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A Preliminary Investigation of an Association Between Dental Restorations and Carcinoma of the Tongue

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The potential association of dental restorations and tongue carcinoma was studied. We reviewed the available pretreatment dental records of 133 patients with carcinoma of the tongue seen at the British Columbia Cancer Agency between 1958 and 1992. 75 patients had teeth adjacent to the ipsilateral side of the cancer (involved side) and the contralateral (control) side of the tongue, resulting in 150 tongue/teeth pairings. Overall there was no significant association between the presence of dental fillings and tongue carcinoma, as the prevalence of bilateral dental restorations was high. Dental restorations were found in 6 patients on the involved side only. Only 1 patient developed a cancer adjacent to normal teeth with contralateral restorations. We feel that this observation merits more study. Meanwhile, careful assessment of dentition and aggressive treatment of dysplastic lesions are warranted.

Keywords: dental restoration, carcinoma of the tongue, metal carcinogenesis

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INTRODUCTION

SQUAMOUS CELL carcinoma (SCC) of the tongue is one of the most common oropharyngeal malignancies in North America [1]. Chronic alcohol consumption and smoking have been causally implicated with carcinoma of the oral cavity. Poor oral and dental hygiene have also been shown to be risk factors of this disease [2]. While it has been the impression of some clinicians that dental restoration may be related to this disease, this impression has not been investigated.

In order to investigate the potential association of adjacent dental restorations with squamous cell carcinoma of the tongue, we conducted a retrospective review of all the available pretreatment dental charts of patients with a diagnosis of squamous cell carcinoma of the tongue. Our aim was to collect a series of patients who have teeth adjacent to both the ipsilateral side of cancer (involved side) and the contralateral side of cancer (control side) in the oral cavity. In order to account for the confounding effects of known aetiologic agents, such as tobacco and alcohol, it was necessary to use the opposite side of the oral cavity of the same patient to serve as control for the microenvironment.

PATIENTS AND METHODS

133 patients diagnosed with SCC of the tongue who were referred to the British Columbia Cancer Agency, Vancouver clinic, for assessment between 1958 and 1992 had pretreatment dental records for review. We excluded 50 edentulous patients and 8 patients who had teeth remaining on only one side of the oral cavity from further analysis. The remaining 75 patients with resultant 150 tongue–teeth pairings constituted the study group.

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RESULTS

The age of the 75 study subjects ranged from 23 to 79 years with a median of 56 years. Seventy-one percent of these subjects were male and approximately 60% of them were regular users of tobacco and alcohol. The location of the cancer was in the anterior two-thirds of the tongue in 75% of the cases, while the remaining cases were limited to the base of the tongue. Approximately two-thirds of the cases presented with limited local disease (stages T1 and T2) without clinical nodal involvement (Table 1).

Table 1. Stage and location of squamous cell carcinoma

Location	
Anterior two-thirds	56 (75%)
Base of tongue	19 (25%)
Stage	
T1	16 (21%)
T2	32 (43%)
T3 & T4	27 (36%)
N0	45 (60%)
N(1–3)	30 (40%)

Table 2. Presence of dental restorations adjacent to squamous cell carcinoma

		Carcinoma		
		Yes	No	
Dental restoration	Yes	57	52	109
	No	18	23	41
		75	75	150

Table 3. Squamous cell carcinoma in patients with asymmetrical dental fillings

		Carcinoma		
		Yes	No	
Dental restoration	Yes	6	1	7
	No	1	6	7
		7	7	14

Dental restorations were found in 109 of the 150 tongue–teeth pairings (Table 2). The presence of a dental filling was not predictive of the presence of an adjacent SCC of the tongue, since the distribution of cancer among those who have had dental restoration was nearly equal.

In the subset of patients who have asymmetrical dental restorations, the location of the SCC of the tongue was more likely to be adjacent to the site of dental restoration, rather than the control side which did not have the dental restoration (Table 3). The probability of this occurring by chance was less than 1 in 17. Table 4 shows the clinical characteristics of the subset of 7 patients; they were seen to be comparable to the remaining study group. The majority of these patients were elderly smokers and drinkers.

DISCUSSION

Although the relationship of amalgams to cancer in general has been investigated [3], to date, the potential role of dental restorations in squamous cell carcinoma of the tongue has not been reported in the literature. In this study, we attempted to investigate this association by controlling for the known aetiological factors, such as alcohol and smoking. This was achieved by using the contralateral noncancerous tongue in the same patient as a control for the microenvironment of the oral cavity. The overall results of this study do not show an association, due to the high prevalence of bilateral symmetrical dental restorations and the overwhelming effect of other risk factors, such as tobacco and alcohol use.

As a potential association may have been obscured by the high prevalence of symmetrical restorations among the study group, a subset analysis of patients who had asymmetrical dental restoration was conducted. The results indicated that SCC of the tongue was more prevalent on the adjacent side of a dental restoration, as opposed to the contralateral side without the dental restoration. This suggests that dental restoration may be a component in the process of carcinogenesis of SCC of the tongue in a small subset of patients. In four of the six cases with a positive association between asymmetrical restorations and SCC, the adjacent restoration was amalgam, one was a posterior composite restoration and one was a rough (fractured) porcelain fused to metal restoration. In the case with a negative association, the restorations were amalgam. Such a hypothesis must be further tested in a larger group of patients by accessing old dental records, prior to referral, of the excluded patients.

The mechanism of carcinogenesis of SCC of the tongue has not been elucidated. Chronic physical irritation of the tongue's squamous epithelium by a rough restoration, analogous to the squamous cell carcinoma of the bladder resultant from bladder stones, may be aetiological [4]. This has been studied in animal models [5]. However, there is no evidence found in the current literature regarding human tumours. In our review, information regarding the surface characteristic of the restorations were available in four of the seven cases and in one case the presence of a rough, irregular restoration was present. Obviously, no conclusions can be made from this one case.

Alternatively, chemical carcinogenesis resultant from the metals found in the dental restorations is plausible. Nickel, which is a major constituent of a nickel–chromium alloy crown, has been demonstrated to leach out of the alloy in significant amounts in salivary solutions [6]. Furthermore, there is abundant information on nickel being carcinogenic in *in vitro* systems, experimental animals and epidemiological studies [7–10]. Crystalline nickel sulphide is a particularly potent carcinogen in *in vitro* systems, owing to active phagocytosis by cultured target cells [11]. Upon cell entry, it has a multitude of effects that are potentially active along the multistep sequence of tumour induction, promotion and progression [12]. Chromium metal and chromic (trivalent) compounds do not appear to be carcinogenic, although

Table 4. Demographics of patients with squamous cell carcinoma and asymmetrical dental fillings

Case	Age (years)	Sex	Location	Stage	Smoker	Drinker
Positive association						
1	68	Male	Anterior	T2N0	Yes	Yes
2	51	Male	Anterior	T3N1	Yes	Yes
3	69	Male	Base	T3N1	Yes	Yes
4	72	Female	Anterior	T3N1	Yes	No
5	38	Female	Anterior	T2N1	Yes	No
6	62	Male	Anterior	T3N0	Yes	Yes
Negative association						
7	59	Male	Anterior	T4N1	Yes	Yes

sparingly soluble chromates (hexavalent chromium compounds) are highly carcinogenic in both animals and humans. This difference appears to reflect the penetrative ability of cell membranes by the different species [9, 13].

The mercury component in dental amalgams has been assessed for local mucosal effects and systemic toxicity [14]. Both the inorganic form, mercury chloride and the organic methylmercury chloride have been shown to be carcinogenic in animal systems. While epidemiological data are sparse, some studies have reported a weak association between mercury exposure and the development of a variety of tumours [15], although no data on squamous cell carcinoma of the head and neck are available. Intratesticular injection of copper sulphate has induced testicular tumours in mice and chicken, but copper has generally not been found to be mutagenic in bacterial systems nor carcinogenic in rodent models that involved intramuscular or intraperitoneal injections [9].

The potential effect of trauma on the development has been assessed in animal models of carcinogenesis. In the hamster cheek pouch model using applications of DMBA, trauma has been shown to promote dysplasia and carcinogenesis [16] and increase the risk of regional lymph node metastasis [17]. Studies in human populations that have assessed the role of chronic trauma in carcinogenesis have indicated that trauma may represent a rare minor risk, but the risk associated with tobacco use and alcohol consumption dramatically overshadows any possible risk from chronic trauma [18–22]. Other studies have found no relationship between denture use and cancer [23, 24]. Evidence of denture irritation has been suggested in rare, isolated cases, and in one case-controlled study [22]. In a case-control study, poor dental status and poor oral hygiene was found to correlate with head and neck cancer [20, 24, 25]. However, whether this is an independent risk factor cannot be determined in most studies. Poor oral hygiene may represent poor oral and medical care or may be a risk factor for cancer, most often overwhelmed by the risk of tobacco and alcohol in most studies [25].

A recent study to assess the use of mouthwash found that risk of oral cancer was increased by 40% in males, and 60% in females regularly using mouthwash after adjusting for tobacco and alcohol use [23]. Risk generally increased according to duration and frequency of mouthwash use, and with the alcohol content of the rinse.

The current study cannot differentiate between the above possibilities. Regardless of the causactive mechanism, dental restorations may act as a possible cofactor in conjunction with other known risk factors such as alcohol and tobacco. Certainly, the overwhelming risk factors for the disease are tobacco and alcohol use. If metals in the amalgam restoration play any role at all, it is a limited role in only a small subset of patients. The relative rarity of the association and the long lag time of carcinogenesis may preclude the conduct of a prospective follow-up study as a practical method of investigation. Development of an oral tumour model for testing the metals in question, analogous to testing other chemical carcinogens implicated in oral cancer, would be necessary [26]. Present clinical efforts should be directed towards more careful assessment of the dentition and treatment of all dysplastic lesions of the oral mucosa.

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