

Case Report

Fusobacterium nucleatum endocarditis: a case report and literature review

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Received October 7, 2022; Accepted February 5, 2023; Epub February 15, 2023; Published February 28, 2023

Abstract: Fusobacteria is anaerobic gram-negative rods, which frequently colonize the oral cavity and can rarely cause deadly diseases in humans. The two most commonly found in this group of bacteria are fusobacterium necrophorum and fusobacterium nucleatum. Only a handful of cases of endocarditis due to fusobacterium have been reported. We describe an 86-year-old male who had a recent tooth extraction presenting to the emergency department with weakness lightheadedness, and pain in his right elbow. He had a low-grade fever of 100.8°. The patient was discharged home but came back less than 24 hours with a fever of 102° and chills and again after the second discharge with sepsis of unknown origin. A week after initial blood cultures were drawn, fusobacterium nucleatum grew in one of two sets and his transesophageal echocardiogram revealed vegetation on his mitral valve. The patient was then successfully treated with a six weeks course of ampicillin-sulbactam. This case is followed by a review of the literature.

Keywords: Endocarditis, bacterial endocarditis, *Fusobacteria* bacteremia

Introduction

Fusobacteria is anaerobic gram-negative rods that frequently colonize the oral cavity [1, 2], but can cause rare and deadly diseases in humans if enters into the bloodstream. The two most commonly found in this group of bacteria are fusobacterium necrophorum and fusobacterium nucleatum [3]. While males appear to be more affected by fusobacterium bacteremia in general, Necrophorum is linked closely with a younger population without comorbidities under 30 years of age. On the other hand, nucleatum has been found to occur in the elderly, especially with the comorbidities of malignancy and dialysis [4, 5]. Fusobacterium has been found to cause periodontal disease, Lemierre syndrome, meningitis, abscesses in different organs, adverse pregnancy outcomes, and various other human diseases. Tonsillitis can be followed by septic thrombophlebitis of the internal jugular vein and then septicemia with septic emboli in the lungs and other sites that can cause life-threatening conditions. Only a handful of cases of endocarditis due to fusobacterium have been reported [6]. The majority of cases of endocarditis are com-

prised of Streptococcus and Staphylococcus species. Enterococcus, pseudomonas, Neisseria, and the HACEK group, which comprises of haemophilus, actinobacillus, cardiobacterium, eikenella, and kingella are the other well-recognized bacterial organisms that cause endocarditis. It is important to recognize Fusobacterium as a potential cause of endocarditis when evaluating a patient with fusobacterium bacteremia as under treatment can be fatal.

Case report

The patient was an 86-year-old male with a past medical history of chronic atrial fibrillation, pacemaker insertion, diabetes mellitus type 2, dyslipidemia, and coronary artery disease with h/o coronary bypass surgery. He had a recent tooth extraction presenting to the emergency department with vague symptoms of weakness in his lower extremities, lightheadedness, and on-and-off pain in his right elbow for a few days. A basic workup at that time did not reveal any significant abnormalities other than a low-grade fever of 100.8°. The patient was given IV fluids and discharged home. The patient returned to the ER within less than 24 hours after being dis-

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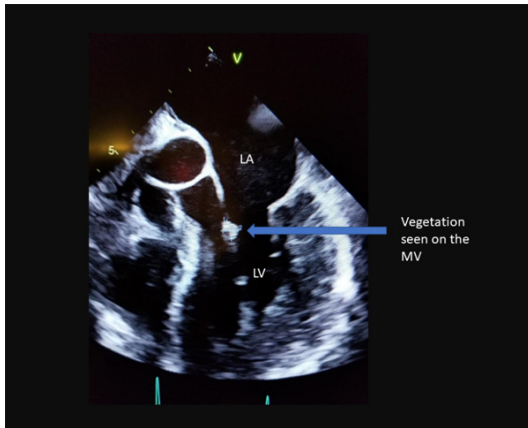


Figure 1. Transesophageal echocardiogram showing vegetation on the mitral valve. LA = Left atrium, L = Left ventricle, MV = mitral valve.

charged with a fever of 102° and chills. The workup again was essentially negative for any focal infection except for hematuria in his urine and an ill-defined 3.2 cm hypoattenuating lesion in the right hepatic lobe on a computer tomography test of his chest, abdomen, and pelvis without contrast. Again, the patient was sent home but returned a third time two days later with high-grade fevers with a max of 104°. Labs demonstrated neutropenia with a WBC of 2.5, lactic acid of 2.2, thrombocytopenia with platelets of 115, elevated liver enzymes with AST-113, ALT-79, and ALP-131, all of which were in the normal range on his labs two days prior. He was admitted for sepsis of unknown origin and started on vancomycin and piperacillin-sulbactam after blood cultures were obtained. Ultrasound of the liver was highly suggestive of an abscess for which a drain was placed by a Radiologist. The patient continued to spike fevers, have pain in his right elbow that was warm and red without a palpable mass, and have negative blood cultures. Repeat imaging showed that his liver abscess remained stable. A week after initial blood cultures were drawn, fusobacterium nucleatum grew in one of two sets. The transthoracic echocardiogram was unremarkable. Given the suspicion of possible septic emboli, a transesophageal echocardiogram was done revealing a 0.6 cm × 0.6 cm vegetation on the anterior portion of the mitral valve (**Figure 1**). The patient was then successfully treated with a six-week course of ampicillin-sulbactam based on the cultural sensitivity and his hepatic drain was discontinued after 2 weeks. The patient recovered and remained asymptomatic after a full course of

antibiotic treatment. Repeat echo 4 weeks after discharge did not show any significant mitral valve abnormality.

Discussion and review

Fusobacterium is a rare cause of bacteremia and an overlooked cause of endocarditis. The patient above presented with fevers, one positive blood culture for fusobacterium nucleatum, and concern for septic emboli given his liver abscess and reoccurring joint pain. High clinical suspicion for possible endocarditis warranted a transthoracic and transesophageal echocardiogram, which later demonstrated mitral valve endocarditis. Without this investigation, the patient would have been undertreated with only 2 weeks of iv antibiotics with the hepatic abscess being labeled the primary source of the infection. The understanding of the complications that occur with fusobacterium organisms is limited given the infrequent cases that are encountered. In an 11-year retrospective study at Calgary Zone of Alberta Health Services (AHS) in Canada, 72 cases of Fusobacterium bacteremia (55 per 100,000 population) were identified with a 10% mortality rate, of which more than half of those deaths were caused by fusobacterium nucleatum [7]. A third of these cases of bacteremia had no focal source of infection. Intrabdominal, hematologic, and obstetrical made up a large portion of the remaining cases of fusiform bacteremia with no reports of endocarditis. It is unclear from the study if an echocardiogram was performed to investigate the cases that had no focal infection. In a 10-year retrospective study conducted in 2012 at Summa Health Systems in Ohio, the second study done in America focusing on Fusobacterium bacteremia, similar findings were seen. 21 of 18,035 blood cultures were positive for fusobacterium species representing 19 separate cases where a gastrointestinal source made up 63.2% of the cases. Genitourinary and pulmonary sources were 15% of the cases and the remaining 21% had no focal source of infection [8]. The 30-day mortality rate in this study was 21.1%. Again, it is unclear in the study what diagnostic testing was performed. Given that fusobacterium has not been recognized as a potential cause for endocarditis, it brings up the question of how many of these cases that have been researched also had endocarditis. Cardiac studies should be strongly considered when encountering patients that become bacteremic with fusobacterium in order to avoid undertreatment.

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The best choice of antibiotic treatment is not known. From the retrospective studies of Lemierre's syndrome, due to rare occurrences, it is impossible to draw a definite conclusion about the efficacy of different antibiotic regimens. Most of our knowledge about antibiotic therapy is from limited few *in vitro* studies with animal and human strains of *F. necrophorum* [9, 10]. Before the availability of antibiotics, Lemierre's syndrome was associated with a high mortality rate of 32%-90%, with embolic events in 25%, and endocarditis in 12.5% of patients [11-13]. It is still a potentially life-threatening disease with a reported mortality of up to 17% with the highest occurring in patients with meningitis with a mortality rate that can reach 30% despite appropriate antibiotic therapy [14]. It is important to consider endocarditis in patients with persistent fever and TEE can be a very helpful tool for substantiating the diagnosis of endocarditis when clinical suspicion needs confirmation.

Conclusion

Fusobacterium is a rare cause of endocarditis. High clinical suspicion for possible endocarditis warrants echocardiographic examination. The best choice of antibiotic treatment is not known but before the availability of antibiotics, Lemierre's syndrome was associated with a high mortality rate.

Disclosure of conflict of interest

None.

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References

- [1] Bennett KW and Eley A. Fusobacteria: new taxonomy and related diseases. *J Med Microbiol* 1993; 39: 246-54.
- [2] Verma D, Garg PK and Dubey AK. Insights into the human oral microbiome. *Arch Microbiol* 2018; 200: 525-540.
- [3] Klug TE, Rusan M, Fuursted K, Ovesen T and Jorgensen AW. A systematic review of *Fusobacterium necrophorum*-positive acute tonsillitis: prevalence, methods of detection, patient characteristics, and the usefulness of the Centor score. *Eur J Clin Microbiol Infect Dis* 2016; 35: 1903-1912.
- [4] Signat B, Roques C, Poulet P and Duffaut D. *Fusobacterium nucleatum* in periodontal health and disease. *Curr Issues Mol Biol* 2011; 13: 25-36.
- [5] Gethings-Behncke C, Coleman HG, Jordao HWT, Longley DB, Crawford N, Murray LJ and Kunzmann AT. *Fusobacterium nucleatum* in the colorectum and its association with cancer risk and survival: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2020; 29: 539-548.
- [6] Shamma NW, Murphy GW, Eichelberger J, Klee D, Schwartz R and Bachman W. Infective endocarditis due to *Fusobacterium nucleatum*: case report and review of the literature. *Clin Cardiol* 1993; 16: 72-5.
- [7] Afra K, Laupland K, Leal J, Lloyd T and Gregson D. Incidence, risk factors, and outcomes of *Fusobacterium* species bacteremia. *BMC Infect Dis* 2013; 13: 264.
- [8] Goldberg EA, Venkat-Ramani T, Hewit M and Bonilla HF. Epidemiology and clinical outcomes of patients with *Fusobacterium* bacteraemia. *Epidemiol Infect* 2013; 141: 325-9.
- [9] Mateos E, Piriz S, Valle J, Hurtado M and Vadillo S. Minimum inhibitory concentrations for selected antimicrobial agents against *Fusobacterium necrophorum* isolated from hepatic abscesses in cattle and sheep. *J Vet Pharmacol Therap* 1997; 20: 21-3.
- [10] Spangler SK and Jacobs MR and Appelbaum PC. Effect of CO₂ on susceptibilities of anaerobes to erythromycin, azithromycin, clarythromycin, and roxithromycin. *Antimicrob Agents Chemother* 1994; 38: 211-6.
- [11] Moreno S, García Altozano J, Pinilla B, López JC, de Quirós B, Ortega A and Bouza E. Lemierre's disease: postanginal bacteremia and pulmonary involvement caused by *Fusobacterium necrophorum*. *Rev Infect Dis* 1989; 11: 319-24.
- [12] Leugers CM and Clover R. Lemierre syndrome: postanginal sepsis. *J Am Board Fam Pract* 1995; 8: 384-91.
- [13] Hagelskjaer LH, Prag J, Malczynski J and Kristensen JH. Incidence and clinical epidemiology of necrobacillosis, including Lemierre's syndrome, in Denmark 1990-1995. *Eur J Clin Microbiol Infect Dis* 1998; 17: 561-5.
- [14] Jacobs JA, Hendriks JJ, Verschure PD, van der Wurff AM, Freling G, Vos GD and Stobberinghet EE. Meningitis due to *Fusobacterium necrophorum* subspecies *necrophorum*: case report and review of the literature. *Infection* 1993; 21: 57-60.