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Case report

Actinomyces europaeus as an emerging cause of necrotizing fasciitis

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ABSTRACT

Necrotizing fasciitis is a type of necrotizing soft tissue infection (NSTI) that can be polymicrobial or monomicrobial in origin. Polymicrobial infections typically involve anaerobes of the Clostridium or Bacteroides family. This case report highlights necrotizing fasciitis caused by an unusual culprit, *Actinomyces europaeus*, which is a gram-positive anaerobic filamentous bacillus that has only been documented in one prior report to cause NSTI. Currently, about half of the hospitals in the United States are equipped to perform antibiotic susceptibility testing for anaerobes, but less than one-quarter of hospitals actually utilize these tests routinely. Thus, it is common for polymicrobial actinomycoses to be blindly treated with antibiotics that are beta-lactamase resistant and active against anaerobes, such as with piperacillin-tazobactam. Here we examine the potential impact of this lack of testing, as well as the evolution of *A. europaeus* to cause necrotizing fasciitis.

Introduction

Necrotizing soft tissue infection (NSTI) describes a range of infections that result in progressive destruction of the skin, subcutaneous tissue, muscle, and fascia [1]. NSTI's are classified into two types. The most prevalent is type 1 which is polymicrobial and usually features a combination of gram-positive cocci, as well as anaerobes, such as Bacteroides and Clostridium, and gram-negative bacilli from the Enterobacteriaceae family. Type 2 is monomicrobial, in which Staphylococcus aureus or group A streptococcus are the most common isolated cause of infection [1].

Here we encountered a rare case of NSTI principally caused by *Actinomyces europaeus*. Actinomyces species occur as normal flora contaminants of the skin, urinary tract, and gastrointestinal tract [2]. In specific, *A. europaeus* is a facultatively anaerobic, gram-positive filamentous bacillus that has been a well-documented culprit of abscesses, decubitus ulcers, and urinary tract infections in the past [2]. The treatment for Actinomycosis is based upon whether the infection is monomicrobial or polymicrobial. Monomicrobial infections are treated effectively with penicillin. However, in polymicrobial infections, accompanying organisms produce beta-lactamase, which hydrolyze penicillin to protect Actinomyces from degradation. Therefore, polymicrobial infections require anaerobic and beta-lactamase coverage, which can be achieved with monotherapy regimens such as piperacillin-tazobactam, carbapenems or other regimens [3]. To our knowledge, this is the second case report of necrotizing fasciitis caused by *A. europaeus*.

Case description

A 60-year-old African-American female with a history of insulin dependent type 2 diabetes mellitus and hypertension presented to the emergency department with hyperglycemia and encephalopathy. The patient's family reported that she was hospitalized the previous week for COVID-19 infection and developed an ischial decubitus ulcer. Three days prior to current presentation, the ulcer worsened and necessitated emergency room treatment. The wound was cleaned, dressed in silver sulfadiazine cream, and she was discharged home with cephalexin and trimethoprim-sulfamethoxazole. Following discharge, the patient began dressing her wound at home with cornstarch and the decubitus ulcer had now progressed to a draining abscess. Overlying the abscess were black eschars and necrotic skin lesions that involved her left-sided lower abdomen, flank, medial thigh, vaginal labia, and buttock. Subcutaneous crepitus was present, and all areas were fluctuant and exquisitely tender. The patient's vitals were as follows: BMI of 35.73, blood pressure of 70/34 mmHg, pulse of 108 beats/minute, respiratory rate of 22/min, temperature of 36.5 °C, and oxygen saturation of 98 % on room air. Her labs revealed a creatinine of 2.9 mg/dL, lactic acid of 10.5 mmol/L, glucose

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of 736 mg/dL, creatine phosphokinase of 340 IU/L, anion gap of 28, and WBC count of 12 × 10^3/μL. Blood cultures and preliminary wound cultures were obtained, and the patient received insulin, normal saline, and empiric antibiotic therapy which included clindamycin, meropenem, and vancomycin. Due to the patient's severe illness, she was taken to the operating room for emergent debridement. Incisions were made down to the myofascial plane where the muscle was spared, but the fascia and overlying tissue were found to be overtly necrotic. All skin, subcutaneous tissue, and fascia were excised along the left-sided buttock, vaginal labia, medial thigh, and flank extending up to the costal margin. Deep tissue biopsies were sent for bacterial cultures. The patient recovered in the ICU and remained on broad spectrum antibiotic therapy. On post-operative days 2 and 4 the patient necessitated further debridement of her left flank and thigh. On post-operative day 5, bacterial cultures showed heavy growth of *A. europaeus* and trace growth of *Peptostreptococcus* species. The diagnosis of necrotizing fasciitis caused by polymicrobial actinomycosis was made, and the antibiotic spectrum was narrowed to piperacillin-tazobactam. However, throughout the subsequent days the patient developed severe respiratory distress with bilateral pulmonary infiltrates. The antibiotic spectrum was extended to include vancomycin, meropenem, levofloxacin, and micafungin, but the patient continued to decline. On hospital day 12, the patient developed multisystem organ failure and ultimately expired.

Discussion

In 2019, Kus et al. [4] documented the first case report of *A. europaeus* as a primary causal agent of necrotizing fasciitis. Two years following the initial case report, we have now encountered an additional case of necrotizing fasciitis caused by *A. europaeus*. Throughout our patient's course of infection, we observed clinical deterioration and recurrent fulminant infection that was unresponsive to the mainstay of treatment, piperacillin-tazobactam. Therefore, we hypothesize that this could reflect a broader trend that *Actinomyces* species are evolving to produce more virulent necrotizing infections. Upon literature review, Smith et al. [5] isolated 87 strains of *Actinomyces* species, 10 of which were *A. europaeus* specifically. Results showed that 20 % of *A. europaeus* strains were resistant to piperacillin-tazobactam and 10 % were resistant to linezolid. Additionally, the study reported that all *A. europaeus* strains were resistant to clindamycin, ciprofloxacin, and ceftriaxone. A separate study [6], isolated 392 strains of *Actinomyces* species, of which 20 strains were *A. europaeus*. While piperacillin-tazobactam was not assessed here, the study concluded that 60 % of strains were resistant to treatment with clindamycin and 100 % of strains were resistant to metronidazole. Overall, uniform susceptibility to carbapenems, vancomycin, aminopenicillins, doxycycline, tigecycline, and penicillin G was observed [5,6]. Table 1 combines the data mentioned above [5,6] to provide a concise view of antibiotics to which *A. europaeus* has displayed resistance.

Actinomyces are slow growing organisms; Incubation takes 5 days before growth appears but can occur at 15–20 days [3]. In the case described, cultures resulted positive for *A. europaeus* after 5 days which is consistent with the literature. While culturing for this type of infection is accessible, one study [7] has shown that only 56% of hospitals in the United States have access to in-house antibiotic susceptibility testing for anaerobes, and only a mere 21 % of those hospitals routinely perform these tests. Furthermore, while all anaerobic blood culture isolates were tested for susceptibility, wound culture isolates were only tested for susceptibility 14 % of the time. Given the low utilization rate of anaerobic susceptibility testing, and the evolution of *A. europaeus* to exhibit antibiotic resistance and cause NSTI, the treatment algorithm for Actinomycosis could transform in the future. Clinicians may be able to specially request anaerobic susceptibility testing at their institutions in the future, provided that the sample is sterile apart from the infection. While treating empirically with a wider spectrum antibiotic, such as a carbapenem, could immediately improve outcomes of polymicrobial actinomycosis, it may also accelerate antimicrobial resistance. Ultimately, this highlights the need for more institutions to adopt and standardize the use of anaerobic susceptibility testing as a routine practice to identify the best treatment for these infections while also maintaining high standards of antibiotic stewardship.

Table 1
Antibiotic susceptibility and resistance exhibited by *A. europaeus*.

Susceptible antibiotics	Resistant antibiotics
Aminopenicillins	Piperacillin-Tazobactam
Carbapenems	Linezolid
Vancomycin	Clindamycin
Tigecycline	Ceftriaxone
Doxycycline	Ciprofloxacin
	Metronidazole

Table 1 provides a concise view of the various antibiotics to which *A. europaeus* has displayed any level of resistance [5,6].

The unfortunate outcome of our patient could be related to a variety of factors including the severity of her infection and her comorbidities. However, due to her worsening despite being placed on appropriate antibiotics, a resistant organism may have also been the culprit.

Conclusion

Necrotizing fasciitis is a devastating infection that must be diagnosed and treated early to reduce mortality. While *A. europaeus* has been a relatively docile anaerobe in the past, it has now developed resistance to numerous antibiotics and evolved to produce necrotizing infections. Thus, adoption of anaerobic antibiotic susceptibility testing as a regular practice would allow the medical community to identify trends in antimicrobial resistance, improve patient outcomes, and maintain antibiotic stewardship moving forward.

CRediT authorship contribution statement

Nathan Anthony: Conceptualization, Investigation, Writing – original draft, Formal analysis, Writing – review & editing. **Nathan Douthit:** Conceptualization, Formal analysis, Writing – review & editing, Supervision. **Allen Foster:** Conceptualization, Supervision.

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Ethical approval

Informed Consent was provided by the family prior to the writing of this case. The case has been deidentified and does not require IRB review.

Consent

The family of the patient whose case is reported provided verbal consent prior to participation.

Author Statement

All authors have read and accepted to/agreed with the conditions posed in the "Instructions to Authors" document. All authors listed above have contributed to the conception and design, the acquisition and interpretation of data, as well as to the drafting and critical revision of the report for important intellectual content. We have each seen the final draft, affirm the originality of the report, and approve of the version to be submitted. We additionally agree that the work has not been previously published or simultaneously submitted for publishing at

any other institution. All authors hereby concur that if accepted for publishing in IDCases that the report will not be published elsewhere in a similar form without consent of the copyright holder.

Declarations of Interest

None.

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Conflict of Interest

All authors declare they have no conflicts of interest.

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