Salivary gland infection with *Candida tropicalis*: antibiotic suppression therapy resulting in selection of uncommon pathogens

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Introduction: *Candida* infection of the salivary glands is extremely rare, and a parotid gland infection with *Candida tropicalis* in an immunocompetent patient has, to the best of our knowledge, never been described before.

Case presentation: A 76-year-old male with known bilateral oncocytic parotid lesions and antibiotic suppression therapy for a vascular endograft infection presented with fever and a tender red mass in the left parotid region. Although a bacterial infection of the parotid gland was suspected at first, cultures of parotid cyst aspirate yielded *C. tropicalis*. Once the Gram stain indicated the presence of yeast cells, fluconazole therapy was initiated. Follow-up after 3 weeks showed resolution of the infection and antifungal therapy was ceased.

Conclusions: With increasing and widespread antibiotic use, this case underlines the emergence of uncommon pathogens by antibiotic selection pressure. This shift in causative pathogens will not only result in an increase in *Candida* infections at known body sites but will also lead to infection of less common anatomical sites. Clinicians should recognize this trend and adjust their differential diagnosis accordingly.

Keywords: antibiotic; *Candida*; cyst; infection; salivary gland; selection.

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Introduction
Infection of the parotid gland most commonly has a viral (e.g., mumps virus) or bacterial origin, the latter often evoked by systemic dehydration or an obstruction of the gland. The bacterial species most likely to cause infection of the parotid gland is *Staphylococcus aureus*, and less commonly infections with *Streptococcus* spp. or anaerobic bacteria are seen. Although *Candida* spp. are known colonizers of the oropharynx, salivary gland infection with *Candida* spp. is extremely rare: only a handful of such cases have been described in the literature. As expected, these cases most commonly involve immunocompromised patients (Even-Tov et al., 2006; Marioni et al., 2003; Stefanopoulos et al., 2003; Raab et al., 1994). However, some cases in immunocompetent patients have also been described (Enache-Angoulvant et al., 2010; Leibowitz et al., 2010). To the best of our knowledge, no case of primary parotid cyst infection with *Candida* spp. and no salivary gland infection with *Candida tropicalis* has been described to date.

Case report
A 76-year-old male presented at the emergency department with fever and a red and tender swollen mass in the left parotid region. He was known to have bilateral oncocytic parotid lesions, as indicated by prior histopathological analysis. His medical history further revealed that 6 months earlier he had undergone vascular surgery and had received a proximal extension of his aortic endograft, which was placed 9 months earlier to treat a thoracoabdominal aneurysm. As the extension of the endograft was suspected to be infected, shortly after its placement

Abbreviation: CT, computed tomography.

The GenBank/EMBL/DDBJ accession number for the 18S rRNA gene sequence of *Candida tropicalis* determined in this study is KR855684.

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amoxicillin/clavulanic acid treatment was initiated. At the time of presentation, the patient had been taking amoxicillin/clavulanic acid 625 mg three times daily per os for 5 months. The oral status of the patient did not reveal any specific oral disease, no oral candidiasis and no periodontal disease were evident, nor were dentures present.

On presentation at the emergency department (day 0), infection of the parotid gland was suspected. Ultrasound examination revealed multiple cystic masses of the left parotid gland. Fine-needle aspiration of three dominant cysts was performed and the pyogenic aspirate was sent to the clinical microbiology and pathology laboratory for analysis (day 0). The differential diagnosis included bacterial parotid cyst infection and bacterial parotitis, and less probably a viral parotitis. The patient was admitted and the treatment with amoxicillin/clavulanic acid per os was switched to intravenous administration of 1200 mg four times daily, and intravenous clindamycin 600 mg three times daily was added.

A Gram stain of the pyogenic aspirate showed yeast cells, which was affirmed by the cytopathology microscopy results, which indicated inflammation and fungal spores with pseudohyphae (Fig. 1). Therefore, at day 1, intravenous fluconazole was added to the treatment regime: 800 mg on the first day, followed by 400 mg per day. After admission, the blood inflammatory parameters initially remained high (C-reactive protein levels >200), and fever and the red tender parotid mass persisted. A computed tomography (CT) scan at day 7 revealed bilateral cystic masses of the parotid gland. The cysts of the left parotid showed thickened walls and surrounding fatty infiltration, indicative of an inflammatory process (Fig. 2a). Multiple calcifications were also seen in the left parotid gland, which may have caused an obstruction, although no salivary dysfunction was clinically present. Meanwhile, culture of the aspirate showed exclusive growth of C. tropicalis, as determined by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (VITEK MS, bioMérieux; Myla database version 3.2.0-2, identification score for C. tropicalis, 99.9), and subsequently the clindamycin therapy was ceased at day 3. The mass spectrometry determination was confirmed by partial sequencing of the 18S rRNA gene, which confirmed the strain to be C. tropicalis (fragment length 265 bp). The final diagnosis was Candida parotid cyst infection. The patient responded well to intravenous fluconazole therapy, and at day 11, the intravenous administration of fluconazole was switched to 400 mg daily per os and the patient was discharged. Amoxicillin/clavulanic acid treatment was reinstated to the pre-admission per os dosing scheme. Follow-up 3 weeks after discharge showed resolution of the infected parotid cysts (Fig. 2b), and the fluconazol therapy was ceased at day 31.

**Discussion**

This is the first report of a parotid gland infection with C. tropicalis. In addition, a primary infection of parotid gland cysts by Candida spp. has, to the best of our knowledge, never been described before. Salivary gland infection with Candida is extremely rare, and often an underlying malignant disease or immunocompromising condition is present. It is of special interest that the infection we described occurred in an immunocompetent patient who received antibiotic suppression therapy. This is attributed to the selection pressure of antibiotic therapy on the oral flora, creating an environment where yeasts can cause opportunistic infections. Candida spp. are part of the normal oral flora, as illustrated by a study of the fungal microbiome in 20 healthy individuals, which showed that 75 % of the cohort harboured Candida spp.: the most abundant species was Candida albicans (40 %), followed by Candida parapsilosis (15 %), Candida tropicalis (15 %), Candida krusei and Candida metapsilosis (5 %) (Ghannoum et al., 2010). Of course, a possible obstruction of the parotid gland may have predisposed to the development of parotid infection in the case presented, but this is also often the case with more common pathogens at this site.

It is well known that broad-spectrum antibiotic treatment affects the human microbiome and changes its composition (Britton & Young, 2014). In an era of ever increasing use of antibiotics, physicians will be increasingly confronted with patients who have an altered composition
of their microbiological flora. This will affect the differential diagnosis, making some pathogens more likely to be the cause of infection, and others less likely. This shift in causative pathogens will not only result in an increase in Candida infections at known body sites (e.g. Candida fungemia or line sepsis), but, as we have demonstrated, will also lead to infection of less common anatomical sites for a specific organism. Therefore, it is of utmost importance for physicians to bear in mind that they will be increasingly confronted with emerging pathogens such as Candida spp.

In conclusion, next to sensible prescription of antibiotic therapy, physicians should also be aware of the effect that antibiotic usage has on the spectrum of possible pathogens causing infectious disease. With the ever increasing use of antibiotics, it is paramount for physicians to have infections with less common pathogens in their differential diagnosis.

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References