Suppurative Parotitis Due to *Candida glabrata*

Case Report and Review of the Literature

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Abstract: We report the case of an insulin-dependent diabetic woman with chronic renal insufficiency who developed *Candida glabrata* suppurative parotitis. Infectious inflammation of the parotid gland is typically bacterial in etiology, and candidal parotitis is a rarely documented finding with only 6 reported cases in the literature. Four cases involved *Candida albicans*; and 2, *C. glabrata*. Furthermore, our patient was uncharacteristically young and without ductal obstruction or other nidus for infection, which makes this case especially unique. We also present a literature review of the previous cases.

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Acute suppurative parotitis most often affects the elderly, severely ill, and immunocompromised but is a recognized albeit uncommon complication of abdominal surgery, especially in the preantibiotic era.[1,2] Perhaps most famously, US President James A. Garfield died of complications of suppurative parotitis after sustaining an abdominal gunshot wound in 1881 during an assassination attempt.[2] The primary cause of acute parotitis is decreased or interrupted salivary flow, which can stem from dehydration, ductal obstruction, certain drugs such as anticholinergics and antihistamines, chronic diseases such as Sjögren syndrome and diabetes mellitus, and sialolithiasis.[3]

The most common pathogens are *Staphylococcus aureus* and, to a lesser extent, α-hemolytic streptococci and enteric gram-negative rods. Rarely anaerobic bacteria, mycobacterium, and fungi can be the causative agents.[4,5] Acute suppurative parotitis is typically characterized by sudden onset of a warm, indurated, erythematous parotid region and is typically unilateral.[4] It has been proposed that one mechanism of parotitis is the retrograde migration of oral pathogens into the salivary ducts and parenchyma due either to decreased salivary flow or obstruction.[5]

CASE REPORT

We describe the case of a 32-year-old woman with a history of insulin-dependent diabetes mellitus complicated by hypertension, chronic kidney disease, nephrosclerosis, and a neurogenic bladder. The patient was being followed up on an outpatient basis by a maxillofacial surgeon for a concerning submandibular mass that had been present for approximately 2 months. The etiology of her right submandibular neck mass was under investigation but was felt to be infectious during this time in which the area was expanding. She was previously treated by the maxillofacial surgeon with a 14-day course of clindamycin. In addition, after little or no improvement, he prescribed a 7-day course of fluconazole, again without resolution of her symptoms or the size of the mass. The patient noticed a worsening of her baseline nausea, night sweats, and recent dizziness associated with the development of this mass.

Upon admission, the patient had a temperature of 96.7°F, blood pressure of 200/102 mm Hg, heart rate of 107 beats per minute, and respiratory rate of 18/min. She was frail and older appearing than her stated age, but was alert and oriented, and in no acute distress. The right submandibular mass, readily apparent on physical examination, was firm, mobile, and irregularly shaped at the angle of the mandible. It was approximately 3.5 to 4 cm in the superior-inferior dimension, 2 cm in width, and tender to palpation.

Laboratory examination revealed the white cell count to be elevated at 18,100 cells per cubic millimeter with 86.2% neutrophils, and the hematocrit was measured at 42.8%. Her bicarbonate level was 17 mEq/L; serum glucose level, 393 mg/dL; serum urea nitrogen level, 33 mg/dL; and serum creatinine level, 4.2 mg/dL. A computed tomographic scan of the neck revealed a large mass associated with the right parotid gland extending inferiorly along the anterior margin of the sternocleidalmastoid muscle deep to the platysma muscle with some regional lymphadenopathy.

A percutaneous needle biopsy of the mass was subsequently performed, which revealed diffuse inflammatory reaction and significant yeast forms. The culture grew *Candida glabrata*, which was resistant to fluconazole, sensitive to all the echinocandins, and also susceptible to voriconazole with a minimum inhibitory concentration of 2. Blood cultures were also performed upon admission, which were subsequently negative for the microorganism. The patient was prescribed oral voriconazole after consultation with Infectious Diseases.

Six days later, an incision and drainage procedure was performed at the bedside because of expansion of the mass and pain. Cultures were again obtained of the thick yellow purulent fluid, which were monomicrobial and grew only *Candida* species. However, further identification was unsuccessful, and the isolate was assumed to be *C. glabrata.* There was immediate relief of the discomfort and swelling, and the patient was to continue on 400 mg daily of voriconazole for 3 months but was lost to follow-up.

DISCUSSION

There are 6 other known cases of candidal suppurative parotitis reported in the literature, obtained using the search engine PubMed with parameters *parotitis* and *candida*, *parotid abscess* and *candida*, *suppurative parotitis* and *candida*, and *parotid gland* and *candida* (Table 1). One case of mixed infection with *Streptococcus pyogenes* and *C. albicans* occurred in

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TABLE 1. Selected Summary of Reported Candida Parotitis Cases

Patient	Age, yr/Sex	Incision and Drainage?	Diabetes?	Pathogen(s)	Treatment	Outcome
Current patient	32/Female	Yes	Yes	*C. glabrata*	Voriconazole	Lost to follow-up
1	75/Female	No; parotidectomy	Yes	*C. glabrata*	Fluconazole	Deceased
2	75/Male	Yes	Yes	*C. albicans*	Fluconazole	Resolution
3	74/Male	Yes	Yes	*C. albicans*	Fluconazole	Resolution
4	59/Male	Yes	No	*C. glabrata*	Fluconazole	Resolution
5	50/Female	No	Yes	*C. albicans* and viridans group streptococcus	Clindamycin and fluconazole	Resolution
6	19/Male	Yes	Yes	*C. albicans* and *S. pyogenes*	Cefuroxime and amphotericin B	Resolution

a 19-year-old man who presented in diabetic ketoacidosis, whereas the other 5 occurred in individuals older than 50 years. Except for one, all cases occurred in patients with diabetes mellitus; the lone exception occurred in a nondiabetic individual with a concomitant parotid Warthin tumor, which may have served as an occult source for the candidal abscess. Stefanopoulos et al report a case of parotid candidal infection stemming from an obstruction of the Stensen duct by a foreign body, which again was a likely precipitating factor in candidal colonization.

Two cases involved only *C. albicans*; 1, *C. albicans* plus viridans group streptococcus; 1, *C. albicans* plus *S. pyogenes*; and 2 others, only *C. glabrata*. In all instances, the patients with candidal parotid infections were originally placed on antibiotics without resolution of their symptoms. One was subsequently treated with amphotericin B with complete resolution of his symptoms, and 3 patients were treated with fluconazole with complete clinical resolution. In the case of the patient with a Stensen duct obstruction, the symptoms did not resolve until the obstruction was detected and removed, despite antifungal treatment with fluconazole. In one case caused by *C. glabrata*, treatment with fluconazole did not lead to clinical resolution, and the patient perished 10 days after initiation of treatment, reportedly from her multiple underlying medical problems, not specifically from the infection.[5–10]

This case illustrates several features that are typical of the other reported candidal parotid abscesses. It occurred in an individual with multiple comorbidities, including diabetes mellitus. Our patient was originally treated with antibiotics as an outpatient, followed by treatment with antifungal therapy, without resolution of her symptoms. She presented with symptoms typical of parotitis. Conversely, in many ways our patient is atypical in that she presented with a 2-month history of parotid mass enlargement rather than an acute onset. She was uncharacteristically young at 32 years, and had no ductal obstruction or parotid tumor to serve as a nidus for fungal infection. Initial treatment by the maxillofacial surgeon included coverage for bacterial infection with clindamycin and fungal infection with fluconazole, with worsening of her symptoms, although fungal susceptibility testing acknowledged that the isolate of *C. glabrata* was resistant to fluconazole. Lastly, *C. glabrata* was isolated from aspiration of her parotid mass, rather than the more common *C. albicans.*

Candida albicans remains the most common isolate of the *Candida* species in a variety of infections. *Candida glabrata* is the second most common fungal isolate in hematogenous fungal infections and has a higher mortality rate.[10] Risk factors for oral colonization of *C. glabrata* are dentures, immunosuppression, antibiotic therapy, and aging.[11] One of the major risk factors for both bacterial and fungal suppurative parotitis is reduced salivary flow. Of note, our patient was not on any medications that reduce salivary flow.

Although whole saliva consists of numerous proteins that play important roles in maintaining good oral health, perhaps none is as important as histatin.[12] Histatins 1, 3, and 5 are prominently secreted by the parotid, submandibular, and sublingual salivary glands[13] and have known antifungal properties, including activity against *C. albicans*.[13,14] Histatin 5 seems to have the most potent fungicidal characteristics of the 3.[15]

Histatins are naturally occurring proteins that may have promising antifungal activity[16] and have a different mechanism of action than azole drugs. These compounds may possess enhanced fungicidal activity against many azole-resistant fungal species, with little or no toxicity. Histatins are being studied for use as components of artificial saliva for patients with salivary dysfunction (such as in Sjögren syndrome) or reduced salivary output (such as in those with diabetes mellitus).[16]

Those individuals with diabetes mellitus, in general, have reduced salivary secretion when compared with healthy individuals.[17,18] Furthermore, diabetic individuals tend to have higher oral yeast counts and higher salivary protein concentrations as well[17] and are at increased risk for oral candidiasis.[19] Those with recurrent oral candidiasis have increased levels of salivary histatins, suggesting that oral candidiasis may modulate salivary histatin levels.[20]

Treatment of this infection is predominantly a combination of surgical drainage and antifungal therapy. Choosing an antifungal agent has become more difficult with the growing resistance of *C. glabrata* to azole antifungal agents, described in the literature as early as 1998.[21–23] Still, there is evidence that *C. glabrata* continues to remain susceptible to voriconazole.[24,25] Moreover, there is evidence that *C. glabrata* is also able to withstand the fungicidal activities of members of the histatin family, including histatins 1, 3, and 5.[26–28] In one study, histatin 5 killed only 62.9% of *C. glabrata* isolates in vitro.[27]

In conclusion, although suppurative parotitis due to *Candida* is a rare event, and much less common in etiology than acute bacterial parotitis, it should be considered in cases of parotitis that remain resistant to traditional antibiotic therapy. In addition, the elderly, diabetic individuals, and others with reduced salivary flow seem to be uniquely at risk for acute parotitis. Although *C. albicans* is a more common cause of suppurative parotitis, concerns for *C. glabrata* resistance to azoles drugs, and the newly mounting evidence for resistance to the fungicidal histatin proteins in our saliva, make treatment complex. Lastly, although histatin-based drugs may be promising future antifungal agents, they may be less successful against inherently resistant *Candida* species such as *C. glabrata.*

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