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Case report

Oral candidosis in Non-Hodgkin's lymphoma: a case report

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Abstract: Though oral candidosis is an opportunistic fungal infection that commonly affects immuno-compromised patients, little is known of its occurrence as a complication of Non-Hodgkin's lymphoma. This paper reports a case of oral candidosis in a 20-year-old Indonesian woman with this lymphoproliferative disease. She presented with acute pseudomembranous candidosis on the dorsum and lateral borders of the tongue, bilateral angular cheilitis and cheilocandidosis. The latter is a rare clinical variant of oral candidosis, and the lesions affecting the vermilion borders presented as an admixture of superficial erosions, ulcers and white plaques. Clinical findings were confirmed with oral smears and swabs that demonstrated the presence of hyphae, pseudohyphae and blastospores, and colonies identified as *Candida albicans*. A culture from a saline rinse was also positive for multiple candidal colonies. Lip and oral lesions were managed with Nystatin. The lesions regressed with subsequent crusting on the lips, and overall reduction in oral thrush. As Non-Hodgkin's lymphoma is a neoplastic disease that produces a chronic immunosuppressive state, management of its oral complications, including those due to oral candidosis, is considered a long-term indication. (J Oral Sci. 45, 161-164, 2003)

Key words: oral candidosis; cheilocandidosis; Non-Hodgkin's lymphoma; nystatin.

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Introduction

Candida, a dimorphic yeast, is a normal commensal of oral and vaginal mucous membranes (1). Within the oral cavity, this opportunistic organism thrives in an acidic environment where it assumes a pathogenic role when the host-commensal relationship is disturbed (2). Local predisposing factors include reduced salivary flow, trauma, epithelial loss, decreased pH and carbohydrate-rich diets (2-4). Systemic predisposing factors are old age, endocrine disturbances, nutritional deficiencies, broad-spectrum antibiotic therapy and long-term corticosteroid therapy (2,5-7).

Of the six candidal biotypes known to infect the human oral mucous membrane, *Candida albicans* represents the most frequently encountered species, both as a normal commensal and as a pathogen (1,2,6,8). It grows in colonies producing true hyphae, pseudohyphae and blastospores. In the oral cavity it can adhere to buccal and labial mucosa, dorsum or lateral borders of the tongue, as well as the hard and soft palate regions, in particular the denture-bearing areas. Other biotypes isolated from oral lesions include *C. tropicalis*, *C. pseudotropicalis*, *C. glabrata*, *C. krusei* and *C. parapsilosis* (1,2,4,6). Switching mechanism of candidal species, as indicated by a variation in colonial forms, is essential for host invasion and proliferation in different body environments (6). Accordingly, altered surface antigenicity eludes the host cell immune response, provides adhesion to oral mucosa and provides potential resistance against antifungal agents (6).

Oral candidosis is a polymorphic disease with many clinical forms. A recent reclassification of oral candidosis has been proposed by Axell et al. (3) (Table 1). This report illustrates three clinical manifestations of oral candidosis, i.e. acute pseudomembranous candidosis, angular cheilitis

and cheiliocandidosis, as seen in an immunocompromised patient.

Case Report

A 20-year-old Indonesian woman diagnosed with Non-Hodgkin's lymphoma was referred to the Oral Medicine Clinic of the Faculty of Dentistry, University of Malaya, Kuala Lumpur for the management of multiple white lesions affecting the dorsum and lateral borders of her tongue, as well as ulcerations of her lips. At presentation, her medical profile included persistent fever for the previous 3 months, malnutrition, dehydration, loss of appetite and loss of weight, decreased urine output for one month with subsequent renal impairment, and generalised weakness. Hematological investigations disclosed abnormal blood film consistent with acute hemolytic anemia. This was associated with low serum iron, folate and B_{12}, abnormal white blood cells and an increased platelet count. Clinical examination revealed generalised facial puffiness with increased melanin pigmentation. Bilateral submandibular lymphadenopathy was present. Both lips were edematous and tender to palpation. There was bilateral fissuring and ulcerations of the corners of the lips, and superficial erosions with white flecks were found on both vermilion borders (Fig. 1). Intraorally, extensive white milk curd-like lesions were present on the dorsum and lateral borders of the tongue (Fig. 2). Oral swabs and smears were obtained for microbiological examinations from the above-mentioned sites.

Table 1 Proposed revised classification of oral candidosis (3)

Primary oral candidosis	Secondary oral candidosis
Acute forms	Oral manifestations of systemic mucocutaneous candidosis (as a result of diseases such as thymic aplasia and candidosis endocrinopathy syndrome)
Pseudomembranous	
Erythematous	
Chronic forms	
Hyperplastic	
Nodular	
Plaque-like	
Erythematous	
Pseudomembranous	
Candida-associated lesions	
Denture stomatitis	
Angular cheilitis	
Median rhomboid glossitis	
Keratinized primary lesions superinfected with *Candida*	
Leukoplakia	
Lichen planus	
Lupus erythematosus	

Microbiological Findings

Culture in Sabouraud Dextrose Agar medium showed multiple pale yellowish dome-shaped colonies identified as compatible with the colony morphology of *C. albicans*. Smears stained with Periodic Acid Schiff reagent demonstrated the presence of hyphae, pseudohyphae and blastospores from all three sites (Fig. 3).

Management

For definitive treatment, Nystatin oral suspension (100,000 IU four times daily) was prescribed. In addition, a gel form of Nystatin was used for the lip lesions. Oral toilet and saline mouthbath were carried out on a regular basis. The lesions regressed considerably after Nystatin therapy, and subsequent culture of swabs taken from the tongue and lips yielded fewer candidal colonies. At the time of reporting, the patient's oral condition was stable and satisfactory.

Discussion

This report describes a case where the onset of Non-Hodgkin's lymphoma occurred first, and oral candidosis presented as a complication of this disease. Three clinical forms of oral candidosis: acute pseudomembranous candidosis or thrush on the tongue, whilst on the lips, cheilocandidosis/candidal cheilitis and angular cheilitis were identified here.

Acute pseudomembranous candidosis represents the most frequently encountered clinical variant of candidosis in the oral cavity (1-4). Extremes of age (i.e. infancy and old age), and underlying debilitating diseases like diabetes mellitus, leukemia and HIV infection are well recognized as the key predisposing factors (1,2,4). In the current case,

Fig. 1 Clinical appearance of the lip lesions. Note the fissuring and ulceration of the angles of the lips (white arrows). The vermilion borders are swollen and show superficial erosions and ulcerations. White flecks are present peripheral to these lesions.

Non-Hodgkin's lymphoma as the underlying debilitating disease is the most obvious precipitating cause. The other etiologic factors considered here were the poor nutritional status of this patient, and her other medically related problems, i.e. dehydration, hematinic deficiencies, renal impairment and acute hemolytic anaemia. All these factors may produce a cumulative state of immunosuppression that in turn may lead to a change in the host-commensal balance with the resultant emergence of pathogenic forms of candida within the oral environment (2,4,8). In general, thrush can affect any part of the oral mucous membrane, but it is more prevalent on the surface of the tongue, buccal and labial mucosa, gingiva, soft palate and oropharynx. In this case, the dorsum and lateral borders of the tongue were the main sites of involvement (2,4). The lesions in thrush are typically described as non-adherent, milk curd or creamy white confluent plaques that can be easily wiped off to leave a raw and erythematous or bleeding base (1,2,4). These features were similarly observed in the present case. The pseudomembranes that were scraped off were verified microscopically to consist of a tangled meshwork of hyphae, pseudohyphae, blastospores, desquamated epithelial cells and debris (2,4).

Angular cheilitis and cheilocandidosis were the two clinical forms of candidosis affecting the lips of this patient. Whilst angular cheilitis a common clinical variant encountered, cheilocandidosis by comparison is relatively rare (5,9). Fissuring, erythema, ulceration and pain at the angles of the lips, as observed in the present patient, were typical of lesions associated with angular cheilitis. As angular cheilitis has a multifactorial etiology, the underlying hematinic deficiencies present in this patient would have contributed to the development of these lesions as well (1,4). Other predisposing causes of angular cheilitis, i.e. loss of vertical dimension with accentuation of the folds at the corners of the mouth as seen in older individuals, were however not observed in this patient (1,9). Staphylococcal infection as a cause of angular cheilitis is a common finding. Twenty percent of angular cheilitis are caused by *C. albicans* alone, 20 percent are associated with *Staphylococcus aureus* alone, and 60 percent are due to a combined infection by *C. albicans* and *Staphylococcus aureus* (10). Concurrent staphyloccoccal infection was not detected in this case.

Diffuse primary infection of the lips is very unusual (4,9). Most of these cases represent secondary candidal infection known as cheilocandidosis or candidal cheilitis. This clinical variant is not well-recognized in part because it is rarely encountered, and also because it does not fall into any of the three major categories of primary oral candidosis, i.e. pseudomembranous, erythematous and hyperplastic (4). In Axell et al.'s proposed reclassification of candidosis, this clinical form was not recognized as well (3). Consequently, little is known of its spectrum of clinical manifestations. Accordingly, in cheilocandidosis, the lesions tend to occur in areas of low-grade trauma (9). Chronic lip licking or sucking can traumatise the vermilion border, precipitating this superinfection (9). The lesions have an ulcerative and granulating appearance (5). In the current case, the patient reported having no chronic lip licking habit. At initial presentation, both her lips were inflamed, swollen and tender. The vermilion borders appeared erythematous and contained scattered irregular areas of erosion, ulceration and bleeding points. Smaller areas of whitish plaques were also observed in association with these lesions. These varied manifestations, i.e. erythematous, ulcerative and plaque-like lesions, probably account for the difficulties underlying the inclusion of this clinical subtype into the standard candidosis classification in current use. Issues relating to the formulation of an acceptable classification

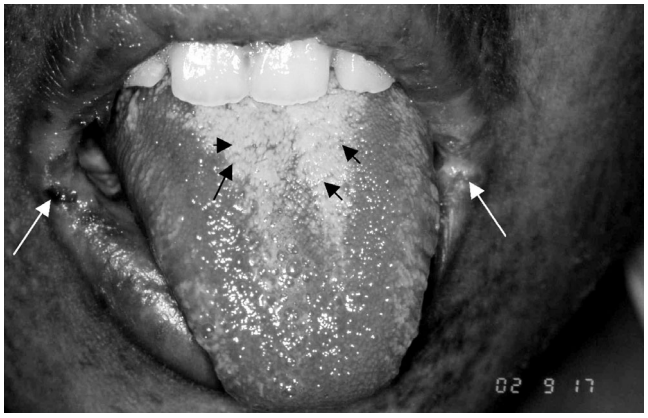

Fig. 2 Pseudomembranous lesions are present on the dorsum of tongue (black arrowheads). Note fissuring and ulcerations at the angles of lips (white arrows).

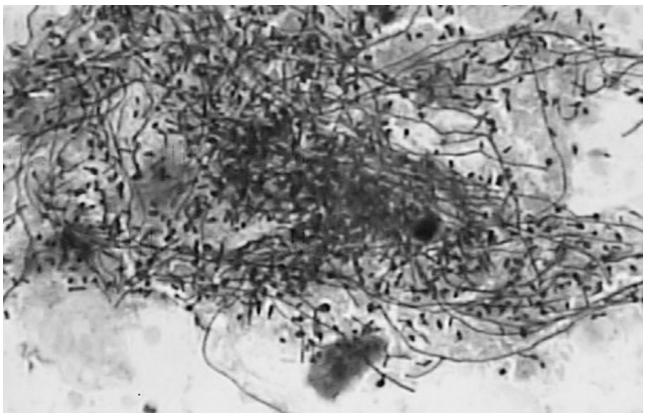

Fig. 3 Smear shows a tangled meshwork of hyphae, pseudohyphae and blastospores. (PAS, × 132)

of oral candidosis have been extensively discussed elsewhere (1,3,4).

Candidosis is a clinical marker of disease progression. Therapeutic responsiveness of this oral complication would depend on whether the underlying disease is in its active or remissive phase. The management of oral candidosis in immunocompromised patients requires systemic antifungal therapy (5,11). In this case, the tongue and lip lesions responded very well to Nystatin, alleviating the necessity of instituting more potent and newer forms of systemic antimycotics at this stage. In general, the presence of species other than *C. albicans* has important therapeutic implications, as susceptibility to antimycotics may be species-related (11). However, as *C. albicans* represented the only species isolated from the oral lesions of this case, this problem was not encountered. As Non-Hodgkin's lymphoma is associated with a chronic state of immunosuppression, oral candidal re-infection is likely, and management of these cases would therefore require long-term follow-up.

In summary, a case of Non-Hodgkin's lymphoma presenting with oral candidosis is described to highlight the varied oral clinical manifestations of this opportunistic infection in an immunocompromised individual, and to draw attention to the less well-known clinical variant, cheilocandidosis.

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