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【 CASE REPORT 】

Fusobacterium necrophorum Endocarditis with Liver Abscesses: A Case Report and Review of the Literature

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Abstract:

Fusobacterium necrophorum is a very rare cause of endocarditis. We herein report a case of *F. necrophorum* endocarditis with liver abscesses in a 51-year-old woman. This is the first reported case of monomicrobial *F. necrophorum* endocarditis to present in a patient over 50 years old. We also reviewed 10 reported cases, including the present case. Our review indicated that anaerobic bacteria, including Gram-negative anaerobic bacilli such as *F. necrophorum*, should be considered in the differential diagnosis of infective endocarditis, especially in patients without preexisting organic heart disease.

Key words: infectious endocarditis, *Fusobacterium necrophorum*, liver abscess

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Introduction

Fusobacterium spp. are obligate anaerobic Gram-negative bacilli that are rare causes of several severe diseases (1, 2). *F. nucleatum* is the most frequent causative species (61%) of *Fusobacterium* spp. bacteremia, followed by *F. necrophorum* (25%). *F. necrophorum* bacteremia typically occurs in younger populations without underlying comorbidities and is usually absent in patients over 40 years old (2).

Endocarditis due to anaerobic Gram-negative bacilli is relatively uncommon. We herein report the first case of *F. necrophorum* endocarditis in a patient over 50 years old and review 9 previously reported cases.

Case Report

A 51-year-old previously healthy woman presented to the emergency room complaining of a fever, weakness and chills. Her vital signs upon admission were as follows: temperature, 40.7 °C; blood pressure, 144/90 mmHg; and pulse rate, 110 beats/minute.

A physical examination showed no abnormalities in her heart or lungs. The abdomen was benign, the liver and spleen were not palpable, and the patient had no tenderness or skin lesions. Although the patient had severe dental and periodontal disease, no pharyngitis or jugular venous thrombophlebitis of the neck were evidenced.

Chest X-ray revealed no infiltrate or congestion. Laboratory tests showed leukocytes, 2,780/mm^3; platelets, 142,000/mm^3; urea nitrogen, 14 mg/dL; and creatinine, 0.77 mg/dL. Liver tests showed aspartate transaminase, 54 IU/L; alanine transaminase, 26 IU/L; lactate dehydrogenase, 254 IU/L; and total bilirubin, 0.6 mg/dL. Serologic studies showed that the patient's C-reactive protein was 10.92 mg/dL, and her rheumatoid factor was 17.0 IU/mL (normal range 0-15.0 IU/mL). Other laboratory findings showed elevated levels of presepsin (584 pg/mL), a specific biomarker in patients with sepsis (normal range 0-313 pg/mL) as well as fibrinogen (563 mg/dL), fibrin degradation products (34.4 mg/L) and D-dimer (10.88 mg/L). Her urinalysis showed 4+ proteinuria and 10-19 red blood cells per high-power field. Two sets of both aerobic and anaerobic blood cultures were obtained from two different sites on the day of admission. Both anaerobic blood cultures grew Gram-negative bacilli within 48 hours; these bacilli were identified by day 6 as *F. necropho-*

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rum. The aerobic blood cultures were sterile. The urine culture obtained on the day of admission was negative.

Initial computed tomography (CT) of the chest and abdomen performed without intravenous contrast showed two 1-cm hypodense lesions on the right hepatic lobe and diffuse swelling of both kidneys. Colonoscopy showed no abnormal findings. An ultrasound examination of the neck showed no evidence of thrombus of the bilateral neck veins. Transthoracic echocardiography revealed 6×7-mm vegetation on the anterior mitral leaflet and mild mitral valve regurgitation (Fig. 1). Repeated CT of the abdomen performed on day 4 of hospitalization showed 2 complex liver lesions enhanced with intravenous contrast, which were 1.4×1.2 cm in S7 and 1.8×1.9 cm in S8, suggesting abscesses. The enhanced lesion in S8 was accompanied by a nonenhanced area in a branch of the right hepatic vein, suggesting hepatic vein thrombus. CT showed no evidence of biliary tract infection (Fig. 2).

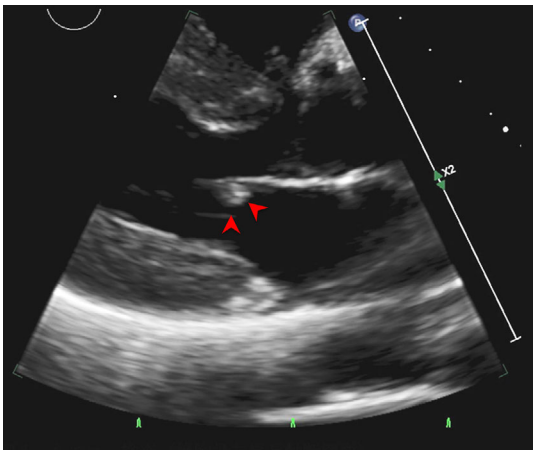

Figure 1. Transthoracic echocardiogram. Image shows 6×7-mm vegetation (arrowheads) on the anterior mitral leaflet.

The patient was administered meropenem starting one day after obtaining the blood culture samples, but it caused drug-eruption. Because the Gram-negative bacilli isolated from both blood culture sets were sensitive to meropenem and ceftriaxone (Table 1), the patient was intravenously administered ceftriaxone starting on day 4. Her temperature appeared to stabilize; however, this improvement was short-lived. Ten days later, she became febrile again (temperature, 39.4 °C). Four more blood culture sets were obtained 9 and 14 days after admission (6 and 11 days after ceftriaxone administration) and were negative. Metronidazole was added to the ceftriaxone on day 16 after admission, and her fever decreased over the next 4 weeks. Metronidazole combined with ceftriaxone was continued for four weeks without side effects.

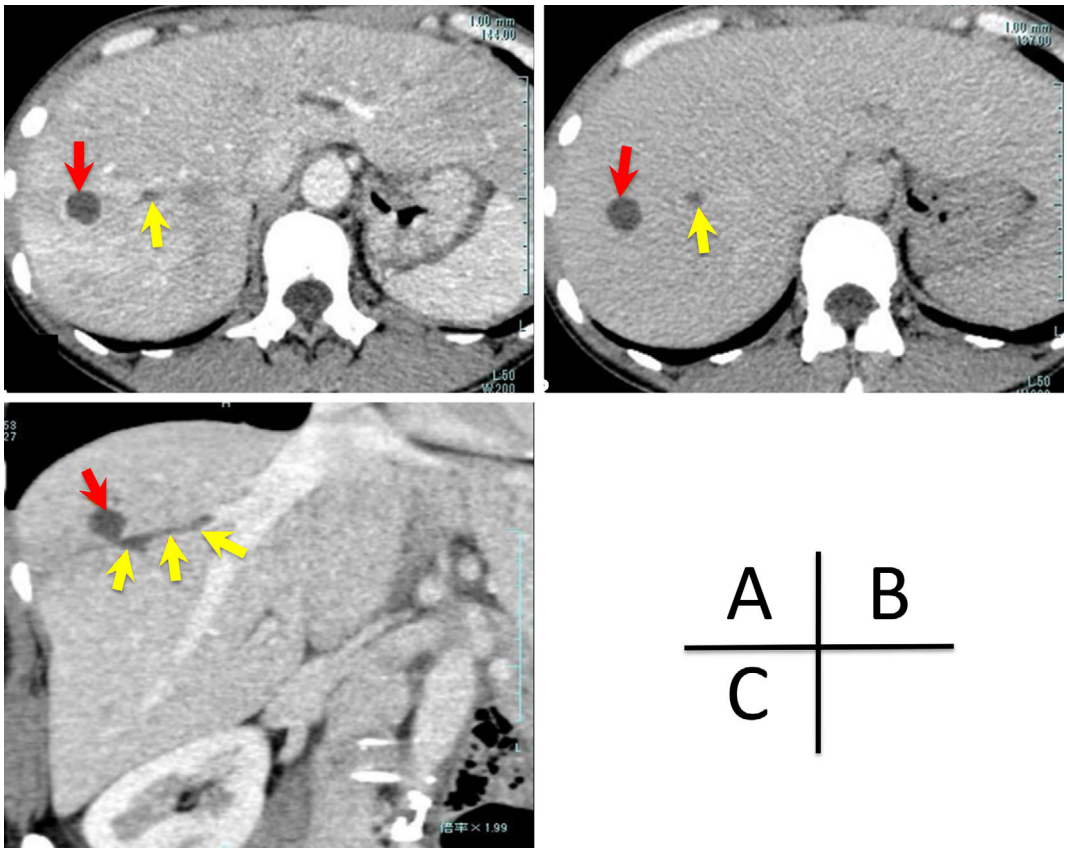

Figure 2. Computed tomography scans of the abdomen demonstrating liver abscesses (red arrows) and hepatic vein thrombus (yellow arrows). A: arterial-dominant phase, B: equilibrium phase, C: portal-dominant phase.

Table 1. Minimum Inhibitory Concentrations (MICs).

Antimicrobial agent	MIC (mg/L)
Benzylpenicillin	≤0.03
Ampicillin	≤0.03
Ampicillin/Sulbactam	≤0.25
Piperacillin/Tazobactam	≤16
Cefoperazone/Sulbactam	≤8
Cefazolin	≤0.5
Ceftriaxone	≤0.06
Ceftazidime	≤1
Cefepime	≤0.06
Cefmetazole	≤1
Flomoxef	≤1
Imipenem/Cilastatin	≤0.06
Meropenem	≤0.06
Minocycline	≤0.12
Clindamycin	≤0.12
Levofloxacin	2
Chloramphenicol	1
Clarithromycin	8
Azithromycin	1

Discussion

Anaerobic bacteria are uncommon causes of infective endocarditis (IE) (2-16%) (3). Anaerobic IE has been associated with a lower frequency of preexisting valvular heart disease than of endocarditis caused by aerobic bacteria (4). The echocardiographic results may be normal in up to half of all cases and therefore cannot be used to rule out an IE diagnosis (5). Anaerobic Gram-negative bacilli attack normal valves more often than do typical microorganisms that cause IE. Underlying cardiac disease is seen only in one-third of *F. necrophorum* endocarditis cases (4, 6, 7).

Major embolic phenomena are a prominent complication of endocarditis caused by anaerobic Gram-negative bacilli (3, 6). Septic embolization to distal sites, which can bring about "metastatic abscesses", is common in patients with such endocarditis (8, 9). Lemierre's syndrome, the usual etiologic agent of which is *F. necrophorum*, involves septic thrombophlebitis of the internal jugular vein, usually secondary to an acute oropharyngeal infection, and is frequently complicated by metastatic abscesses. Although the lung is the most common metastatic target, other reported

Table 2. Published Data on Patients with Monomicrobial *Fusobacterium necrophorum* Endocarditis.

Case No.	References	Reported year	Age/ sex	Presumed infection source	Prior cardiac abnormalities	Valve involved	Complications	Treatment/outcome
1	16	1983	16/F	URTI	Not stated	Vegetation on prolapsed mitral valve	Meningitis with 12th cranial nerve paresis and sphenoidal sinusitis	Penicillin and metronidazole /survived
2	17	1992	2/M	Pneumonia	None	Severe MR	Pyopneumothorax, chest wall abscess and CHF	Vancomycin, ceftazidime and metronidazole/ survived after MVR
3	5	1992	2/M	Pneumonia	None	Severe MR due to chordal rupture	Pneumothorax, lung abscesses	Vancomycin, ceftazidime and metronidazole/ survived after MVR
4	18	2007	20/M	Enteritis	None	Vegetation on aortic valve, mild AR	None	Penicillin/survived
5	19	2010	20/F	URTI	Unable to identify	Vegetation on mitral valve, severe MR	Pneumothorax	Cefotaxim and levofloxacin/ died after MVR
6	20	2011	25/M	Pharyngitis	None	Vegetation on tricuspid valve	Lung abscesses, abscess in gluteal region with myositis and fasciitis, facial vein thrombosis	Clindamycin and penicillin / survived
7	9	2011	25/M	URTI	Bicuspid aortic valve	Vegetation on aortic valve, severe AR	Liver and splenic abscesses	Piperacillin/tazobactam/ survived after AVR
8	15	2013	34/M	Dental procedure	None	Vegetation on mitral valve	Cerebral infarction and acute respiratory distress syndrome	Vancomycin, ceftriaxone and metronidazole/died
9	21	2020	49/M	Unable to identify	None	Vegetation on aortic valve, no AR	Lung and liver abscesses and kidney infarction	Piperacillin/tazobactam/ survived
Our case			51/F	Dental and periodontal disease	None	Vegetation on mitral valve, mild MR	Liver abscesses	Ceftriaxone and metronidazole/survived

M: male, F: female, URTI: upper respiratory tract infection, MR: mitral regurgitation, CHF: congestive heart failure, MVR: mitral valve replacement, AR: aortic regurgitation, AVR: aortic valve replacement

sites of disseminated septic embolism include the systemic joints, muscles, kidneys, liver and spleen associated with abscesses (9, 10). *F. necrophorum* can produce endotoxins and leukotoxins and affect platelet aggregation, which is thought to cause the distinguishing clinical features (11, 12). Our patient had a severe dental infection and liver abscesses accompanied by hepatic vein thrombus. Because the liver abscesses may have been associated with biliary tract infection or a rectal lesion, CT and colonoscopy were performed but showed no evidence of the source of the patient's bacteremia. Brain CT and magnetic resonance imaging had not been performed, as the physical examination showed no abnormality in neurological findings.

Historically, *F. necrophorum* has more than 50 synonyms owing to inadequate reporting of microbiological details and confusion pertaining to the nomenclature in earlier eras (13, 14). Unsophisticated anaerobic culturing methods are thought to have led to the misattribution of a causal role to organisms such as streptococci. Thus, *F. necrophorum* was not always reliably identified in cases reported before 1950 (14, 15). Table 2 summarizes the clinical features and hospital courses of previously published cases of monomicrobial *F. necrophorum* endocarditis as well as those of our case. Some cases in which a monomicrobial infection could not be confirmed were excluded from Table 2. To our knowledge, nine cases other than our own have been reported since 1980 (5, 9, 15-21). Six of these patients had no history of valvular heart disease. Metastatic abscesses were identified in 6 of the 10 total patients, including our patient. Five of the 10 patients were treated successfully with medication alone, without the need for valve replacement. The mean age of the 9 previously reported patients was 21 years old, ranging from 2-49 years old. Ours is the first reported case of monomicrobial *F. necrophorum* endocarditis in a patient over 50 years old.

F. necrophorum can be difficult to culture and requires prolonged incubation under strict anaerobic conditions (5, 8, 22, 23). Stuart and Wren (5) reported that *F. necrophorum* should be considered as a causative bacterium along with other microorganisms known to cause culture-negative endocarditis if IE is suspected clinically but aerobic cultures are negative while the heart is structurally normal.

Although *F. necrophorum* is susceptible to many antibiotics *in vitro*, the clinical response may be much slower than this sensitivity suggests (8, 17). Regardless of the infectious focus, *Fusobacterium* bacteremia should be treated with combination therapy consisting of a third-generation cephalosporin and additional antibiotics against anaerobes, as *Fusobacterium* infections are often polymicrobial and may be caused by beta-lactamase-producing strains (3, 6, 9, 23, 24). Metronidazole was administered to four of the nine previously reported patients with *F. necrophorum* endocarditis. Kuppalli et al. (22) reported that metronidazole has good tissue penetration, and the combination of ceftriaxone and metronidazole can successfully treat *F. necrophorum* infections. Metronidazole appeared effective in our patient.

Conclusion

We treated a 51-year-old patient with *F. necrophorum* endocarditis. In the differential diagnosis of IE in patients without preexisting valvular heart disease, anaerobic bacteria, including Gram-negative anaerobic bacilli such as *F. necrophorum*, should be considered as possible causative organisms, regardless of the patient's age.

The authors state that they have no Conflict of Interest (COI).

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