

Analysis of Fusobacterial Bacteremia Patients During 1998 and 2000:  
Presenting as Co-Existence of Mixed Infections

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Abstract

*Fusobacterium* spp. has been recognized as pathogens. It is therefore important for clinicians and microbiologists to be aware of this infection and its clinical spectrum. We described nine cases of documented fusobacterial bacteremia. We analyzed those clinical and microbiological data. We used the description analysis. The male to female ratio was 8. The mean age was 44.2 years-old. The mean length of stay in hospital was 14.6 days. Clinically, 5 patients had fever and shock occurred in 3 patients. The clinical presentations for the fusobacteria were as following: 3 patients from liver abscess, 2 patient from peritonitis, 1 patient from the soft tissue infection, and 1 patient from the meningitis. Two patients were primary bacteremia. There were three *F. mortiferum*, two *F. necrogenes*, two *F. necrophorum*, one *F. nucleatum*, and one *F. varium*. Three patients died, and 6 patients survived. The mortality rate for fusobacterial bacteremia was 33.3% (3/9). The clinical manifestation of those cases was variable. If microbiological reports are fusobacteria, clinicians should pay attention to mixed infection, not only fusobacteria. (J Intern Med Taiwan 2004; 15: 161-166)

Key Words : *Fusobacterium*, Bacteremia

Introduction

*Fusobacterium* have been recognized as pathogens<sup>1</sup>. The species of fusoacteria seen most often in clinical infections are *F. nucleatum*, *F. necrophorum*, *F. mortiferum*, and *F. varium*<sup>1</sup>. Fusobacteria are frequently isolated from abscesses, gynecologic infections, and wound infection<sup>1</sup>. There is little literature about fusobacterial bacteremia in Taiwan. We reported on nine patients with documented fusobacterial bacteremia. If microbiological report shows fusobacteria, physicians

should pay attention to mixed infection, not only fusobacteria.

## Materials and Methods

A cross-sectional study of fusobacterial bacteremia was conducted by searching the medical records of Changhua Christian Hospital from 1 January 1998 to 31 December 2000. During this period, infectious diseases specialist assessed all patients with a diagnosis of fusobacterial bacteremia, and reviewed all of the patients. The following details were recorded: age, sex, date of admission, severity of underlying disease, date of infection, diagnosis, clinical feature, result of susceptibility test, response to therapy, and outcome.

### Clinical evaluations

The clinical status of the patients at admission and during the subsequent hospital stay was obtained from patient charts. The source of infection was determined according to clinical and microbiological evidence. We then categorized the source of infection according to its originating site, for example liver abscess, meningitis, peritonitis, and soft tissue infection. Primary bacteremia was defined as bacteremia with no apparent original source.

### Microbiological investigations

Blood culture was performed for every patient with suspected sepsis. We used the BACTEC NR-860 system (Beckton Dickinson Diagnostic Instrument Systems, USA) for detecting pathogens. The Gram-stain showed the polymorphic morphology. The organism grew on CDC ANA agar (BBL, Sensi-Disc; Becton Dickinson, Cockeysville, MD). We also did the antibiotic susceptibility test, including the kanamycin, colistin, and vancomycin. The API-20A kit (bio Merieux Vitek, Hazelwood, MO) was done for further identification. The antibiotic susceptibilities used the disk diffusion method (BBL, Sensi-Disc; Becton Dickinson, Cockeysville, MD) and was done according to guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) 2. We tested with  $\beta$ -lactams (penicillin, amoxicillin-clavulanate, cefmetazole, piperacillin-tazobactam, flomoxef and imipenem-cilastatin), clindamycin and metronidazole.

## Results

We analyzed 9 patients with documented fusobacterial bacteremia between 1 January 1998 and 31 December 2000. The male to female ratio was 8 (8:1). The mean age was 44.2 years-old (range: 25-69). The mean length of stay in hospital was 14.6 days (range: 1-21). The demography of those 9 patients showed at Table. There were three *F. mortiferum*, two *F. necrogenes*, two *F. necrophorum*, one *F. nucleatum*, and one *F. varium*. Clinically, 5 patients had fever and shock occurred in 3 patients at the onset of the fusobacterial bacteremia. The clinical presentations for the fusobacteria were as follows: 3 patients from liver abscess, 2 patient from peritonitis (including 1 patient was appendicitis), 1 patient from the soft tissue infection, and 1 patient from the meningitis. Two patients were primary bacteremia. In every cases, empirical antibiotics were commenced at the onset of clinical signs of infection. The antibiotics were ex-changed to those indicated by susceptibility tests. The results of antimicrobial susceptibility tests of all 9 fusobacterial strains were susceptible to metronidazole and clindamycin. Of the 9 patients, 3

patients died, and 6 patients survived. The mortality rate for fusobacterial bacteremia was 33.3% (3/9). The co-existence of other microorganisms was listed at Table. During the study period, there was no outbreak of fusobacterium. There was no Lemierre's syndrome in our study.

#### Discussion and Conclusions

Clinical manifestations of fusobacterial infection were variable in our study. Brook I et al. described the fusobacterium spp has been recognized as pathogen 1. Fusobacteria are frequently isolated from abscesses, gynecologic infections, and wounds infection 1. In our study, there were three patients with liver abscess, two patients with peritonitis, one patient with wound infection, but no patient with the gy-necologic infections.

The microbiological characteristics of the fusobacteria were changeable. Grossly, the fusobacteria are long and thin organisms with tapered ends, and have typical fusiform morphology. Fusobacteria may grow in 20 percent bile. Fusobacteria are pale-staining gram-negative bacilli with diversity of cell shapes and colony morphology. *F. varium* displays pleomorphism, with spheroid swelling along irregularly stained filaments and round dorms. *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 in the intestinal tract and is occasionally isolated from intra-abdominal infection. It may be implicated in infection throughout the body, but with some predilection for lower respiratory tract, head and neck, periodontium, gingival, and central nervous system 4. We thought that the route of entry for that patient could arise from the gastrointestinal tract.

In our study, there were three *F. mortiferum*, two *F. necrogenes*, two *F. necrophorum*, one *F. nucleatum*, and one *F. varium*. The species of fusoacteria seen most often in clinical infections are *F. nucleatum*, *F. necrophorum*, *F. mortiferum*, and *F. varium*. *F. nucleatum* is the predominant fusobacterium sp. Of the seven fusobacteria encountered in human infections, *F. nucleatum* is isolated most often. Those are important pathogens, particularly in head and neck and lower respiratory infections. *F. necrophorum* may be very virulent in certain types of infections. In postanginal sepsis ( Lemierre's syndrome 5 ) ,the infection begins with a membranous tonsillitis and proceeds septicemia with metastatic infection that can include lung abscess, pleural empyema, liver abscess, osteomyelitis, and purulent arthritis 4. In our study, there was no Lemierre's syndrome.

Most fusobacteria remained susceptible to penicillin, but  $\beta$ -lactamase production has been noted in those organisms following penicillin therapy 3. A growing resistance of fusobacteria to penicillins has been noticed in the past decades 6. The main mechanism of resistance of fusobacteria is through the production of the enzyme  $\beta$ -lactemase. Testing for antimicrobial susceptibility and the ability to produce  $\beta$ -lactamase of fusobacteria can assist in the selection of proper antibiotics 1. We had not tested the  $\beta$ -lactamase for those nine fusobacteia because of no available kit. Only two endpoint-determining susceptibility test methods for anaerobic bacteria are recommended 7. One is the agar dilution method, and the other one is broth microdilution method. We used the disk

diffusion test because of no adequate equipment.

The parenteral antimicrobials that can be used in most infectious sites are clindamycin, metronidazole, chloramphenicol, cofoxitin, penicillin ( i.e. ampicillin, ticarcillin, piperacillin),  $\beta$ -lactam plus a  $\beta$ -lactamase inhibitor ( i.e. ampicillin plus sulbactam, piperacillin plus tazobactam), and a carbape-nem ( i.e. imipenem-cilastatin, meropenem). The duration of therapy for anaerobic infections, which are often chronic, is generally longer than for infections caused by aerobes. Clinical judgement, personal experience, safety and patient compliance should direct the physician in the choice of the appropriate antimicrobial agents. In our study, the length of therapy generally ranged between two and six weeks, but should be individualized depending on the response. If microbiological laboratory reports fusobacteria , physicians should pay attention to mixed infection, not only fusobacteria.

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分析 1998 到 2000 間梭狀桿菌菌血症病患：以混合感染表現

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## 摘 要

梭狀桿菌 (*Fusobacterium*) 是一種病原菌，但是對於臨床醫師與醫檢師而言並不常見，本研究是針對梭狀桿菌進行分析。收集梭狀桿菌菌血症病患並進行分析其臨床表現與微生物學特徵。總共有 9 位病患。平均年紀為 44.2 歲，平均住院日數為 14.6 天。臨床上 5 位病患有發燒，3 位發生休克。感染來源分別為：3 位來自肝膿瘍 (liver abscess)、2 位來自腹膜炎 (peritonitis)、1 位來自軟組織感染 (soft tissue infection)、與 1 位來自腦膜炎 (meningitis)；其他 2 位沒有明顯感染來源。分離出來的梭狀桿菌分別為 3 株 *F. mortiferum*、2 株 *F. necrogenes*、2 株 *F. necrophorum*、1 株 *F. nucleatum*、與 1 株 *F. varium*。均為混合感染。總共有 3 位病患死亡，梭狀桿菌菌血症死亡率為 33.3% (3/9)。梭狀桿菌菌血症臨床表現複雜，如果微生物實驗室發出梭狀桿菌報告，臨床醫師應該注意是否為混合感染 (mixed infection)，不能只針對梭狀桿菌進行治療。

**Table 1. The characteristics of those nine fusobacterial bacteremia patients**

number	age	sex	diagnosis	chief complaints	isolate	The same specimen <sup>*a</sup>	Isolate	The co-existence of the isolate <sup>*b</sup>	Route of entry	Treatment(days)	prognosis
1	26	M	Liver abscess	Fever for 2 days	<i>Fusobacterium varium</i>	1) <i>Corynebacterium sp</i>	<i>Fusobacterium varium</i>	<i>nil</i>	Liver abscess	Cefmetazol(21), metronidazole(21)	Survive
2	54	M <sup>*4</sup>	Lung cancer, Uremia, DM, CADs/p	S.O.B. <sup>*1</sup> for 1 day	<i>F. nucleatum</i>	<i>Nil</i>	<i>F. nucleatum</i>	1) <i>MRSA</i> ; 2) <i>Klebsiella pneumoniae</i> ; 3) <i>Pseudomonas aeruginosa</i> ;	Uncertain	Cefmetazole(14)	Expired
3	45	M	Liver abscess	RUQ <sup>*2</sup> pain for 4 days	<i>F. necrophorum</i>	<i>Nil</i>	<i>F. necrophorum</i>	1) <i>Klebsiella pneumoniae</i>	Liver abscess	Cefmetazole(2), augmentin(16)	Survive
4	25	M	Liver abscess	Fever for 2 days	<i>F. necrogenes</i>	<i>Nil</i>	<i>F. necrogenes</i>	1) <i>Fusobacterium necrophorum</i>	Liver abscess	Cefmetazole(5), augmentin(22)	Survive
number	age	sex	diagnosis	chief complaints	isolate	The same specimen <sup>*a</sup>	Isolate	The co-existence of the isolate <sup>*b</sup>	Route of entry	Treatment(days)	prognosis
5	50	M	Esophageal cancer	Coma for 1 day	<i>F. necrogenes</i>	1) <i>beta-streptococcus, non-ABCDE F</i>	<i>F. necrogenes</i>	<i>Nil</i>	Uncertain	Cefuroxime(1)	Expired
6	37	M	Acute appendicitis	Fever and LLQ <sup>*3</sup> pain for 1 day	<i>F. mortiferum</i>	<i>Nil</i>	<i>F. mortiferum</i>	1) <i>Staphylococcus epidermitis</i> ; 2)	Appendicitis	Unasym+anygyn(7), augmentin(7)	Survived

*Br. D*  
*non-enterococ-*  
*us; 3)*  
*Bacteroides*  
*fragilis; 4) E.*  
*coli; 5)*  
*Pseudomonas*  
*aeruginosa*

number	age	sex	diagnosis	chief complaints	isolate	The same specimen* <sup>a</sup>	Isolate	The co-existence of the isolate* <sup>b</sup>	Route of entry	Treatment(days)	prognosis
7	42	M	Cervical spine injury with quadriplagia	Weakness and fever for 3 days	<i>F. mortiferum</i>	1) <i>Corynebacterium sp;</i> 2) <i>Clostridium clostridiumforme</i>	<i>F. mortiferum</i>	Nil	Soft tissue abscess	Cefmetazole(6), imipenem(9)	Expired
8	50	M	Lymphoma	Abdominal pain for 1 day	<i>F. mortiferum</i>	1) <i>Corynebacterium sp.;</i> 2) <i>beta-streptococcus, non-ABCDE</i>	<i>F. mortiferum</i>	Nil	Intra-abdominal infection	Cefmetazole+metronidazole(14), metronidazole(7)	Survived
9	69	F <sup>*5</sup>	Meningitis	Fever for 7 days	<i>F. necrophorum</i>	1) <i>Corynebacterium sp</i>	<i>F. necrophorum</i>	nil	Meningitis	Ceftriaxone(7), imipenem(14)	Survived