Actinomyces neuii, An Uncommon Bacterial Isolate From A Neck Abscess

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ABSTRACT

Actinomyces neuii is an emerging opportunistic pathogen. Previously unrecognized or mis-identified, it has been reported more frequently in recent years as the causative agent of significant infection due to the application of modern technologies such as MALDI-TOF MS or DNA sequencing. Most of the *Actinomyces* species, including *A. neuii*, are susceptible to β–lactam antibiotics. However, other species-specific resistance makes accurate identification important to treatment considerations. We report a 78-year old male with an infected sebaceous cyst of the neck from which *A. neuii* was recovered. The patient's initial empiric treatment with trimethoprim-sulfamethoxazole was not effective. Clinical resolution was achieved after surgical incision and drainage of the abscess and a short course of cephalexin. This case report aims to increase awareness of this uncommon potential pathogen among primary care physicians and illustrates the utility of correct organism identification with regard to clinical management.

INTRODUCTION

Actinomyces neuii was first described in the 1980s as a diphtheroid (i.e. pleomorphic) non-spore forming Gram-positive rod that was classified in the Centers for Disease Control (CDC) fermentative coryneform group 1. It was very rarely reported in the literature as a causative agent of infections as it was likely dismissed as a commensal or incidental finding due to its coryneform morphology. In 1994 it was reassigned to the *Actinomyces* genus based on 16S rRNA gene sequencing of CDC group 1 and group 1-like isolates (1). Especially since the advent of highly accurate, user-friendly methods of microbial identification in clinical laboratories -- like matrix assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) -- *A. neuii* has been reported in association with, and as the etiologic agent of clinically significant infections (2-4).

More than twenty-five *Actinomyces* species have been reported as human commensals. They are part of the normal flora of the human oropharynx, skin and the gastrointestinal and genitourinary tracts, but they can become opportunistic pathogens when the host epithelial barrier is disrupted (5). The majority of *Actinomyces* species are facultative anaerobes that grow branching filaments and produce "sulfur" granules (aggregates of bacteria and host proteins) in tissue. Biochemically, they show negative reactions in catalase and urease tests. However, *A. neuii* is aerotolerant, catalase positive, and does not produce "sulfur" granules. Microscopically, colonies show predominantly diphtheroid morphology, arranging in either clusters or V/Y shapes without filament formation (1). These features of *A. neuii* challenge correct identification if identification is based solely on morphology and biochemical methods. Accurate identification is best facilitated by newer methods including MALDI-TOF MS or PCR-based profiling (6, 7). Most *Actinomyces* species including *A. neuii* are susceptible to β–lactam antibiotics. However, species-specific resistance is reported for other agents, making accurate identification potentially important to therapeutic decisions (8, 9).

CASE DESCRIPTION

A 78-year old male with a past medical history of paroxysmal atrial fibrillation, type II diabetes mellitus, chronic obstructive pulmonary disease, and cerebrovascular accident with residual left sided deficits, presented with a tender left sided neck mass of two weeks duration. The patient had been taking an empiric course of trimethoprim-sulfamethoxazole prescribed by his primary care physician for five days prior to the visit. Physical examination revealed a 3.0 x 3.0 cm fluctuant mass that upon pressure discharged purulent and sebaceous material, prompting a clinical diagnosis of an infected sebaceous cyst. The lesion was incised and drained and the patient was sent home with a prescribed regimen of cephalexin. A wound swab was sent to the hospital microbiology lab for culture. After this first surgical incision and drainage and a full course of empiric cephalexin treatment the patient was reported to have no pain, warmth or residual erythema at the site of the abscess. Complete excision of the residual cyst was performed at a follow up visit. The clinical diagnosis of sebaceous cyst was confirmed by histological evaluation.

Within five days incubation, cultures recovered small white catalase-positive colonies that grew preferentially under aerobic conditions. The organisms were Gram-positive, and diphtheroid without spores or filaments. MALDI-TOF MS identified the isolate as *A. neuii*.

DISCUSSION

Even though *A. neuii* has been reported and/or reviewed in microbiology and infectious disease journals in recent years (2), due to its low incidence it may still remain a novel pathogen to many primary care physicians as well as to diagnostic laboratory staff. Its emergence as an opportunistic pathogen in a variety of infections merits attempts to increase awareness of *A. neuii* and the importance of its accurate identification in clinical specimens. A presumptive identification of *Actinomyces* may be determined from direct examination of clinical specimens (e.g. by Gram-stained smear preparations). However, suspicion of an actinomycosis on the part of the clinical provider and the laboratory is important because the atypical microscopic morphology of *A. neuii* may cause it to be mistaken for a *Corynebacterium* species and/or dismissed as commensal contaminant. The colonial morphology of culture growth may help presumptive identification, although this too is not definitive. An aerotolerant actinomycete may be unexpected by laboratory staff and the catalase-positive reaction of *A. neuii* will mimic that of a *Corynebacterium* species. Traditional biochemical methods of identification to the species level are difficult to do and commercial phenotypic kits lack the ability to accurately identify many *Actinomyces* species. Proteomic profiling by MALDI-TOF MS or DNA sequencing are now preferred methods for accurate identification of *Actinomyces* (5).

The recent attention to *A.neuii* has been due in part to these new, more exacting methods of microbial identification (2, 3, 6). Since its discovery and taxonomic assignment, *A. neuii* has been implicated in various clinically significant monomicrobial and polymicrobial infections. Commonly it has been reported in association with skin and soft tissue infections presenting with abscess (10), as in this present case. It has also been implicated in infections involving exposure to mucocutaneous or skin flora, including infections of the genitourinary tract, prosthetic devices and catheters, and post-operative endophthalmitis (11-15). A sporadic case of cutaneous actinomycosis has been reported for *A. neuii subsp. anitratus* in association with anti-tumor necrosis factor alpha (anti-TNF-alpha) drug therapy (6). *A. neuii* has been reported in bloodstream infections (3) and rare cases are reported for *A. neuii* being the sole causative agent in native heart valve endocarditis and chronic pericarditis (16), suggesting that the species can be a player in severe invasive disease.

The majority of *A. neuii* isolates are susceptible to β-lactam antibiotics. It is worth mentioning that *Actinomyces* species do not produce β-lactamase, therefore a β-lactamase inhibitor does not add any clinical benefit to the antibiotic regimen unless the patient has a polymicrobial infection warranting this option (17). Like other *Actinomyces*, *A. neuii* also is expected to be susceptible to vancomycin but is intrinsically resistant to metronidazole and is often less-susceptible to clindamycin (8, 9). One study of clinical isolates supports the consideration of carbapenems and tetracyclines as alternative treatment options (9). Importantly, resistance has been reported for *non-neuii Actinomyces* species for several antibiotic agents including aminoglycosides, ceftriaxone, clindamycin, fluoroquinolones, and rifampicin (17-19). Accurate speciation of an *Actinomyces* isolate recovered in a clinical specimen is important to inform determination of clinical significance and empiric management decisions prior to susceptibility testing.

The mainstay treatment for *A. neuii* infection generally follows those for other *Actinomyces* species. For skin and soft tissue infections antibiotic therapy can be an

adjunct to surgical intervention, as it was in our case.

In summary, *A. neuii* is a heretofore mis-identified and under-recognized opportunistic pathogen. It is now implicated in a range of infections thanks to new methods of accurate microbial identification and a heightened awareness of its pathogenic potential. Proper identification of the species and recognition of its etiologic role is important to a therapeutic approach and prognosis. Although typically susceptible to β-lactams, serious infections may warrant susceptibility testing to assure optimal management.

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