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Case Report
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Oral Candidiasis Turns to Oral Cancer - A Rare Clinical Presentation

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Abstract

Oral carcinogens like tobacco and alcohol are well recognized risk factors associated with development oral precancerous lesions and subsequent cancer of the upper aerodigestive tract. The role of infection and chronic inflammation is also a recognized as being significant in cancer development. It has a well accepted fact that white patches of oral mucosa, which are super infected with Candida, have a greater probability of undergoing malignant transformation than those that are not infected. There are less case reports with association between chronic fungal infection and development of cancer. Here with, we report a case of chronic Candidial infection which was diagnosed and initially treated as chronic oral Candidiasis which on follow up turned into oral sqamous cell carcinoma.

Introduction

Indian subcontinent shows the highest prevalence of oral cancer among all cancers in men, while it is the sixth most common cancer worldwide [1]. On an average possibly about 8-8.5% men and 4-8.1% women will develop oral cancer in their lifetime in developing countries [2]. Oral cancer is a multifactorial disease though most of the times it is preceded by some premalignant lesions or conditions for varying length of time. Interestingly they share some etiological factor with oral cancer, particularly the use of tobacco or other carcinogens addiction.

Infection has a considerable role in cancer development, causing approximately one in five malignancies worldwide [3,4]. Bacteria like Helicobacter pylori, viruses like Human Papilloma Virus (HPV), chronic hepatitis B and C infections, and herpesvirus, Epstein-Barr virus (EBV), causes cancer due to chronic infections [5]. The literature on etiological relationship between fungal infection and cancer are less, although for many years Candida species have been implicated in various epithelial cancers. Candidal infection does not appear to be a risk factor for dysplastic cervical lesions or cervical carcinoma [6] and most interest in Candida and carcinogenesis is related to oral and esophageal carcinoma [5]. The possible association between Candida species and oral neoplasia was first reported in the 1960s with later reports suggesting a link between the presence of Candida albicans in the oral cavity and the development of oral squamous cell carcinoma [7]. In actuality epithelial dysplasia improves after elimination of Candida species from infected tissue also supports this contributory association [8].

The aim of this case report is to add in the literature of a rare case presentation of chronic oral Candidiasis which converts into oral cancer on follow up.

Case Presentation

A 60 years female reported to department of oral medicine with a chief complaint of burning sensation in mouth since 4-5 years. On taking detailed case history she revealed she was alright 4-5 years back when she started experiencing burning sensation in mouth. Burning sensation was present when she uses to take spicy food which decreases on taking sweet food or sweets. Patient was advised to take capsule Becosule for burning sensation by their relatives, but burning sensation still persisted after taking medications once daily for few days. Now in last 15 days she visited to a dentist for extraction of her mobile teeth in upper front region of jaw. After extraction of her teeth, Dentist referred her to our institute for her complains regarding burning sensation in mouth and for a white lesion on palate and tongue. No history of trauma, weakness, stress or weight loss. Patient was asthmatic and taking inhaler for the same since last 7 to 8 years (beclomethasone dipropionate). Patient was also hypertensive since last 3 years and on medication for the same (Tablet Amlodipine

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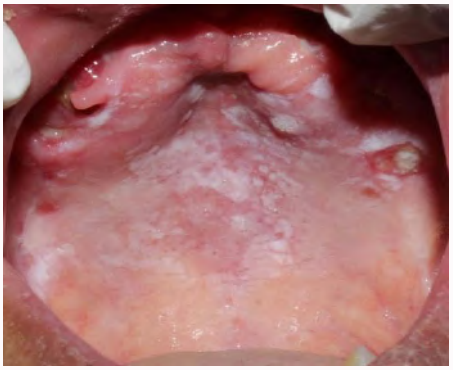

Figure 1: Lesions on palate.

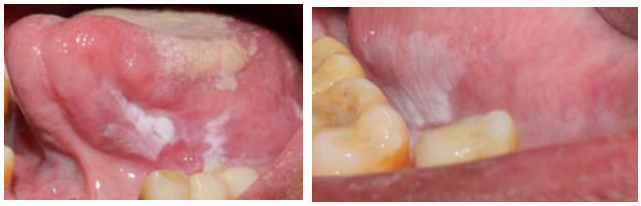

Figure 2: Lesions on left and right ventral surface of tongue.

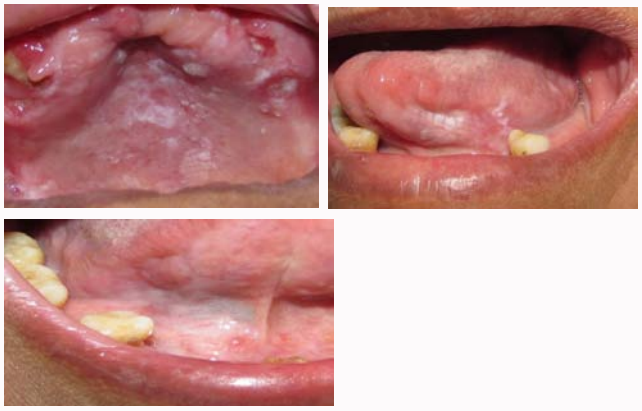

Figure 3: Healing lesions on follow up visit after topical antifungal applications.

5 mg). In general physical examination she was normal with all vital parameters within normal limits.

On examination of her intraoral lesions, white slightly scrapable lesion noted involving complete palate which was also extending on maxillary alveolar ridge in some sites (Figure 1). White non scrapable lesion was also noted on right and left ventral surfaces of tongue (Figure 2). There was coating on dorsal surface of tongue. Based on her history and clinical presentation provisional diagnosis of Pseudomembranous Candidiasis on palate and chronic hyperplastic Candidiasis on right and left ventral surface on tongue was made. Patient was subsequently started with topical antifungal, symptomatic treatment and kept on follow up. After 1 month follow up lesions was resolving on palate and ventral surfaces of tongue (Figure 3). Patient was again called after 15 days. Lesion was still better in follow up visits while non healing lesion was seen on maxillary anterior region of jaw (Figure 4). Patient was given symptomatic treatment for that but lesion was not healing so we had opted for incisional biopsy which was turned as well differentiated squamous cell carcinoma on histopathologic examination (Figure 5). Patient was advised CT scan

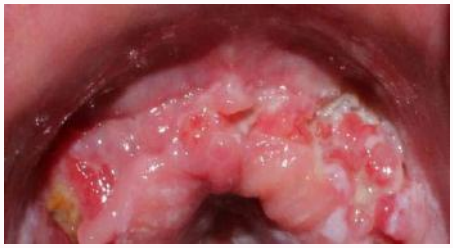

Figure 4: Non healing socket in maxillary anterior region on follow up visits.

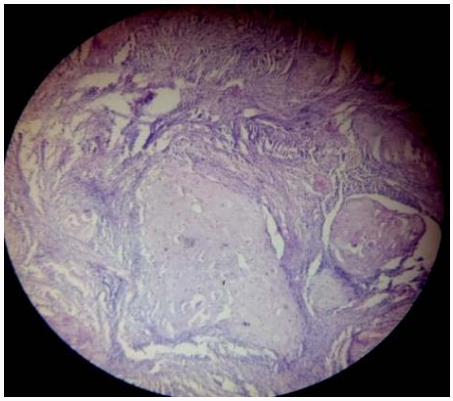

Figure 5: Histopathlogic picture.

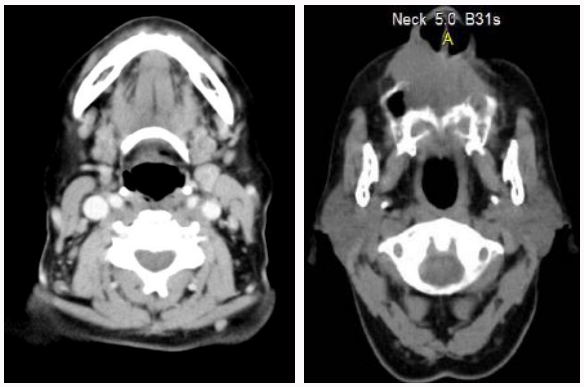

Figure 6: CT scan showing extent of lesion.

(Figure 6) and surgical treatment was done. Patient is still on follow up and no recurrence noted till date.

Discussion

Cancer is Latinized from Greek word 'Karkinos', meaning a crab, representing how carcinoma extends its claws like a crab into the adjacent tissues. Cancer is the second most leading cause of mortality in economically developed countries and the third most leading cause of death in developing countries [2]. It is estimated that more than one million new cases are being detected annually in the Indian subcontinent. 92-95% of all oral malignancies are oral squamous cell carcinomas. Anyone can develop cancer; however the risk of being diagnosed with cancer increases with age & exposure to risk factors [9]. Longer people live the more possible it is for a sporadic mutation to occur in their genome, leading to genetic alterations that may lead to a malignant phenotype [9].

Oral cancer is a multifactorial disease and along with many potentially malignant disorders, chronic oral Candidiasis is rarely

but can transfer into oral cancer. An imbalance between Candida albicans, virulence factors and host defenses often due to specific defects in the immune system causes Candida albicans to colonize, penetrate, and damage host tissues [10]. There are two proposed mechanisms by which C. albicans can invade keratinocytes. In the first mechanism, the secretion of degradative enzymes by the fungus, chiefly aspartic proteases that digest epithelial cell surface components and thus allow the physical movement of hyphae into, or between, host cells. The second proposed mechanism involve the E-cadherin pathway in which induction of epithelial cell endocytosis, Candida albicans stimulates keratinocytes to produce pseudopod-like structures that encircles the fungus and depicts it into the cell in a process [5]. Candida has capacity to induce oral cancer by directly producing carcinogenic compounds, like nitrosamines [11]. Such a carcinogen will attach with DNA to form adducts with bases, phosphate residues, and/or hydrogen bonding sites which leads to miscoding or irregularities with DNA replication [12]. The point mutations thus induced may triggers the specific oncogenes and instigate the development of oral cancer [5]. According to a study by Krogh et al. [13] they proposed that some Candida species isolated from leukoplakia lesions are capable of producing potent carcinogen N-nitrosobenzylmethylamine (NBMA). The tubular hyphal of Candida albicans might be important as its structure allows entrance of precursors from saliva and a discharge of the nitrosamine product to keratinocytes which is a potentially initiator for oral cancer [13]. Although, in a mouse model of oral carcinogenesis Dwivedi et al. [14] found that infection with Candida albicans in itself is not capable of inducing dysplasia or oral cancer. In another study on rat and mouse oral squamous cell carcinoma models, Candida albicans had been shown to act as a promoter of oral carcinogenesis where carcinogenesis was initiated by repeated association of 4 nitroquinoline 1-oxide (4NQO) [15]. There is a constant debate on association between cancer and chronic inflammation since many years. There are multiple interactions between tumor cells and stromal cells for a tumor growth and invasion. There are many stromal events that may contribute to carcinogenesis by initiation of specific proteolytic enzymes, which are capable to degrade components of the basement membrane and/or fibrous stroma [16]. According to literature Candida albicans has ability to secrete specific proteinases, which are capable of degrading basement membrane and extracellular matrix [17]. Candida albicans has also been established to degrade E-cadherin, which is a transmembrane glycoprotein, important in bonding of adjacent keratinocytes [18]. From the above discussion we can correlate that these findings have implication not only on the potential for Candida albicans on tissue invasion, but also on the potential to enhance the invasion of genetically altered epithelial cells, firstly by minimizing the keratinocyte cohesion and then by supplementing their passage through the basement membrane.

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