CLINICAL VIGNETTE

Cutibacterium acnes Isolated from Neck Mass: True Infection or Contaminant?

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Case Report

A 31-year-old male had chronic neck pain due to cervical disc disease and underwent C5-C7 disc replacement in Germany. There were no complications during the perioperative period, although he noted persistent neck stiffness after surgery. MRI neck obtained six months post surgery showed only postoperative change without other significant abnormality.

Fifteen months after surgery, he noticed a mass on the right side of his neck, with some tenderness. He initially presumed it was from a muscle strain when he exercised at the gym. Because the mass persisted, after a month he was evaluated with lab tests including normal CBC, C-reactive protein and erythrocyte sedimentation rate. Additional tests including HIV, quantiferon, syphilis, and fungal serology markers were negative. Ultrasound revealed a heterogeneous mass in the right neck at level IV near the posterior lower pole of the right thyroid lobe. The neck mass biopsy reported acute lymphadenitis with histiocytic and plasmacytic proliferation, which was nonspecific for inflammatory or infectious process. The culture from the biopsy sample isolated *Cutibacterium acnes* (*C. acnes*). He did not receive any specific treatment given the unknown clinical significance of the *C. acnes*.

The neck mass gradually increased in size, but was no longer tender. Follow up MRI six months later found two heterogeneously enhancing masses in the right neck. The process in the right tracheoesophageal groove had a slender pedicle tracing back to the right ventral C6-C7 disc space, at the site of prior discectomy and artificial disc. The radiologist reported the imaging findings as nonspecific but could represent an indolent infection or inflammatory response arising from the C6-C7 disc level and artificial disc. The MRI also noted the mass adjacent to the right lobe of thyroid had a similar appearance. This could be an extension of the same process beyond the paravertebral space, although a direct communication was difficult to appreciate. After spinal surgery evaluation, he underwent C6 vertebral biopsy. Four ml of hemopurulent fluid was aspirated and the C6 vertebral body was biopsied. The aspirated sample culture isolated *C. acnes*. Pathology reported granulomatous inflammation and granulation tissue with prominent acute inflammation/purulence, with fragments of degenerated inflamed collagenous tissue. Special stains for bacteria, acid fast bacilli and fungi were negative. The biopsy sample was also sent to the University of Washington for universal PCR sequencing, and *C. acnes* was detected. This established the diagnosis of prosthetic vertebral osteomyelitis and abscess with *C. acnes* infection more than two years after the original surgery.

The patient was followed by spinal surgery and infectious disease specialists. The ideal treatment recommendation is surgery with hardware removal and debridement, followed by long-term antibiotic treatment. However, because this patient was at high risk for surgical complications, he elected alternative treatment with intravenous antibiotics followed by long-term oral antibiotic suppression. If the antibiotic treatment was unsuccessful, he would consider surgery. He received intravenous daptomycin and ceftriaxone for 8 weeks, followed by oral amoxicillin as long-term suppression. By the end of the intravenous antibiotic treatment, the mass on his right neck had decreased in size. Repeat neck MRI confirmed the decrease in peripherally enhancing fluid collections in the right neck lateral to the right thyroid lobe and medial to the right common carotid artery and jugular vein. The collections appear to be communicating along the superior margin with a fistulous tract extending from the posterior aspect of the collections to anterior C6-C7 disc space. He remained clinically stable without complete resolution. We continue to closely monitor his symptoms and MRI findings on long term antibiotic suppression.

Discussion

C. acnes is a slow growing, gram positive pleomorphic rod that grows best anaerobically. It usually inhabits human skin, sebaceous glands, nasopharynx, gastrointestinal, and urologic tracts. It has low virulence and is frequently considered as a blood and tissue culture contaminant.[1] However with improved diagnostic techniques and better criteria to define infection, *C. acnes* is increasingly recognized as true pathogen rather than a contaminant.

Serious infections with *C. acnes* include CNS shunts and prosthetic joint replacements of shoulder, hip, or knee.[2-4] In spite of its low virulence, *C. acnes* is capable of adherence and biofilm formation. This plays an important role in the pathogenesis of infection with this organism. The majority of patients with *Cultibacterium* prosthetic joint infections (PJI), have infiltration of the glycocalyx with adherence to the implant surface.[5-7] Recently, there has been increased interest in *C. acnes'* role in spine pathology.[8] It has been identified as a pathogen in native spine infection and osteomyelitis, which has implications in the management compared with more common-

ly recognized pathogens. In addition, it is hypothesized that *C. acnes* may play a role in degenerative disk disease and the development of Modic end plate changes found on MRI.[8]

Cutibacterium implant associated infection (IAI) disproportionately affects males, probably reflecting the different distribution of body hair between sexes.[9-12] Despite adequate preoperative skin antisepsis procedures, perioperative contamination occurs as *Cutibacterium* species usually reside in the sebaceous glands located in dermal skin layers.[13] Other risk factors for *Cutibacterium* IAI include age below 54 years, body mass index below 22kg/m^2, and thoracic instrumentation.[14]

A long interval between surgery and onset of symptoms or diagnosis of *Cutibacterium* infection has been noted. Most *Cutibacterium* infection occurs late after implantation, hence it is classified as delayed or late infections.[15,16] A case-control study on spinal IAI by Grossi, et al reported the median time of infection recognition was post-operative day 843 in those with *C. acnes* infection, and 23 days in those with infections due to other pathogens.[14]

The definition criteria and clinical characteristics of IAI caused by *Cutibacterium spp* are poorly known. The methods to detect this pathogen include prolonged incubation of microbiological specimens,[17] application of novel techniques for biofilm detection, such as sonication of explanted materials[18] , and implementation of molecular assays.[19] An incubation period of 14 days in both aerobic and anaerobic culture media is needed for the growth of this pathogen.[20] Some authors recommend even longer incubation time of 21 days,[21] however, this prolongation results in an increased risk of contamination. Non-microbiological findings may support the clinical suspicion of *Cutibacterium* orthopedic IAI, in spite of normal laboratory and negative microbiological tests, including radiological features such as early loosening, heterotopic ossifications, or insufficient bone consolidation.

Eradication of IAI is best achieved by a combination of both appropriate antimicrobial and surgical treatment. Due to its broad antimicrobial susceptibility, the majority of *Curibacterium* orthopedic IAI can be theoretically treated with one-stage revision, providing that the surrounding soft tissue is not compromised and all foreign material and dead tissue can be removed during debridement.[22] However, the surgery, especially when it involves the vertebrae may result in complications. Because of risk of complications, surgery may not be the first-line treatment option. This presents a challenge in antibiotic management. The widespread use of antibiotics in acne may induce *C. acnes* strains with cross-resistance to various antibiotics, leading to clinical impact in all diseases caused by *Cutibacterium species*.[23] Emergence of *Cutibacterium species* resistance to antibiotics has been reported[24] and antimicrobial susceptibility testing is essential if the pathogen is isolated from the deep tissue samples.

Unlike other patients with vertebral osteomyelitis or IAI, our patient did not present with neck or spinal pain, but only with a neck mass. Although the culture of the neck mass biopsy sample isolated *C. acnes*, the relationship between the neck mass and the unrecognized spinal IAI could not be determined until the return of the vertebral biopsy. Due to the high risk of surgical hardware removal/replacement and debridement, we elected to try antibiotic treatment initially. This management is suboptimal given the higher risk for initial treatment failure as well as risk of recurrence following the cessation of antibiotics. Long-term oral antibiotic suppression may reduce the risk of infection recurrence. Close monitoring of his symptoms and serial neck MRI imaging will help to early identify recurrence of infection and vertebral damage. Conversion to surgical treatment will be inevitable once the treatment failure is documented.

In summary, due to the heterogeneous, subtle and atypical clinical presentation, the diagnosis of *C. acnes* IAI is often delayed. Clinicians must carefully weigh situations to judge culture results, and should not routinely dismiss *C. acnes* as contaminant in patients with prior arthroplasty or spinal hardware placement and the pathogen is isolated near or in the surgical areas. Conventional microbiological tests have limited sensitivity. In order to identify the potential *C. acnes* infection, it is imperative to request and wait for results of prolonged enrichment cultures to aid microbiologic diagnosis.

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