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Case Report

A Rare Case of *Candida glabrata* Cervical Spondylodiscitis

Angelina Hong, MD[1]; Ali Tariq Alvi, MD[1]; Lily Hyunjung Lim, MD[1]; Pallavi Aneja, MD[1]

Author affiliations are listed at the end of this article.

Correspondence to: Angelina Hong, MD (angelina.hong@hcahealthcare.com)

Abstract

Introduction
Invasive candidiasis can lead to numerous life-threatening sequelae. *Candida glabrata* is the second-most common causative species of invasive candidiasis. This species possesses a high risk for persistent infection and candidemia. An uncommon complication of invasive candidiasis is spondylodiscitis and can rarely affect the cervical spine.

Case Presentation
The patient is a female in her late 50s with a complex medical history inclusive of chronic obstructive pulmonary disease, chronic pain, multiple abdominal surgeries, prolonged intensive care unit admission, and administration of total parenteral nutrition and broad-spectrum antibiotics who presented with complaints of worsening neck pain. She was last hospitalized 3 months prior and found to have *C glabrata* fungemia but was nonadherent to antifungal therapy.

She was found to have advanced C5-6 spondylodiscitis and an epidural abscess. Her surgical cultures grew *C glabrata*. Despite surgical intervention and antimicrobial therapy, she clinically deteriorated and acquired septic shock with multiorgan failure.

Conclusion
This is a rare case of cervical spondylodiscitis caused by a deep-seated *C glabrata* infection.

Keywords
Candidiasis; invasive; *Candida glabrata*; cervical spondylodiscitis; discitis; spondylitis

Introduction
Candidiasis is a fungal infection caused by any *Candida* species and can be local or systemic.[1] Invasive candidiasis is characterized by a *Candida* bloodstream infection and can lead to a deep-seated infection with significant sequelae (eg, osteomyelitis, abscess formation). It can lead to ophthalmologic abnormalities, such as endophthalmitis and chorioretinitis, or spondylodiscitis, an infection of the vertebrae and the intervertebral disc spaces.[1] Invasive candidiasis is approximated to affect over 250 000 people yearly.[2] Recent studies suggest the incidence of candidemia is 2 to 14 cases per 100 000 people.[2] It is most commonly caused by *Candida albicans* but can also be caused by *C glabrata*, *C tropicalis*, *C parapsilosis*, and *C krusei* as well as other species. Infection by these 5 named species comprises approximately 90% of cases.[2,3]

C glabrata is the second-most common causative species next to *C albicans*.[1] Whereas the overall incidence of *C albicans* candidemia is declining, *C glabrata* is growing in prevalence, particularly in the United States and Europe.[2,3] *C glabrata* is estimated to comprise 24.3% of invasive candidiasis cases in North America.[4] Those at higher risk of *C glabrata* infection include elderly patients with a history of malignancy, diabetes, and/or a history of prior azole

or echinocandin therapy.[2,3] In addition to these variables, there are multiple other risk factors associated with invasive candidiasis in general, such as central venous catheter access, prolonged intensive care unit stay, total parenteral nutrition, hemodialysis, broad-spectrum antibiotic use, solid organ tumors or transplantation, glucocorticoid use, chemotherapy, and abdominal surgery.[2,3]

Candidemia is associated with high mortality rates, approximated to be 40% or greater, and is even higher in the intensive care unit.[1,2] *C glabrata* in particular is known to have a growing resistance to azole antifungals and thus echinocandin therapy is recommended as a first-line treatment and is associated with reduced rates of mortality compared to other antifungal regimens.[3-6] Because of its resistance and various virulence factors, *C glabrata* is a very aggressive species and possesses a high risk for persistent infection and candidemia.[1,2] This rare case describes a female in her late 50s who developed cervical spondylodiscitis secondary to *C glabrata* hematogenous dissemination.

Case Presentation

The patient was a female in her late 50s with a complex medical history inclusive of chronic obstructive pulmonary disease, chronic pain, opioid dependence, multiple abdominal surgeries, prolonged intensive care unit admission, administration of total parenteral nutrition, use of broad-spectrum antibiotics, and recent *C glabrata* fungemia who presented with a chief complaint of neck pain that radiated to her upper extremities bilaterally. She was discharged from the hospital a few months prior with intravenous antifungal therapy but was nonadherent to this treatment plan and did not complete antifungal therapy or infectious disease follow-up.

The patient was afebrile and hemodynamically stable upon admission to the hospital. On physical exam, she was noted to be frail and chronically ill in appearance but alert and oriented to person, place, and time. She had 4/5 muscle strength in her upper extremities bilaterally and endorsed paresthesia in both of her hands. Laboratory values were significant for elevated inflammatory markers with an erythrocyte sedimentation rate of 69 mm/hr and a C-reactive protein level of 3.6 mg/dL. Magnetic resonance imaging of the cervical spine revealed advanced C5-6 spondylodiscitis and an epidural abscess (**Figure 1**).

The patient underwent an anterior C5-C6 total corpectomy, C4-C7 discectomy, anterior C4-C7 fusion, epidural abscess evacuation, and C4-T1 posterior cervical laminectomy on hospital day 3. She received empiric antimicrobial therapy, including intravenous micafungin. Blood cul-

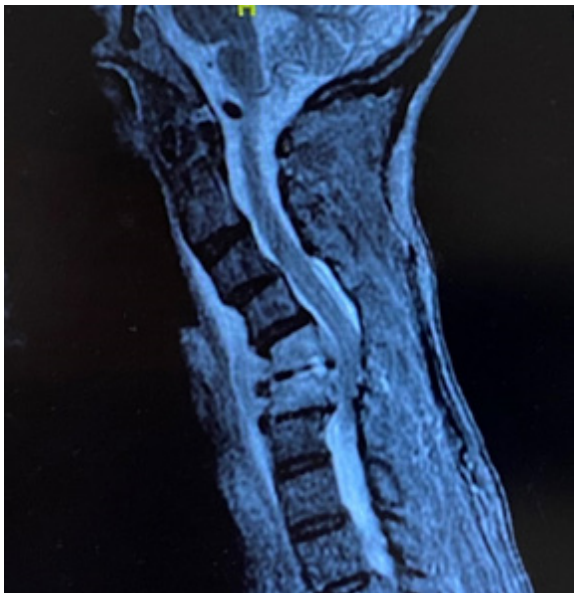

Figure 1. The patient's magnetic resonance imaging of her cervical spine demonstrated classic findings of spondylodiscitis at the C5-C6 level, with vertebral phlegmon and abscess, both anteriorly and posteriorly and extending circumferentially, with resulting cord compression.

tures obtained on admission were negative. Surgical cultures obtained from her neck and spine grew *C glabrata* and were found to be sensitive to micafungin. Empiric antibiotics, vancomycin, and cefepime were discontinued on hospital day 7 after the surgical cultures grew *C glabrata*.

On hospital day 10, postoperative day 7, the patient developed acute hypoxic and hypercapnic respiratory failure with altered mentation and was intubated. She developed multiorgan failure and was started on pressor support for suspected septic shock. She was transferred to the intensive care unit. Despite maximum vasopressor support and stress-dose steroids, she continued to deteriorate. Goals of care were discussed with family members, who decided to proceed with hospice on hospital day 10.

Discussion

This is a unique case of invasive candidiasis leading to cervical spondylodiscitis. Cervical spondylodiscitis can cause severe neurologic debilitation and typically requires surgical intervention with appropriate antimicrobial therapy to have the possibility of recovery.[7] Although this patient's blood cultures, drawn upon presentation to the emergency department, were negative, her surgical cultures were all positive for *C glabrata*. The patient likely had retained a deep-seated *C glabrata* infection secondary to her previous episode of fungemia, and her treatment was complicated by antifungal nonadherence upon her previous discharge.[1]

Spondylodiscitis of fungal etiology is very rare. There are a few reported cases of lumbar and thoracic spondylodiscitis secondary to *Candida* infection, but there is scarcer documentation of cases involving the cervical vertebrae.[8,9] Fungal spondylodiscitis in general, regardless of the affected area of the spine, is estimated to compose about 0.5-1.6% of all spondylodiscitis cases.[9] We found only 1 case report by Bonomo et al in 1996 that reported a cervical epidural abscess with surgical cultures positive for *C glabrata* and complicated by osteolytic changes in the C3 and C4 vertebrae.[10] The patient's blood cultures were negative. However, she had a history of a recent tumor resection in the hypopharynx.[10] Thus, her infectious source may have been from the retropharyngeal space or hematogenous or lymphatic spread from the oral tissues.[10] Other reported cases of fungal cervical spondylodiscitis did not involve cultures positive for *C glabrata* but rather other species such as *C albicans*.[11]

Our patient had multiple risk factors for *C glabrata* colonization. She had a history of multiple abdominal surgeries, was previously hospitalized in the intensive care unit, required total parenteral nutrition, and received broad-spectrum antibiotics in the past. Genetics also play a role in determining patient susceptibility to invasive candidiasis. There are a handful of select allele variations that significantly impact cytokine pathways and other pro-inflammatory variables, thereby regulating susceptibility to systemic fungal infection.[1] Early and appropriate antifungal therapy is critical, as is treatment adherence and close follow-up.[12] In addition to the growing resistance to azole antifungals, cases of echinocandin resistance are also increasing in number.[12] In such cases, amphotericin B would be indicated as the alternative regimen.[12] Thus, antifungal stewardship continues to be a crucial component in the management of invasive candidiasis and suppressing the rates of antifungal resistance.[12]

We suspect the patient's acute decline postoperatively on hospital day 7 was multifactorial, given her numerous medical comorbidities. She was on appropriate antifungal therapy, as her surgical cultures grew *C glabrata* sensitive to micafungin. In addition to episodes of delirium postoperatively with worsening functional status, she also required a complex multimodal pain regimen due to her high opioid tolerance. Polypharmacy likely played a role in her altered mentation and acute-on-chronic hypercapnia. This, in addition to a possible aspiration event, contributed to her respiratory failure and intubation before her rapid deterioration.

Conclusion

Invasive candidiasis can have many severe complications and affect various organ systems, with diverse clinical presentations. Based on our literature review, this is only the second documented case of spondylodiscitis affecting the cervical area secondary to a deep-seated *C glabrata* infection. With this case report, we hope to provide insight to internists who encounter similar clinical presentations.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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Author Affiliations

1. HCA Florida Westside Hospital, Plantation, FL

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