Gerodontology

Case report

Oral candidiasis mimicking an oral squamous cell carcinoma: report of a case

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Oral candidiasis is a significant problem in immune-compromised patients. The most common forms of mucosal candidiasis are oropharyngeal, oesophageal and vaginal, and more than 90% of HIV positive persons will manifest at least one episode of oropharyngeal candidiasis. Local and systemic factors such as uninterrupted daily use of a prosthesis by patients, smoking habit, as well as high glucose intake may contribute to the development of the lesion. The aim of this article is to report an uncommon case of oral candidiasis presenting an aggressive clinical behaviour in a 64-year-old male patient, with a significant smoking habit and a medical history of non-controlled diabetes. The lesion affected the hard and soft palate of the right side, revealing erythematous and ulcerated areas, elevated borders and central portions resembling necrosis, mimicking the clinical features of oral squamous cell carcinoma. However, the correct diagnosis of oral candidiasis was obtained after histopathological and cytological examinations and the patient was easily treated with traditional antifungal drugs and correction of his glucose levels.

Keywords: *Candida*, diabetes, tobacco, prosthodontics.

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Introduction

Oral candidiasis is the most common opportunistic oral infection in humans[1] and it has received increasing attention, presumably due to its increased prevalence worldwide[2]. The majority of infectious episodes are caused by *Candida albicans*, a dimorphic fungal commensal organism of the gastrointestinal and lower female reproductive tracts. *Candida albicans* asymptomatically colonises epithelial surfaces presumably in the blastoconidia form that it takes in nature. As a result of this exposure, many healthy individuals have developed detectable *Candida*-specific immunity, which presumably protects against infection[3]. However, numerous studies have shown that several *Candida* species possess a multitude of virulence mechanisms leading to successful colonisation and infection of the host[2,4–6].

Several predisposing factors have been recognised as being potentially involved in the development and, above all, in the chronicity and/or relapse of this infection. Therefore, a predisposition to oral candidal colonisation and candidiasis is increased with xerostomia, immunodeficiency, denture wearing and tobacco smoking. In addition, it has been suggested that a high carbohydrate diet and diabetes mellitus may predispose to oral candidiasis[1].

Oral squamous cell carcinoma (OSCC) is one of the most common types of cancer in the world, accounting for more than 95% of all malignant neoplasms in the oral cavity. It is a significant problem in many parts of the world as its high incidence, unsatisfactory 5-year survival rate and because treatment can result in severe functional defects[7,8]. Clinically, OSCC usually presents as an asymptomatic chronic ulcerative lesion with

elevated borders and areas of tissue necrosis, mainly affecting elderly patients with a smoking habit.

The aim of this article is to report a case of oral candidiasis with an atypical presentation resembling an OSCC in a 64-year-old male diabetic patient.

Case report

A 64-year-old male patient was referred by a general dental practitioner with the chief complaint of a ''hole in his palate'', which under clinical evaluation led his dentist to suspect an OSCC. During the anamnesis the patient reported smoking more than 60 cigarettes per day, not being an ethanol user, but had no other contributory past medical or dental history. On intraoral evaluation, a large lesion affecting the posterior portion of the hard palate and the anterior portion of the soft palate of the right side, presenting with erythematous and ulcerated areas, elevated borders and central portions resembling necrosis was observed (Fig. 1). Because of the clinical presentation, the previous hypothesis of OSCC was maintained.

Incisional biopsy was performed and the histopathological analysis revealed an unspecified chronic inflammatory process, ulcerative areas and hyphae of *C. albicans* (Fig. 2), confirmed by a cytological examination using the periodic acid-Schiff (Fig. 3).

The patient underwent blood-fasting glucose dosage to evaluate the presence of diabetes mellitus and the results revealed a laboratory value of 543 mg/dl, higher than the normal value, thus being referred to an endocrinologist. The patient's treatment comprised the use of nystatin 500 000 IU, four times daily for 10 days, retaining the drug in the mouth for some minutes before swallowing. In addition, the patient was asked to change his prosthesis, as well as adopting preventive measures such as not sleeping wearing his prosthesis and to wash it at least once daily. After 10 days of treatment, the patient presented with a good repair process taking place, returning after 25 days with his hard and soft palates completely healed (Figs 4 and 5).

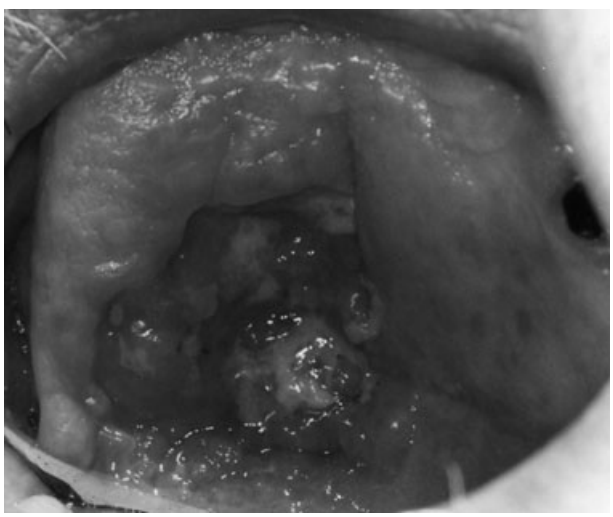

Figure 1 Clinical presentation of a large lesion with erythematous and ulcerated areas, elevated borders and central portions resembling necrosis.

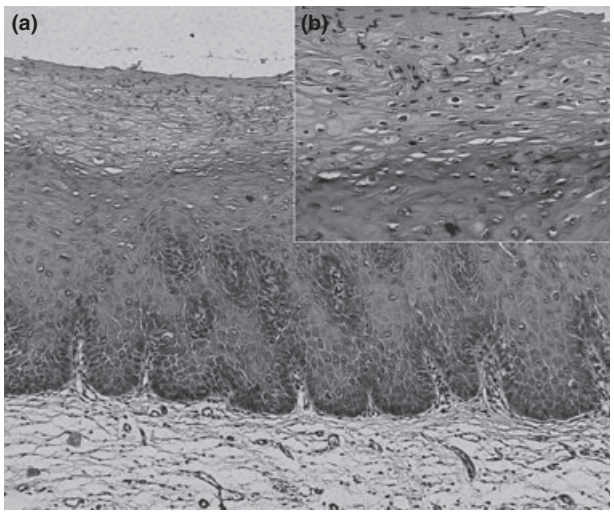

Figure 2 Histopathological analysis using the periodic acid-Schiff staining revealing the presence of hyphae of *Candida albicans* in the superficial layer of the epithelium. (a) Original magnification × 20. (b) Original magnification × 40.

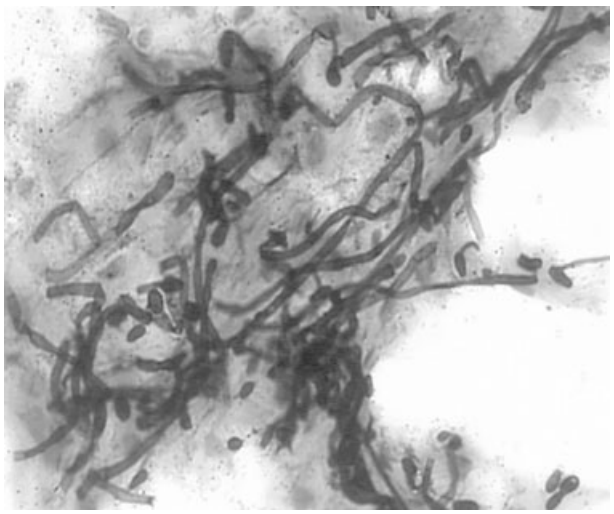

Figure 3 Presence of hyphae of *Candida albicans* in the cytological examination.

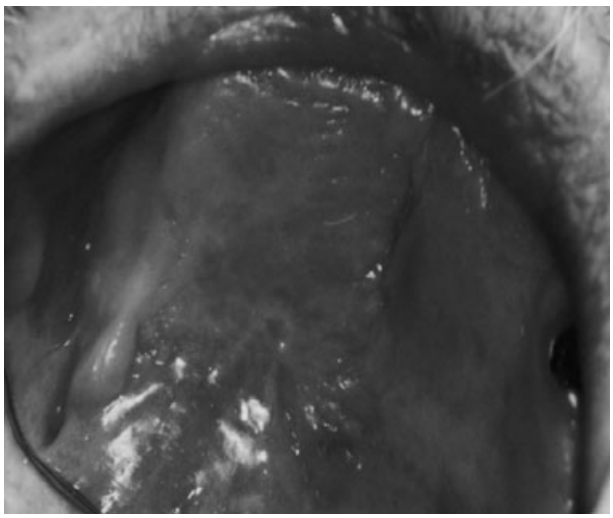

Figure 4 Hard and soft palate completely healed after 25 days of treatment.

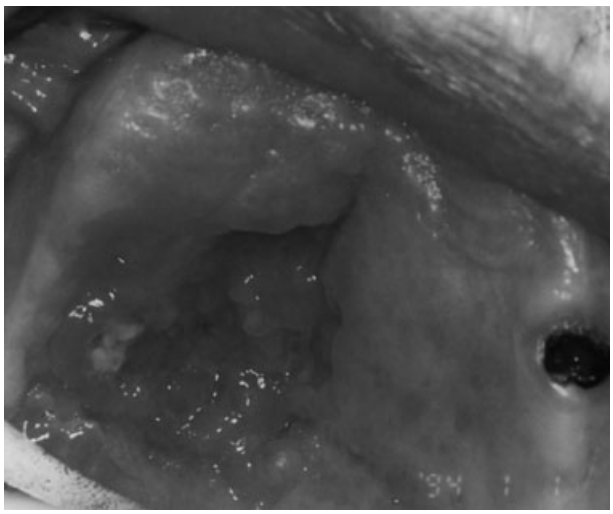

Figure 5 Good repair process ten days after treatment beginning.

Discussion

As a constituent of the normal human microflora, the fungus *C. albicans* is harboured in the mucous-lined body organs in approximately 40–60% of population. Although non-albicans *Candida* species are emerging as significant pathogens, *C. albicans* still occupies the top of the list for causing all forms of candidiasis[9]. This fungus may change from commensal to a pathogenic microorganism in the mouth in relation to oral and systemic conditions, hence, once the host is afflicted with any immune-compromising condition, for example, diabetes mellitus, neutropenia, AIDS, it will become more liable to candidiasis. In addition, other factors that lead to a disturbance of the local environment of the oral cavity can predispose the individual to candidiasis[9,10].

In the present study, we reported a case of oral candidiasis where the association of a variety of factors linked to the patients' systemic health and local environment disturbances led to the development of a lesion with an atypical clinical presentation with ulcerated areas, elevated borders and portions resembling necrosis mimicking an OSCC.

It is known that tobacco use is the main risk factor for OSCC acquisition and different studies have shown that tobacco use increases OSCC risk up to seven times when compared with the general population, and alcohol in combination with tobacco raises that risk to 15 times[11–13]. The majority of the patients affected by OSCC are reported to be active smokers or have smoked previously. Therefore, in the present case the high amount of cigarettes smoked daily by the patient, associated with the clinical presentation of the lesion, contributed to the OSCC hypothesis reached by his dentist and maintained by us before the result of the incisional biopsy.

The habit of cigarette smoking is clearly recognised as a predisposing factor for oral candidiasis[6]. In a recent study, Shin *et al.*[14], using 180 healthy subjects, found a significant relationship between cigarette smoking and oral candidal carriage, and it was observed that the more heavily the individual smoked, the more likely they were to carry *Candida* in the oral cavity. However, the exact mechanism by which candidal carriage may be affected by cigarette smoking is not yet fully established. It has been suggested that smoking may lead to localised epithelial alterations, increasing oral epithelial keratinisation and subsequent enhancement of hydrophobicity, which may predispose the smoker to higher oral yeast colonisation[6,15]. An alternative hypothesis is that smoking depresses the activity of oral leucocytes and reduces gingival exudate with the consequence that the carriage of leucocytes and immunoglobulins, important in inhibiting the colonisation of *Candida* in the oral cavity, is likely to diminish and enhance candidal colonisation[6].

Increased salivary glucose has been implicated as an independent risk factor for increased oral candidal carriage. Salivary glucose may form chemically reversible glycosylation products in tissues during hyperglycaemic episodes. It is possible that accumulation of such glycosylation products on buccal epithelial cells may increase the number of available receptors for *Candida*, favouring yeasts

growth. Furthermore, tobacco smoke increases adrenaline levels in blood, and blood glucose levels in diabetic smokers were significantly higher than non-smokers due to the effect of smoke on adrenaline[6,16]. In this line of view, it can be suggested that the association between smoking habit and the elevated glucose levels of the patient in the present case, favoured the onset of a lesion with an aggressive clinical presentation.

It is fully recognised that the qualitative and mainly quantitative alterations of saliva play a primary role in the development of oral candidiasis. Saliva contains a variety of anti-candidal agents such as transferrin, lactoferrin, secretory immunoglobulin A (sIgA), defensins and histatins (*Candida* adhesion-inhibiting proteins)[1,16]. Both stimulated and non-stimulated saliva flow rate and levels of anti-candidal agents decrease gradually with age. The reason for this depends on senile hypofunction of the parotid and submandibular glands, on systemic disease and, especially, on the side effects of medication. More than 400 drugs can give rise to xerostomia or salivary gland hypofunction, this probably being most frequent or pronounced in geriatric patients, which present with oral candidiasis prevalence ranging from 34 to 51%. Although our patient did not report the use of any drug that could lead to salivary hypofunction, his age may have contributed to a decreased salivary flow, favouring the lesion development.

There is also a large body of evidence indicating that *Candida* is able to adhere to acrylic resin dentures and that this is the first step that may lead to the development of the infectious process and may ultimately result in varying degrees of denture stomatitis of the adjacent mucosa. Without this adherence, microorganisms would be removed from the oral cavity when saliva or food is being swallowed[16].

Poor denture hygiene by patients is common and by virtue of the lack of local saliva and high level pH, *Candida* can easily proliferate beneath and within the denture acrylic. Previous studies have likewise found that dentures may predispose to oral candidal carriage, particularly in older persons who are more likely to be partially or fully edentate, representing a significant risk factor for subsequent clinical disease[1]. Hence, the long and uninterrupted use of a prosthesis by the patient, associated with the lack of satisfactory hygiene may have significantly favoured the carriage of *Candida* hyphae, contributing to fungal infection. In addition, the absence of an appropriate fit of the prosthesis because of its long period of use could be associated with palatal trauma, therefore, altering the mucosal surface and allowing a direct mucosal insult by tobacco smoke, facilitating fungal entry into the adjunct mucosa and consequent candidal colonisation.

There is a likelihood that more people will be at risk of oral candidiasis as a consequence of increasing lifespan, greater use of immune-suppressive therapies and the wider range of drugs that can give rise to hyposalivation. In view of these changes, there is a need to establish more specifically target people at risk of oral candidiasis in order to provide them with an appropriate preventive programme[1]. In the present case, the uninterrupted daily use of the prosthesis by the patient for more than 20 years, his advanced age, his smoking habit, as well as the high glucose dosage might have contributed for the candidal colonisation and the development of candidiasis. In conclusion, dentists must be aware of older patients presenting with lesions with atypical features, and that it is extremely important and necessary that an incisional biopsy examination be performed in these cases.

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