Fusobacterium varium Bacteremia Associated with Liver Abscess: A Case Report

Chang-Hua Chen[1,2], *Li-Chen Lin*[2], *Chun-Eng Liu*[1,2], *Tzuu-Guang Young*[1,2]

We describe one case of documented *Fusobacterium varium* bacteremia associated with liver abscess. The patient presented with fever as the only clinical manifestation. An abdominal echogram revealed one hypoechoic lesion over S_7 segment. Blood culture yielded *F. varium*. Cefmetazole was prescribed accordingly for 21 days combined with echo-guided aspiration of the abscess successfully controlled the infection. Physicians should be aware of *F. varium* bacteremia in patients presenting with liver abscess. (*Changhua J Med* 2003;**8**:123-127)

Key words: *Fusobacterium varium*, bacteremia, liver abscess

Introduction

Fusobacterium varium is an uncommon pathogen and often results in multiple clinical manifestations such as abscess, wound infection and others [1]. Liver abscess is one of the most frequent complications [1]. *F. varium* bacteremia associated with liver abscess is rare in Taiwan. We report a patient with documented *F. varium* bacteremia associated with liver abscess. Physicians should consider this infectious agent in the differential diagnosis of in liver abscess.

Case Report

The patient was a 26-year-old male from Changhua County who was in his usual state of good health before he was admitted to our hospital on December 11, 2000 due to a persistent fever for three days. He smoked one pack of cigarettes daily for the past five years, and he drank six cans of beer daily for the past 3 years. During his medical history, he admitted to drinking a folk wine (虎頭蜂酒) three days before, but he denied drinking ground water. Diarrhea, abdominal pain, nausea, and vomiting did not develop during this period. On admission, he was severely ill. His blood pressure was 102/60 mm Hg, heart rate 120 beats/min, respiration rate 24/min, and oral temperature was 37.3 °C. His breath sounds were clear. The abdomen was soft without local tenderness. Laboratory data revealed white blood cell count (WBC) was 8,700/mm^3 with 80% neutrophils, and C-reactive protein (CRP) was 5.26 mg/dL. Biochemical analysis showed aspartate aminotransferase was 51 IU/L, alanine transaminase was 45 IU/L, and total bilirubin was 0.2 mg/dL. Renal function tests revealed blood urea nitrogen was 37.5 mg/dL and creatinine was 2.8 mg/dL. Chest radiography did not demonstrate any abnormalities. Initially, minocycline 100 mg IV every 12 hours was administered because we suspected a rickettsial infection. On the second admission day, an abdominal sonogram showed one hypoechoic lesion (3.0 cm x 2.9 cm) over S_7 segment (Figure 1). Because the blood culture grew gram-negative bacilli, then cefmetazole 2 gm every 12 hours IV was prescribed instead of minocycline. Aspiration of the liver abscess could not be performed because it lacked liquefaction. The patient's fever subsided on the fifth admission day.

Anaerobic blood cultures (BACTEC NR-860 system, Becton Dickinson Diagnostic Instrument Systems, USA) grew Gram-negative bacillus, and the Gram-stain showed pleomorphism, spheroid swelling, and round bodies (Figure 2). The organism grew on CDC ANA agar (BBL, Sensi-Disc, Becton Dickinson, Cockeysville, MD). The antibiotic disk patterns were sensitive to kanamycin and colistin, but resistant to vancomycin (Figure 3). API-20A kit (bio Merieux Vitek, Hazelwood, MO) was used for further identification. The biochemical characteristics summarized in Table 1 show that this

[1] Division of Infectious Disease, Department of Internal Medicine, [2] Infection Control Committee, Changhua Christian Hospital, Changhua , Taiwan

Received: September 12, 2002 Revised: December 23, 2002 Accepted: February 18, 2003

Reprint requests and corresponding to: Dr. Tzuu-Guang Young, Division of Infectious Disease, Department of Internal Medicine, Changhua Christian Hospital, 135 Nanhsiao Street, Changhua 500, Taiwan.

organism is *Fusobacterium varium*. The test for antibiotic susceptibility used the disk diffusion method (BBL, Sensi-Disc, Becton Dickinson, Cockeysville, MD) following the guidelines of the National Committee for Clinical Laboratory Standards [2]. Results were listed in (Table 2). The colonoscopy did not find any abnormality. Follow-up laboratory data showed a WBC of 13,400/mm^3 with 80% neutrophils and CRP was 9.52 mg/dL. The level of alanine transaminase increased to 54 IU/L while creatinine decreased to 1.2 mg/dL. On the 11th admission day, the patient developed a fever that subsided only after echo-guided aspiration of the liver abscess. He was given cefmetazole for 21 days and discharged on January 5, 2001. We prescribed oral metronidazole 500 mg QID for another 21 days. A repeat abdominal sonogram showed resolution of the abscess. The patient remained well during the following three months.

Figure 1. Abdominal echogram showed one hypoechoic lesion (3.0 X 2.9 cm) over S$_7$ segment.

Figure 2. The morphology of the Gram-negative bacilli showed pleomorphic, spheroid swelling, and round bodies (Gram stain, 400 X).

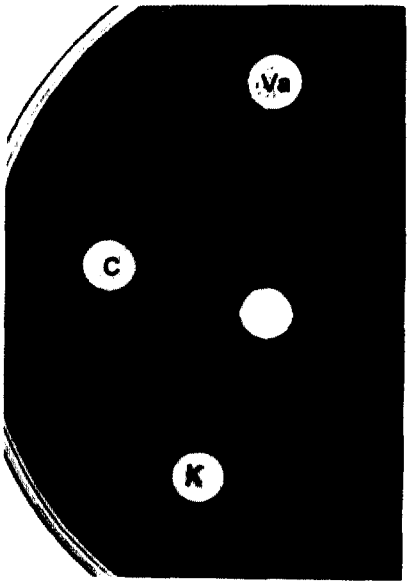

Figure 3. The antibiotic patterns were sensitive to kanamycin and colistin, but resistant to vancomycin.

Table 1. Biochemical characteristics of this isolated strain

Test	results
Morphology	rod
Spore formation	–
Catalase	–
Gram reaction	pink
Urease	+
Indole	–
Esculin hydrolysis	–
Gelatin hydrolysis	–
Gelatin hydrolysis	–
Acid from	
Glucose	–
Lactose	–
Maltose	–
Mannitol	–
Xylose	–
Sucrose	–
Salicin	–
Arabinose	–
Trehalose	–
Glycerol	–
Cellobiose	–
Gluconate	–
Melezitos	–
Raffinose	–
Mannose	+
Sorbitol	–

Table 2. Antibiotic susceptibility of Chromobacterium violaceum isolates

Antimicrobial agents	Susceptibility of isolates
penicillin G (Aqua penicillin)	Sensitive
Ampicillin-clavulanate (Augmentin)	Sensitive
Ampicillin-sulbactam (Unasyn)	Sensitive
Piperacillin-tazobactam (Tazocin)	Sensitive
Imipenem-cilastatin (Tienam)	Sensitive
Cefmetazole (Cefmetazon)	Sensitive
Flomoxef (Flumarin)	Sensitive
Metronidazole (Flagyl)	Sensitive
Clindamycin (Cleocin)	Sensitive

Discussion

Fusobacteria are pale staining, gram-negative, filamentous, obligate anaerobic bacilli from the family Bacteroidaceae. They have diverse cell shapes and colony morphology. Some fusobacteria like *F. varium* may grow in 20% bile. *F. varium* is pleomorphic with spheroid swellings along irregularly stained filaments and round bodies. *F. varium* produces a colony with an opaque center and translucent, irregular margin that resembles a fried egg.

Fusobacteria are catalase negative, indole variable, sensitive to kanamycin and colistin, but resistant to vancomycin [1,3,4]. *F. varium* is indigenous flora of the intestinal tract occasionally isolated from an intra-abdominal infection. It is commonly implicated in serious infections throughout the body, but with some predilection for the lower respiratory tract, head and neck, periodontium, gingiva, and central nervous system [4]. We believe the route of entry for this patient was through the gastrointestinal tract.

The pathogenesis of fusobacterium infection has been investigated in previous studies [5]. Hofstad T et al. attempted to determine factors that contribute to the pathogenicity of fusobacterium by comparing certain virulent characteristics. A lipopolysaccharide endotoxin formed by fusobacterium, contributes to abscess formation [5]. The lipopolysaccharide of fusobacterium strains resembles aerobic gram-negative rods structurally. Most strains have strong biological activity. *F. necrophorum* produces a leukocidin that hemolyzes red blood cells of humans and other animals. Phospholipase A and lysophospholipase produced by *F. necrophorum* may play a role in pathogenesis [4].

The species of Fusobacteria seen most often in clinical infections are *F. nucleatum*, *F. nephrophorum*, *F. moriferum*, and *F. varium*. *F. nucleatum* is the predominant Fusobacterium species and it is often associated with oral, pulmonary, and intra-cranial infections [1]. Fusobacteria have also been frequently isolated from abscesses, the female genital tract, blood, and wound infection [1]. Of the seven Fusobacterium encountered in human infections, *F. nucleatum* is isolated most often as a pathogen in head, neck, and lower respiratory infections. *F. necrophorum* may produce virulent disease. In postanginal sepsis (Lemierre's syndrome) [6], the infection begins with a membranous tonsillitis and proceeds to septicemia with distal metastatic infections that include lung abscess, pleural emphysema, liver abscess, osteomyelitis, and purulent arthritis [4]. This patient presented only with a liver abscess not Lemierre's syndrome probably due to his early diagnosis and treatment.

Most Fusobacteria are susceptible to penicillin; however, penicillin resistance has increased usually because of β-lactamase production [3]. Testing for antimicrobial susceptibility and ability to produce β-lactamase can determine the best proper antimicrobial agent for treatment [1]. In our case, β-lactamase was not produced by the pathogen. So cefmetazole was used for treatment.

In general, Fusobacteria are more susceptible to antimicrobial agents than *Bacteroides fragilis*. Resistance, however, has appears in some species of Fusobacteria. Some strains of *F. nucleatum* and *F. mortiferum* produce β-lactamase, and more than 50% of *F. varium* strains are resistant to clindamycin. Fusobacterium produce L-form colonies on exposure to cell wall-active antimicrobial agents. These appear as transparent growths on agar dilution susceptibility tests, and cause ambiguous interpretation of the minimal inhibition concentration. The organism in our case did not display this transparent growth. Metronidazole, imipenem, the β-lactamase inhibitor combinations, and second- and third-generation cephalosporins are active against most strains [4]. Only two endpoint-determining susceptibility-testing methods for anaerobic bacteria are recommended. One is the agar dilution method, and the other one is the broth microdilution method [8]. We used the disk diffusion test.

In summary, many parenteral antimicrobials are available to treat anaerobic infections including clindamycin, metronidazole, chloramphenicol, cofoxitin, penicillin, β-lactam plus a β-lactamase inhibitor and carbapenem. Anaerobic infections, which are often chronic, require a longer treatment time than for infections caused by facultative anaerobes. Clinical judgment, personal experience, and patient compliance will help to determine the appropriate antimicrobial agent. The duration of therapy ranges from 2 to 4 weeks, which can be individualized depending on the patient's response.

In cases of lung abscesses, treatment may be required for up to 8 weeks. We treated this patient for 6 weeks. Although *F. varium* is an uncommon pathogen, physicians should consider this infectious agent in the evaluation of liver abscess.

References

1. Brook I: Anaerobic Bacteria. In: Armstrong D, Cohen J eds. Infectious Diseases. 1st ed. London : Mosby, 1999.
2. NCCLS: Performance standards for antimicrobial susceptibility testing: eighth information supplyment. NCCLS document M21-T. Villanova, PA: National Committee for Clinical Laboratory Standards,1992.
3. Lorber B: *Bacteroides, Provotella,* and *Fusobacterium* Species. In: Mandell GL, Bennett JE, Dolin R ed. Principles and Practice of Infectious Diseases. 4th ed. New York: Churchill Livingstone, 1995: 2195-204.
4. Baron EJ, Peterson LR, Finegold SM: Bailey & Scott's Diagnostic Microbiology, 9th ed. New York: Mosby, 1994;37:524-50.
5. Hofstad T: Virulence determinants in non-spore-forming anaerobic bacteria. Scand J Infect Dis 1989; (supple 62):15-24.
6. Lemierre A: On certain septicemias due to anaerobic organisms. Lancet 1936;I:701-3.
7. Rosenblatt JE, Briik I: Clinical relevance of susceptibility testing of anaerobic bacteria. Clin Infect Dis 1993;16(suppl 4):S446-8.
8. NCCLS: Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard-fifth edition. NCCLS document M11-A5. NCCLS, 940 West Valley Roads, Suite 1400, Wayne, Pennsylvania, USA 2001.

肝膿瘍合併 *Fusobacterium varium* 菌血症：個例報告

陳昶華[1,2]　林麗眞[2]　劉尊榮[1,2]　楊祖光[1,2]

我們描述一例因爲肝膿瘍合併 *F. varium* 菌血症的個案。在臨床上病患只有發燒，腹部超音波發現在 S_7 有一處病兆，血液培養長出 *F. varium*。我們使用 cefmetazole 以及在超音波指引下抽掉肝膿瘍，成功地治療這位病患。臨床醫師在肝膿瘍病患應該注意有可能是 *F. varium* 感染。 (彰化醫學　2003;**8**:123-127)

關鍵詞：*Fusobacterium varium*，菌血症，肝膿瘍

台灣彰化，彰化基督教醫院 [1]內科部感染科，[2]感染控制小組
受文日期：91 年 9 月 12 日，修改日期：91 年 12 月 23 日，接受刊登：92 年 2 月 18 日
索取抽印本請聯絡：楊祖光醫師，台灣，彰化市 500 南校街 135 號，彰化基督教醫院，內科部感染科。