

Epidemiology and Clinical Outcomes in Patients with *Fusobacterium* Bacteremia in a Tertiary Care Hospital

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Abstract

Background: *Fusobacterium* are anaerobic gram negative bacilli, and are normal flora of the oral, gastrointestinal (GI), respiratory, and vaginal mucosa. Infection with *Fusobacterium* occurs as a result of disruption of mucosal surfaces, most often in the elderly, and patients (pts) with medical comorbidities. *Fusobacterium* bacteremia (FB) accounts for 0.9% of all bacteremia cases, with a mortality rate of up to 47.4%. We described the epidemiology and outcomes of pts with FB at a tertiary care hospital in the United States – this is the second study on FB to be conducted in the US in 30 years.

Methods: A 10-year retrospective study was conducted in pts with FB at Summa Health System in northeastern Ohio. Demographic, clinical, laboratory, treatment, and outcome data were collected. Fisher's Exact Test and T-test were utilized for statistical analysis.

Results: Nineteen pts with FB were identified. The frequency of FB during this period was 0.01%. The mean age was 58.6 years and 16 pts were >40 years old. Sixteen pts were Caucasian, and 10 pts were female. The most common comorbidities were cardiovascular disease (CVD) and immunosuppression. The most common presenting variables were GI complaints, sepsis, hyperthermia, leukocytosis, and elevated creatinine. The infection sources were GI, genitourinary, respiratory, and unclear in 21.0%. Eighteen patients were treated with antibiotics, with 78.9% on appropriate antibiotic regimens. Thirteen pts required ICU, and 7 pts were mechanically ventilated. The 30 day mortality was 21.1%. Elevated creatinine and mental status changes were associated with a significantly higher mortality ($p=0.0181$ and 0.0374 respectively). CVD, diabetes, and ICU admission were associated with a significant increase in length of hospital stay (LHS), ($p=0.0017$, 0.0010 , and 0.0379 respectively).

Conclusions: FB had a very low prevalence at Summa Health System (1:10,000 cases). Increased creatinine and mental status changes were associated with a significant increase in mortality. CVD, diabetes, and ICU admission were associated with a significant increase in LHS.

Introduction

- Fusobacterium* are obligate anaerobic gram negative bacilli which inhabit oral, gastrointestinal (GI), upper-respiratory, vaginal, and colonic mucosa as part of the normal flora (1).
- Fusobacterium* infections occur through disruption of mucosal surfaces from trauma, tumor, or prior infection, which causes oropharyngeal disease, pleuropulmonary infection, and bacteremia (1).
- Fusobacterium* bacteremia (FB) accounts for 0.9% of all human bacteremia cases, is thought to arise predominantly from a GI focus, and is associated with a variable mortality, ranging from 0% to 47.4% (1-5)
- Immunocompromised patients, the elderly, diabetics, patients with renal insufficiency, and patients with cardiovascular disease (CVD), are at increased risk for developing FB, and also carry a worsened prognosis (1, 4).
- This study aims to describe the epidemiology, risk factors, and outcomes of patients with FB in a tertiary care hospital in northeast Ohio.
- This is the second study of FB conducted in the United States in 30 years.

Materials and Methods

- A 10-year retrospective study of patients with FB from 2001 through 2010 was conducted at Summa Health System – a 658 bed community teaching hospital in northeastern Ohio.
- Demographics (gender, race, age), comorbidities, clinical presentation, blood culture results, laboratory data (white blood cell count [WBC], hemoglobin & hematocrit, and creatinine), radiological findings, and treatment measures were collected from all patients.
- The source of bacteremia was identified for each patient based on the history, clinical findings, and radiological reports.
- The outcome measures recorded include 30-day mortality, length of hospital stay (LHS), and admission to the ICU.
- Bivariate Fisher's Exact Test and bivariate T-test were utilized for statistical analysis.

Results

- Nineteen patients with FB were identified. Twenty-one out of 182,285 total blood cultures grew *Fusobacterium* sp (0.01%)
- Mean age was 58.6 years old, (range = 24 to 97 years old). Gender distribution was 52.6% female.
- All patients with FB had at least one comorbid condition. The most common condition was CVD, present in 63.2% of patients (Table 1).
- The most common presenting variables included GI complaints (63.2%), sepsis (32.0%), hyperthermia (47.4%), leukocytosis (63.2%), and elevated creatinine (42.1%). In one case, the positive blood culture was an incidental finding.
- Poly-microbial bacteremia occurred in 5 cases (26.3%).
- The source of FB infection was GI in 63.2% of cases, and unknown in 21.1%.
- Eighteen of 19 patients were treated with antibiotics. Three patients (15.8%) were treated with inappropriate antibiotic regimens.
- Eleven patients (57.9%) were admitted to the ICU, 7 patients (36.8%) required mechanical ventilation. No factors were significantly associated with ICU admission.
- Four patients (21.1%) died within 30 days of hospitalization. Factors significantly associated with increased mortality included creatinine>1.2, and mental status changes (Table 2).
- The mean length of hospital stay (LHS) was 13.8 days, ranging from 1 day to 50 days. Increased LHS was significantly associated with diabetes, CVD, and ICU admission (Table 3).

Tables

TABLE 1: *Fusobacterium* Bacteremia Patient Characteristics

| Characteristic | Number | Percentage |
|------------------------|--------|------------|
| Age (>65) | 8 | 42.1 |
| Race (White) | 16 | 84.2 |
| Gender (Female) | 10 | 52.6 |
| Cardiovascular disease | 12 | 63.2 |
| Diabetes | 3 | 15.8 |
| COPD | 4 | 21.1 |
| Smoker | 4 | 21.1 |
| Cancer | 3 | 15.8 |
| Chemotherapy | 2 | 10.5 |
| Steroid therapy | 5 | 26.3 |

COPD = Chronic Obstructive Pulmonary Disease

TABLE 2: Factors Associated with Increased Mortality in Patients with *Fusobacterium* Bacteremia

| | Favorable Outcome | | Death | | Total | Significance |
|------------------------|-------------------|-------|-------|-------|-------|--------------|
| | n=15 | n=4 | n=19 | n=19 | | |
| Diabetes | 2000 | 0000 | 1579 | 10000 | 2105 | 1.0000 |
| COPD | 2000 | 2500 | 2105 | 10000 | 2105 | 1.0000 |
| Cancer | 1333 | 5000 | 2105 | 1783 | 2105 | .1783 |
| Immunosuppression | 3333 | 5000 | 3684 | 6027 | 3684 | .6027 |
| GI Infection | 5333 | 10000 | 6316 | 2451 | 6316 | .2451 |
| Cardiovascular Disease | 6000 | 7500 | 6316 | 10000 | 6316 | 1.0000 |
| Sepsis | 2667 | 5000 | 3158 | 5573 | 3158 | .5573 |
| Leukocytosis | 5333 | 10000 | 6316 | 2451 | 6316 | .2451 |
| Elevated Creatinine* | 2667 | 10000 | 4211 | 0181 | 4211 | .0181 |
| Septic Co-infection | 2000 | 5000 | 2632 | 2722 | 2632 | .2722 |
| Mental Status Change* | 1333 | 7500 | 2632 | 0374 | 2632 | .0374 |
| ICU Admission | 6000 | 5000 | 5789 | 10000 | 5789 | 1.0000 |

*p<0.050

COPD = Chronic Obstructive Pulmonary Disease

GI = Gastrointestinal

Leukocytosis = WBC >11,000 cells/microL

Elevated Creatinine = Creatinine > 1.2 mg/dL

TABLE 3: Factors associated with increased Length of Hospital Stay in patients with Patient Variables in *Fusobacterium* Bacteremia

| | LOS (days) | | Significance |
|-------------------------|------------|---------|--------------|
| | Mean | p-value | |
| Diabetes* | | | |
| Yes n=3 | 35.333 | .0010 | |
| No n=16 | 9.813 | | |
| COPD | | | |
| Yes n=4 | 19.250 | .3932 | |
| No n=15 | 12.400 | | |
| Cancer | | | |
| Yes n=4 | 11.250 | .6849 | |
| No n=15 | 14.533 | | |
| Immunosuppression | | | |
| Yes n=7 | 16.143 | .5936 | |
| No n=12 | 12.500 | | |
| GI Infection | | | |
| Yes n=12 | 13.583 | .9184 | |
| No n=7 | 14.286 | | |
| Cardiovascular Disease* | | | |
| Yes n=12 | 20.000 | .0017 | |
| No n=7 | 3.286 | | |
| Clinical Sepsis | | | |
| Yes n=6 | 10.000 | .4255 | |
| No n=13 | 15.615 | | |
| Leukocytosis | | | |
| Yes n=7 | 15.500 | .5088 | |
| No n=12 | 11.000 | | |
| Elevated Creatinine | | | |
| Yes n=11 | 16.375 | .5109 | |
| No n=8 | 12.000 | | |
| Septic Co-infection | | | |
| Yes n=5 | 12.786 | .5914 | |
| No n=14 | 16.800 | | |
| Mental Status Change | | | |
| Yes n=5 | 13.800 | .7959 | |
| No n=14 | 13.857 | | |
| ICU Admission* | | | |
| Yes n=11 | 18.909 | .0379 | |
| No n=8 | 6.879 | | |

*p<0.050

COPD = Chronic Obstructive Pulmonary Disease

GI = Gastrointestinal

Leukocytosis = WBC >11,000 cells/microL

Elevated Creatinine = Creatinine > 1.2 mg/dL

Discussion

- The first US case series of FB was described in 1983 (6). At least 7 other similar case-series focusing on FB have been published elsewhere since that time (1-5, 7, 8).
- FB is a rare clinical event, ranging from 0.19% to 0.90% of blood cultures (2, 6). Incidence of FB in this study was even lower, at 0.01%.
- A wide age-range is noted amongst FB patients, with most studies including adolescents and the very elderly (1, 4, 6-8). Patients in this study likewise span greater than 70 years.
- Mean age of FB patients is often greater than 55 years old (1, 4, 5). Older patients also predominated in this study, with a mean age of 58.6 years old, and a near-equal gender distribution.
- FB is frequently found in patients with neutropenia or neoplastic malignancy (30.8% to 45.6%) (1, 2, 4-8). This is comparable with our study, where 36.8% of FB patients had immunosuppression from malignancy or systemic steroid use.
- FB can result from genitourinary infection (5% to 35%) (1, 5-9). In this study, 10.5% of patients' FB was derived from an obstetric or gynecological source.
- While GI infection is a common source of FB, the infectious source is unknown in up to 38.6% of cases (1, 5, 7). GI infection in our study was the most common source of FB (63.2%), with an unknown infectious source in 21% of patients.
- A GI source of infection demonstrated no statistically significant correlation with the negative outcomes analyzed.
- Polymicrobial bacteremia was a common finding in our study (26.3%), as well as other published studies (28.5% to 43.1%) (1, 4-7). All concomitant organisms in our study consisted of normal mucosa flora (10).
- Polymicrobial bacteremia was not significantly associated with worsened outcomes in this study, nor in the other FB case-series (1, 5-7).
- Four patients (21.1%) died within 30 days of FB diagnosis. Mortality rates of other studies ranged from 0% to 47.4% (1-8).
- Elevated creatinine and mental status change were significantly associated with mortality.
- ICU admission was required in (68.4%) of cases, indicating that FB occurred in patients with very poor health.
- While no significant correlation existed between the analyzed factors and ICU admission, patients who presented to the ICU generally had sepsis, GI source of infection, and greater LHS.
- LHS averaged nearly 2 weeks (13.8 days), again indicating that FB patients are generally in poor health.
- Diabetes, CVD, and ICU admission were significantly associated with increased LHS.

Conclusions

- FB is an uncommon event (1:10,000 cases).
- Greater than half of the cases had CVD, presented with GI complaint, and had leukocytosis.
- The most common infectious source was GI.
- Thirty day mortality was 21.1%, and 68.4% of cases required ICU admission.
- Increased creatinine and MS changes were associated with a significant increase in mortality.
- CVD, diabetes, and ICU admission were associated with a significant increase in LHS

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