Fusobacterium Mortiferum Bacteriemia In Newly Diagnosed Chronic Lymphocytic Leukemia

Authors Casey Reulbach PGY-III, Ascension Genesys Hospital, Grand Blanc, USA; Mai Truong PGY-II, Internal Medicine, Ascension Genesys Hospital, Grand Blanc, USA; Anton Juncaj PGY-V, Hematology/Oncology, Ascension Genesys Hospital, Grand Blanc, USA; Advisor: Reginald Sandy, Ascension Genesys Hospital, Grand Blanc, USA

Ascension Genesys Hospital
Medical Education
Grand Blanc, MI

Ascension Genesys Hospital

Introduction

The Genus Fusobacterium are fastidious Gram-negative, anaerobic bacilli (1-3) commonly found in the oral cavity, female genitourinary tract, and alimentary tract. Clinically, *F. nucleatum* and *F. necrophorum* are more frequently observed human pathogens (3-5). Studies determined the incidence of bacteremia of 0.55 cases per 100,000 population per year (5-7). However, Fusobacterium are also linked to abscesses, peripheral infections, Lemierre's syndrome, mesenteric vein thrombosis, and septic shock (1, 5, 8-11). *F. nucleatum* has also been a rare cause of bacteremia in patients with hematologic malignancies, specifically leukemia and lymphoma, with neutropenia and oropharyngeal mucositis being main risk factors in this patient population (12). Additionally, the species *F. nucleatum* may be linked to colorectal cancer by promoting tumorigenesis and affecting chemotherapeutic resistance (13). Here, we describe a case of a man who presented with multiple complaints and was found to have newly diagnosed chronic lymphocytic leukemia (CLL) and later blood culture positivity for *Fusobacterium mortiferum.*

Case Presentation

- A 60-year-old male with past medical history of hypertension, tobacco use disorder, and alcohol use disorder was evaluated for malaise, onset 2 weeks prior to his presentation.
- Associated symptoms of generalized weakness, altered mental status, nausea, non-bloody emesis, decreased P.O. intake, unintentional weight loss (40 lbs, 3 months), bilateral flank pain, and ground-level fall.
- Reported generalized weakness caused unwitnessed fall, no LOC, struck left knee. No AC. Does not follow with PCP.
- Social history was remarkable for drinking ~ 5-6 beers daily, smoking 0.5 packs of cigarettes daily (20 pk/yr), and occasional marijuana use.
- Vitals upon arrival: BP 92/58, HR 68, Temp 98.8 F, RR 14, SpO2 100% on RA.
- Physical exam: trace bilateral lower extremity edema, A&Ox2 (person, time). No focal neurological deficits, petechia, or palpable splenomegaly.

Initial Labs/Imagining

- Chemistry 14 profile: Sodium 129 mmol/L, potassium 9.8 mmol/L and BUN/creatinine 76 mg/dL/2.31 mg/dL respectively (No prior for comparison).
- AST/ALT: 206/103 U/L respectively
- CBC: WBC 1058.4 K/cmm, Hgb 3.6 g/dL, and platelets 48 K/cmm
- PT/INR: 16.7 sec/1.49 respectively
- Troponin: 0.35 ng/mL (repeat 0.04 ng/mL, 0.02 ng/mL)
- Ammonia level: 100 uMol/L
- Fibrinogen: 164 mg/dL
- Uric acid: 20.4 mg/dL
- Lactic acid: 2.40 mmol/L (repeat 2.0 mmol/L, 2.0 mmol/L)
- Urine analysis: Negative
- LDH: 2486 IU/L

- XR left knee: Negative
- XR chest: Showed no acute cardiopulmonary processes
- CT brain: Negative
- CT abdomen and pelvis: Showed extensive multicompartmental abdominal pelvic adenopathy highly concerning for lymphoproliferative disorder, periaortic adenopathy measuring 11 x 5 cm, hepatosplenomegaly, and a non-obstructing left kidney stone.

Hospital Course

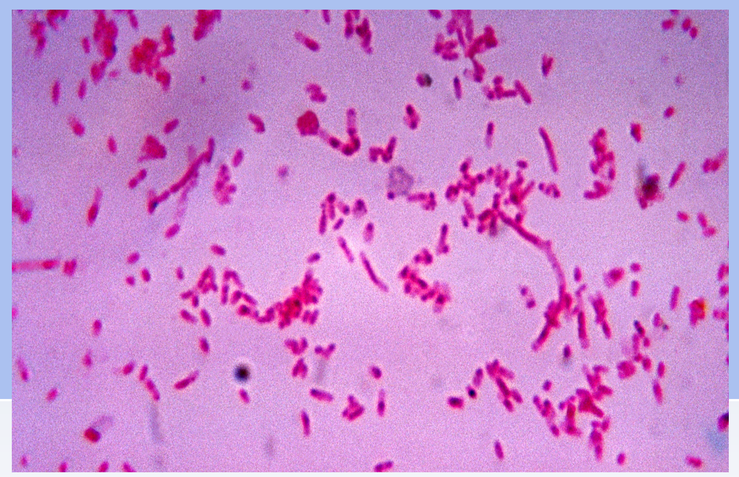
Emergency Department:

- Received 2u pRBC, septic fluid bolus, Ceftriaxone, Vancomycin, Rasburicase
- Nephrology and Hematology/Oncology contacted for Hyperkalemia, leukocytosis, and bicytopenia with leukapheresis and hydroxyurea ordered. Peripheral slide morphology revealed leukocytosis with marked absolute and relative lymphocytosis composed primarily of small mature appearing lymphocytes.

Hospitalization:

- Day 1: Bone marrow biopsy performed. Aspirate unable to be collected, suspected packed marrow. Flow cytometry and cytogenetics sent to UofM.
- Days 2-6: The patient received 3u pRBC (total 5u pRBC) and 1u platelets. Leukapheresis 6x session (goal WBC < 10 K/cmm).
- Day 7: Flow cytometry/cytogenetics resulted, findings consistent with CLL/SLL.
- Day 8: Transferred out of ICU. New odynophagia consistent with oral thrush appreciated on exam. Nystatin ordered. One episode of self-resolving epistaxis.
- Day 9: Tmax of 101.8 F, new onset rash to trunk and bilateral lower extremities. Repeat CXR worsening pulmonary vascular congestion. Empirically Vancomycin and Cefepime started. ID consulted.

Fusobacterium mortiferum



- Day 10-12: Repeat blood cultures taken on day 9 revealed gram-negative rods (2/2 cultures, later discovered to be Moraxella nonliquefaciens after patient expired), continued on Vancomycin and Cefepime. Repeat (third set) blood cultures on day 12. ID recommended removal of right IJ Quinton catheter as a possible source of infection, and plan of repeat blood cultures after removal. Final blood culture results pending. Transthoracic echocardiogram showed LVEF of 60 to 65% and no evidence of vegetations.
- Day 13: Developed acute encephalopathy with increased ascites and suspected underlying liver disease (previous ammonia level 100). Increasing respiratory distress, tachypnea, and tachycardia. Lactulose ordered. Transferred back to ICU for respiratory distress. Condition continued to deteriorate and a family elected for comfort measures only (CMO). CMO orders were placed and patient expired. Repeat blood cultures that were taken on day 12 resulted 4 days after the patient expired, and grew Fusobacterium mortiferum.

Discussion

Here we presented a case of a patient with newly diagnosed CLL whose blood cultures showed gram negative rods but identification of the specific pathogen was not discovered until post-mortem.

- Anaerobic bacteremia is an increasingly prevalent issue in neutropenic patients with hematologic malignancies over the last few years (12).
- 5% of all gram negative bacteremic cases in severely neutropenic patients were identified as Fusobacterium nucleatum (12).
- Increased risk populations: hematologic malignancies, dialysis patients; with dementia, chronic obstructive lung disease, diabetes, and heart disease following closely behind.
- While rare, infection with Fusobacterium species can be life threatening. Goldberg et al. in the US showing a 21% thirty-day mortality rate that was associated with an increase in serum creatinine and altered mental status, as observed in our patient (6).

Conclusion

- Fusobacterium mortiferum and other Fusobacterium species are clinically important and a seemly rare cause of bacteremia in patients with hematologic malignancies.
- Initial treatment with broad spectrum antibiotics (i.e. metronidazole or carbapenems) should be started and tailored to final culture results as there appears to be a wide-range of resistance among the different Fusobacterium species (4, 5).
- A case report documented in Japan showed successful response to intravenous Imipenem/Cilastatin 2.0 g/day in a 68 year old Japanese man with a history of hepatitis C and alcohol abuse who was found to have blood cultures positive for Fusobacterium mortiferum, Streptococcus constellatus, Bacteroides thetaiotaomicron, and non-spore-forming anaerobic gram-positive bacillus during his hospitalization. Patient completed seven days of antibiotic therapy, with resolution of fever and a return to baseline of hepatorenal function (14).
- As literature is limited in cases with Fusobacterium bacteremia, it is important to document such cases as they come in efforts of bringing awareness to the pathogen to promote use of empiric antibiotics in specific high risk patient populations for ultimately, a quicker recovery.

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