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Yeast organisms associated with human oral leukoplakia.

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Abstract

Oral leukoplakia is a lesion of variable clinical behaviour and a malignant transformation rate of 3-6%. Leukoplakia exhibits various histologic features, hyperkeratinization being the most consistent. As yeast organisms have been encountered in a high proportion of leukoplakia cases, a causal role has been suggested for these organisms. Candida albicans is by far the most commonly isolated yeast from leukoplakia, but also other Candida species as well as Torulopsis and Saccharomyces species may be encountered. The species composition of the mycoflora in leukoplakia does however not differ from that of normal oral mucosa. Subspecies differentiation of C.albicans has revealed the existence of different oral strains between individuals and further, strain differences of C.albicans in leukoplakia and in normal mucosa have been observed. This procedure may lead to isolation and identification of the yeast organisms causally associated with leukoplakia.

Introduction

Oral leukoplakia is a white patch that cannot be characterized clinically or pathologically as any other disease (1). Prevalence rates of leukoplakia range from 20 to 1160 cases per 10,000 people, and malignant transformation in up to six per cent of leukoplakia cases has been observed in long-term studies involving observation periods of one to 11 years (2). Tobacco is a recognized cause of leukoplakia, but in addition numerous studies during the last two decades have pointed to yeasts, in particular Candida species, as causative agents of the disease (2,3).

Yeasts constitute a prominent part of the oral microflora, with isolation frequencies in the range of 2-37 per cent in healthy subjects, according to a recent review (4). The mean frequency, weighted according to the number of subjects in each study, was 14.3 per cent for yeasts, 10.3 per cent for Candida albicans. In studies of the oral yeast flora in hospital patients the weighted mean frequency was 45.2 per cent for all yeasts, 42.9 per cent for C.albicans. The quantitative outcome of isolation studies is heavily influenced by the technique used, and it appears that imprint culture technique is more sensitive than impression cultures and isolation from saliva (5). Species, and subspecies identification requires isolation of the fungal organism, whereas histologic

investigation of tissue sections and microscopy of smears can only provide a tentative genus identification at best.

Leukoplakia studies employing microscopic examination of fungal organism

By use of histologic examination of biopsies or microscopy of smears from cases of leukoplakia studies in a number of countries have revealed the presence of yeast cells, in the range 10 to 85 per cent (Table 1). The yeast cells in the reported studies are generally described as forming pseudohyphae, a morphologic feature characteristic of the genus Candida. In a few studies (6, 12) has the fungal organism been isolated and identified (See following section).

Table 1. Yeast cells observed in oral leukoplakia using histologic examination of smears or biopsies

Country	Number of samples	Presence of yeast cells (in %)	Reference
Denmark	64	38	6
U.K.	138	11	7
Denmark	235	23	8
Denmark	98	31	9
India	723	7	10
West Germany	656	13	11
U.K.	13	85	5
West Germany	103	10	12

Leukoplakia studies employing isolation of fungal organism

By use of swabs from leukoplakias, and normal oral mucosa for comparison, and inoculation on mycological agar media, yeasts have been isolated from the majority of samples (Table 2). C.albicans was the dominating species encountered, making up 67-80% of the isolated yeast flora. The remaining part of the flora included other species of Candida, as well as species of Torulopsis and Saccharomyces. It is evident from Table 2 that there is no obvious difference in the species composition between leukoplakia and normal mucosa, as one would expect, if yeasts were performing a causal role in leukoplakia. However, the hypothetical leukoplakia-inducing property might not be species related, but merely a characteristic of subspecies, or strains. Preliminary data from a study, designed to persue this

aspect, is shown in table 3 (13). The species C.albicans is subdivided into strains by a recently developed system, based on the performance of strains in nine biochemical tests (14). According to the performance in the tests the strain under investigation is designated a code of three-digit numbers. If two strains differ in three or more tests, they are considered to be different strains. Thus the C.albicans strains isolated from Case 1, 3, 4, and 5 are all different (Table 3). Further, three of the four C.albicans strains from Case 5 are different.

Table 3. Distribution of yeasts and C.albicans strains[a]

Case	Site	Yeast	C. albicans strain code
1	leukoplakia	C. albicans	153
	normal mucosa	C. albicans	173
2	leukoplakia	C. tropicalis	
	normal mucosa	none	
3	leukoplakia	C. albicans	243
		T. glabrata	
	normal mucosa	C. albicans	053
		T. glabrata	
4	leukoplakia	C. albicans	377
	normal mucosa	C. albicans	377
5	leukoplakia	C. albicans	163; 243
	normal mucosa	C. albicans	553; 553

[a] Adopted from 13

Conclusion

Although yeasts, particularly Candida albicans frequently have been found associated with leukoplakia, opinions are divided as to the significance of the organisms as a causal factor in the lesion. The yeasts may be just secondary invaders, but it is noteworthy that treatment of leukoplakia with fungicides in some cases causes regression of the lesions (3, 15). Further, the histologic picture of yeast-associated leukoplakia resembles that of other Candida infections in the oral cavity. However, the elucidation of the causal association between leukoplakia and yeasts would be greatly enhanced by isolation and identification of yeast strains with leukoplakia-inducing potency in animal models, and the application of a strain differentiation system for C.albicans may be a first step in this direction.

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