Squamous Cell Carcinoma of the Gingiva Associated with a Special Type of Smokeless Tobacco "Maraş Powder": Case Report

Dumansız Tütün "Maraş Otu" Kullanımı ile İlişkili Oral Skuamöz Hücreli Karsinom

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Geliş Tarihi/*Received:* 05.02.2011
Kabul Tarihi/*Accepted:* 19.04.2011

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ABSTRACT The major risk factors in the etiology of oral squamous cell carcinomas are alcohol and tobacco. In addition to cigarette smoking smokeless tobacco is also considered carcinogenic and is strongly associated with various oral pre-cancerous lesions and oral cancers. In the eastern Mediterranean region of Turkey, a kind of smokeless tobacco called 'Maraş Powder' is used instead of cigarette. It is applied between the lower labial mucosa and gingiva. Maraş powder is obtained from a tobacco plant species known as Nicotiana rustica Linn and the ash of wood. This case report presents a 60-year-old male patient whose visible painless white lesion in the attached gingiva was first noticed during the periodontal examination and who was finally diagnosed with squamous cell carcinoma in the mucogingival region of the left mandibular jaw. The patient was disease-free after 22 months of follow-up. This case report indicates that tumoral lesions require special attention and early diagnosis is necessary for an improved survival rate.

Key Words: Gingiva; tobacco, smokeless; mouth neoplasms

ÖZET Oral skuamöz hücreli karsinomaların eityolojisinde başlıca risk faktörleri tütün ve alkoldür. Sigara dışında, dumansız tütünün karsinojenik yapıda olduğu ve çeşitli prekanseröz lezyonlar ve ağız kanserleri ile kuvvetli bir bağlantısı olduğu düşünülmektedir. Türkiye'de dumansız tütün olarak "Maraş Otu", özellikle Akdeniz bölgesinin doğusunda sigara yerine bukkal mukoza üzerine yerleştirilerek kullanılmaktadır. "Maraş Otu" Nikotina rustica Linn adı verilen bir bitki ve kül karışımından oluşan bitkisel bir tozdan elde edilir. Bu raporda, 12 yıl süre ile "Maraş Otu" kullanımı öyküsü olan, 60 yaşında bir erkek hastanın sol alt çene premolar mukojinjival bölgesinde saptanan ve skuamöz hücreli karsinom olarak tanımlanmış olan lezyon bildirilmektedir. Yirmi iki ay süresince takip edilen hasta halen sağlıklıdır; metastaz veya nüks tanımlanmamıştır. Bu bağlamda, vakada erken tanının prognoz yönünden önemi ve oral lezyonların tanısında patolojik tetkiklerin gerekliliği vurgulanmaktadır.

Anahtar Kelimeler: Dişeti; tütün, dumansız; ağız tümörleri

Turkiye Klinikleri J Dental Sci 2011;17(3): 310-4

Alcohol and tobacco are the major risk factors in the etiology of oral squamous cell carcinomas.[1,2] In addition to cigarette smoking, smokeless tobacco like betel quid and areca nut in Southeast Asia are considered carcinogenic and are implicated as being strongly associated with various oral precancerous lesions and oral cancers.[3,4] Smokeless tobacco products do not cause disorders of airways related to smoking (e.g. chronic obstructive pulmonary disorders, pulmonary cancer)[5] but are known to cause toxic effects particularly cancer and other cellular and DNA changes, either at the placement sites or by indirect systemic effects. On

the other hand, these products contain a large array of carcinogens among which nitrosamines are the strongest.[3] The metabolites of nitrosamines, particularly nitrosonornicotine (NNN) and 4-(methylnitrosamino)-1-(3 pyridyl)-1-butane (NNK) are found locally in the saliva in the oral cavity and in body fluids of smokeless tobacco users.[3,6]

In the eastern Mediterranean region of Turkey, a kind of smokeless tobacco6 called 'Maraş Powder' is used instead of cigarette. It is applied between the lower labial mucosa and gingiva for 4-5 min. It may be repeated many times during the day and some people may even go to sleep with it in their mouths. It is commonly used by males and females with varying age and education levels. There are some differences between Maraş Powder and other smokeless tobacco types in terms of their preparation and usage. Most of the smokeless tobacco products are prepared from Nicotina tabacum L. and none of them contains ash. However, Maraş Powder is obtained from Nicotiana rustica Linn. The leaves of Nicotiana rustica Linn are powdered, mixed, crushed with the ash obtained from the oak, walnut tree at a ratio of 1/2 or 1/3 and humidified before its use. There is strong evidence that Maraş Powder plays an important role in the etiology of oral and pharyngeal carcinomas, gingivitis, leukoplakia, and epithelial dysplasia in the oral mucosa.[6-8]

This article presents a 60-year-old male patient with squamous cell carcinoma in the mucogingival region of the left mandibular jaw who was sucessfully operated. The patient was disease free after 22 months of follow-up. The squamous cell carcinoma is one of the very rare cases of gingival cancer, which may be related to habitual consumption of Maraş Powder in different geografical regions and cultures of the world and underlines the importance of early differential diagnosis and treatment for long-term survival.

CASE REPORT

A 60-year-old male patient was referred by his general dental practitioner for a painless lesion on the mucogingival line and attached gingiva of the left mandibula. Clinical examination revealed a white ulcerated painless lesion (Figure 1, 2). Periodontal status was clinically determined by the plaque index, the gingival bleeding index, the clinical attachment level, the probing pocket depth and by radiographic examinations.[9,10] The mean plaque index score was 2 and bleeding on probing score was 1.Attachment loss was 4 mm and the mean pocket depth was 5 mm. Radiologic examination revealed horizontal bone loss (Figure 3).

Clinically, there was no submandibular and submental lymphadenopaty. The lesion was first noticed by the patient 2 months prior to his presentation. It was slowly increasing in size but it did not cause any symptoms.

Medically, the patient suffered from hypertension and diabetes mellitus. He was using 2 mg prazosin (alpha receptor blocker) and glimepride (oral antidiabetic) daily. He was well-educated and

FIGURE 1, 2: Intraoral photographs of the patient before biopsy. Lesion is on the mucogingival line and gingiva is white around the lesion.

FIGURE 3: Panoramic x-ray before treatment. Horizontal bone loss especially around right maxillary molars. No bone loss around left mandibular premolars (tumor region).

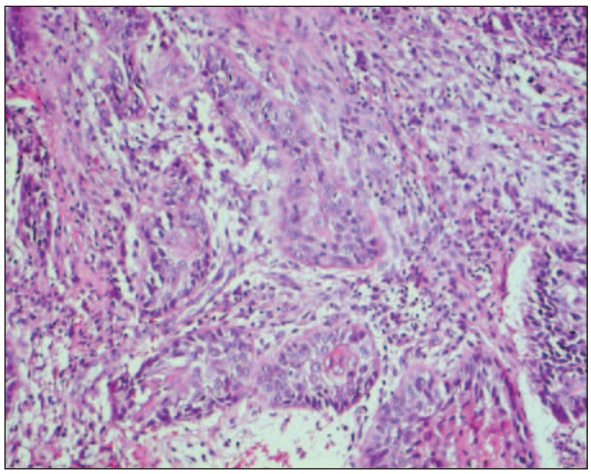

FIGURE 4: Photomicrograph of invasive tumor.

there was no history of cigarette and alcohol consumption. He mentioned that he had a stressful work-life and has been using Maraş Powder for 15 years. He applied a small amount of powder via cotton pellet between the lower buccal mucosa and attached gingiva during the day and even while sleeping in the last two years. An incisional biopsy of the ulcerated lesion was performed under local anesthesia.

Microscopic evaluation of the gingival specimen revealed a neoplastic invasive proliferation of the surface epithelium with a thick layer of parakeratin, marked dysplasia and a thickened spinous cell layer along with islands and strands of malignant epithelium. Tumor region and strands were composed of atypical epithelial cells with hyperchromatic large vesicular nuclei. Keratin pearl formation and atypical mitosis were present in some regions of the tumor. The diagnosis of the specimen was well-differentiated squamous cell carcinoma (Figure 4).

Maxillofacial and neck computed tomography analysis was normal except for right maxillary sinusitis.

Sunsequently the patient was referred to the otorhinolaryngology Department of the University Hospital where he underwent marginal mandibulectomy and left selective neck dissection with the excision of the involved areas. Final histopathologic examination of the specimen confirmed the diagnosis of squamous cell carcinoma with tumor-free margins and lymph nodes. The patient was treated with 6000 gray (Gy) total dose of radiotherapy. Tomographic examination of the head and neck region 22 months after the operation was normal with no residual disease or any recurrence. He was disease-free after two years of diagnosis and is still under control (Figure 5, 6, 7).

DISCUSSION

Smokeless tobacco products can cause oral mucosal lesions, gingival recession, squamous cell carcinoma, verrucuos carcinoma, leukoplakia, and erythroplakia and they may play a role in the development of cardiovascular disease, peripheral vascular disease, hypertension and peptic ulcers.

FIGURE 5: Panoramic x-ray after 22 months. Teeth 31,32,33,34 were extracted during the operation.

FIGURE 6,7: Intraoral photograps of the patient after two years of treatment; the appearence of gingiva and the tumor region.

The etiology of the lesions may be traumatic, mechanical and chemical.[3,11] Squmous cell carcinomas are not frequent and attribute for less than 10 % of the oral cavity carcinomas.

Oral cancer has one of the lowest five-year survival rates among the major types of cancer, including breast, skin, prostate, uterus and urinary bladder cancers. Early diagnosis is crucial to an improved survival rate. If lesions are detected when they are small and localized, and are treated expeditiously, survival rates up to 70-90% can be achieved.[12]

Differential diagnosis includes epithelial displasia, bening mucosal pemphigoid, periodontal-endodontic lesions and lichen planus.[13]

In our case the lesion was white, ulcerated and pocket-like with the location overlapping with the Maraş powder application site in the oral cavity, suggesting that the powder is a precipitating factor. The powder is made of a plant N. rustica Linn, which is similar to N. tobacum L regarding alcaloid composition. Nevertheless, nicotine content of this plant is about 6-10 fold higher,[5] and this may be the reason to prefer N. rustica Linn. The ash blended while preparing the Maraş powder facilitates the absorption of nicotine from the oral mucosa by making the medium alkaline.[14] Unlike cigarette smoking, nicotine continues to be absorbed for more than 30 minutes even after Maraş Powder is removed from the mouth. For cigarette smoking on the other hand, nicotine absorption ceases when smoking is finished.[15] Although it is more addictive than smoking (or tobacco), its negative impacts on human health could not yet be understood. In a study including 92 patients, Okur and coworkers reported that 46 patients with mild, 15 patients with moderate and 12 patients with severe gingival recessions among Maraş Powder users of less than one year. Furthermore, authors suggested that some of the white lesions like leukoplakia, eritroplakia and aftous lesions present in 22 patients, might be considered precancerous lesions.[8] In our case we also observed gingival recessions and desquamation in the oral mucosa possibly due to the chronic trauma of powder positioning.

Tombak reported that a similar kind of smokeless tobacco used in Sudan might play an important role in the etiology of oral squamous cell carcinoma and might be associated with salivary gland cancers. Due to its oral use, the chronic stimulation of the lenfoid tissues in the oral mucosa may be associated with increased gingivitis, leukoplacias and oral cancer incidence. Similarly, reports indicate that it has a stronger potential of leading to addiction compared to cigarette smoking because of its higher nicotine concentration and prolonged mean usage time.[14]

Smokeless tobacco products are implied in the etiology of gingival squamous cell carcinomas, which develop in about 12.4% of the population

over 65 years of age.[1,12] These cancers have good prognosis in early stages of diagnosis. In this respect, it is important to be aware of the usage of different kinds of smokeless tobacco products worldwide. Among these toombak, shamma, mishri, gutkha, naswar, khiwam and zarda are well known.[3,4] Here we reported an early diagnosed and succesfully treated gingival squamous cell carcinoma case, which is presumed to be caused by Maraş Powder, a smokeless tobacco product popular in the eastern Mediterranean region of Turkey.

Acknowledgement

The authors wish to thank Dr.S.Elif Gültekin from Gazi University Department of Pathology for her helpful comments in the preparation of this mauscript.

REFERENCES

1. Seoane J, Varela-Centelles PI, Walsh TF, Lopez-Cedrun JL, Vazquez I. Gingival squamous cell carcinoma: diagnostic delay or rapid invasion? J Periodontol 2006;77(7):1229-33.
2. Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for oral cancer in newly diagnosed patients aged 45 years and younger: a case-control study in Southern England. J Oral Pathol Med 2004;33(9):525-32.
3. Warnakulasuriya KA, Ralhan R. Clinical, pathological, cellular and molecular lesions caused by oral smokeless tobacco--a review. J Oral Pathol Med 2007;36(2):63-77.
4. Fasanmade A, Kwok E, Newman L. Oral squamous cell carcinoma associated with khat chewing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104(1):e53-5.
5. Güven A, Köksal N, Büyükbeşe MA, Cetinkaya A, Sökmen G, Aksu E, et al. Effects of using a different kind of smokeless tobacco on cardiac parameters: "Maraş Powder". Anadolu Kardiyol Derg 2003;3(3):230-5.
6. Erenmemişoğlu A. Turkish smokeless tobacco "Maraş Powder." Prev Med 1999;28(6):616-7.
7. Buyukbese MA, Koksal N, Guven A, Cetinkaya A. Effects of smokeless tobacco "Maras powder" use on respiratory functions. Tohoku J Exp Med 2004;204(3):173-8.
8. Okur E, Yıldırım I, Kılıç MA, Şaşmaz S. [Clinical changes in the oral cavity resulting from smokeless tobacco (Maraş Powder)]. Turkish Journal of Ear Nose and Thorat 2004;13(3-4):72-6.
9. Silness J, Loe H. Periodontal disease in pregnancy. II. correlation between oral hygiene and periodontal condtion. Acta Odontol Scand 1964;22:121-35.
10. Ainamo J, Bay I. Problems and proposals for recording gingivitis and plaque. Int Dent J 1975;25(4):229-35.
11. Reichart PA, Philipsen HP. Betel Chewer's Mucosa-a review. J Oral Pathol Med 1998; 27(6):239-42.
12. Pitiphat W, Diehl SR, Laskaris G, Cartsos V, Douglass CW, Zavras AI. Factors associated with delay in the diagnosis of oral cancer. J Dent Res 2002;81(3):192-7.
13. Yoon TY, Bhattacharyya I, Katz J, Towle HJ, Islam MN. Squamous cell carcinoma of the gingiva presenting as localized periodontal disease. Quintessence Int 2007;38(2):97-102.
14. Aral M, Ekerbicer HC, Celik M, Ciragil P, Gul M. Comparison of effects of smoking and smokeless tobacco "Maras powder" use on humoral immune system parameters. Mediators Inflamm 2006;2006(3):85019.
15. Tabak L. Is smokeless tobacco less harmful than smoking? Anadolu Kardiyol Derg 2003;3(3):236-7.