade 3/6 pansystolic murmur was audible at the apex. The abdomen was not tender to palpation, and without hepatosplenomegaly. In an examination of the extremities, his right shoulder was swollen, tender, and had limited motion with local heat. The white blood cell count was 33,600/mm³, with 95% polymorphonuclear leucocytes. His HbA1c was 8.4%, his GOT 31 U/L, his GPT 26 U/L and his Alk-P 152 IU/L. X-ray examination of the chest and right shoulder were normal. Urine culture revealed no growth but blood culture grew colonies of *S. bovis* (grown on 3 separate sets). The clinical course, pathogens, treatments, and diabetic control in this patient are shown in Table 1.

RESULTS

Initially the patient received intravenous penicillin-G plus gentamicin for suspicion of subacute infective endocarditis but the source was undefined. On the second hospitalization day, a 2-D echocardiogram showed flailed posterior mitral valve due to chordare rupture with new moderate to severe

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Table 1. Clinical course, pathogens, treatments and diabetes mellitus control in this patient

	Year-month	1997-11	1998-2	1998-10	1999-2	2002-4
HbA1c (%)		9.1	8.7	8.6	8.2	8.4
Symptoms and signs		Fever, chills, abdominal pain	Fever	Fever, chills	Fever, chills	Shoulder pain, fever, chills
Infection sites		Liver abscess	Liver abscess	Liver abscess	Liver abscess	Right shoulder osteomyelitis, infective endocarditis, splenic abscess
Isolated bacterial strain		Abscess culture: <i>K. pneumoniae</i> Blood culture: no growth	Abscess culture: <i>K. pneumoniae</i> Blood culture: no growth	Abscess culture: <i>K. pneumoniae</i> Blood culture: no growth	Abscess culture: <i>K. pneumoniae</i> Blood culture: no growth	Blood culture: <i>S. bovis</i>
Drug susceptibility		Cephalosporin (1st, 2nd, 3rd generation) Aminoglycoside Ciprofloxacin	Cephalosporin (1st, 2nd, 3rd generation) Aminoglycoside Ciprofloxacin	Cephalosporin (2nd, 3rd generation) Aminoglycoside Ciprofloxacin	Cephalosporin (2nd, 3rd generation) Aminoglycoside Ciprofloxacin	Penicillin 1st generation cephalosporin Aminoglycoside Ciprofloxacin Vancomycin
Treatment		Intravenous cephalosporin and pigtail drainage	Intravenous cephalosporin and pigtail drainage	Intravenous cephalosporin and pigtail drainage	Intravenous cephalosporin and pigtail drainage	Intravenous penicillin and gentamicin

mitral regurgitation. Infective endocarditis was diagnosed by Duke criteria (11). On the third day, a bone scan and gallium-67 scan were done and revealed an active bone lesion in the right clavicle, and acromion end of the right scapula and right humeral head. On the fourth day, bloody stool was noted. His history showed that he had suffered bloody stool 5-6 times over the previous 6 years (i.e., since 1997), but he did not pay attention to it because it was sporadic. A giant colon villotubular adenoma more than 4 cm in size at 30 cm from the anal verge was found and polypectomy was performed by sigmoidoscopy. On the fifth day, a contrast-enhanced abdominal computer tomogram examination disclosed a silent splenic abscess. The patient received a combination antibiotic treatment with penicillin-G and gentamicin. His fever and chills subsided after the second day of hospitalization. On the seventh day, improvement of leucocytosis, right shoulder pain and limitation of movement were observed. Gentamicin was discontinued after a 2-week course, while intravenous penicillin-G was given for 4 weeks. The right shoulder symptoms were complete recovery and the follow-up abdominal echographic exams showed complete resolution of the splenic abscess. The patient was discharged in good condition and is doing well at present.

DISCUSSION

The association of *S. bovis* endocarditis with carcinoma of the colon is well known. Several possible mechanisms have been proposed to account for this association. Increased colonization along with disruption of the mucosa may favor *S. bovis* bacteremia (5). The adhesion of *S. bovis* to either endothelial cell or extracellular matrix components may contribute to infective endocarditis (6).

K. pneumoniae is the leading cause of liver abscess in diabetic patients in Taiwan (1-3). However, the pathogenesis has not been completely elucidated. Delamaire et al. demonstrated that all steps of polymorphonuclear neutrophil functioning, including adherence, chemotaxis, phagocytosis, and bactericidal activity, were altered in diabetic patients (7), who are more susceptible for *K. pneumoniae* infection. Severe hyperglycemia would alter neutrophil metabolism by

diverting NADPH from superoxide production into the aldose reductase-dependent polyol pathway that connects glucose into sorbitol and thus would impair opsonophagocytosis of type III group B streptococcus (4). This hypothesis could also be applied to the susceptibility to infection of *S. bovis* in diabetic patients. *K. pneumoniae* and *S. bovis* are both colonizers of the human gastrointestinal tract. Like *S. bovis* infection, colonic tumor may play an important role in pathogenesis of *K. pneumoniae* liver abscess, as our case presented with recurrent *K. pneumoniae* liver abscess and later developed complications of endocarditis, osteomyelitis, and silent splenic abscess as a result of *S. bovis* bacteremia originated from colon tumor.

In our case, the patient had a history of four episodes of *K. pneumoniae* liver abscess. However, there was no infective endocarditis or osteomyelitis as a complication of liver abscess in any of his previous *K. pneumoniae* infections. Probably that a lower adherence ratios of *K. pneumoniae* to heart valves comparable with streptococci may explain the result (8).

Splenic abscess, osteomyelitis, and multiple embolisms are more frequent with *S. bovis* infection than with other pathogens of infective endocarditis. Silent splenic abscess, which was disclosed by an abdominal CT scan in this study, has also been reported to be more prevalent among patients with *S. bovis* infection (9). Our case presented musculoskeletal symptoms and fever as the initial signs, but did not have left upper quadrant abdominal pain or tenderness. Most cases have back pain with spondylitis, but our case was characterized by right shoulder pain instead. This may have been the result of decreased immunocompetency due to diabetes mellitus or to a preexisting skeletal disease related to his playing basket ball every day.

To the best of our knowledge, there has been only one other case report describing a *K. pneumoniae* liver abscess in a diabetic patient with occult colonic malignancy (10). The real incidence of colon tumor in such cases may be underestimated. In this diabetic case, according to the 6-year-history of intermittent bloody stool and improvement after polypectomy, we speculate that the recurrent *K. pneumoniae* liver abscess may have been related to the underlying occult

colon tumor, which was disclosed many years after the further complication of *S. bovis* endocarditis. Our case suggested that it is worthwhile to investigate the possible association between *K. pneumoniae* liver abscess and occult colon tumor.

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