

Squamous Cell Carcinoma of The Gingiva: A Case Report and Literature Review

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ÖZET

Gingivanın skuamöz hücreli karsinomu: Vaka sunumu ve literatür taraması

Skuamöz hücreli karsinom (SCC) oral kavitede en sık görülen ve farklı klinik belirtiler ile karakterize malign epitelyal bir neoplazmdir. SCC displastik oral skuamöz epitelinden doğmaktadır. SCC patogenezi göz önüne alınırsa oluşan lezyon için pürüzsüz ve sağlam bir yüzey olağan değildir. 52 yaşında kadın hasta dişetinde büyüme şikayeti ile Marmara Üniversitesi Diş Hekimliği Fakültesi Oral Diagnoz Kliniğine yönlendirilmiştir. Hastanın tıbbi anamnezinde herhangi bir sistemik hastalık olmadığı öğrenilmiştir. Ayrıca lenfadenopati tespit edilmemiştir. Sol maksiller birinci molar bölgede bukkal ve palatinal mukozada verrüköz bir görüntü oluşturan lezyon ve dokuda hipertrofi izlenmiştir. Klinik muayeneye ek olarak ilgili bölgeden önce smear biyopsi ve sonrasında ise insizyonel biyopsi alınmıştır. Histopatolojik inceleme sonucunda lezyonun 'skuamöz hücreli karsinom' tanısı ile malign karakterde olduğu saptanmıştır. Sonuç olarak hasta lezyonun cerrahi operasyon ile elimine edilmesi için Kulak, Burun, Boğaz (KBB) departmanına yönlendirilmiştir.

Anahtar sözcükler: Skuamöz hücreli karsinom, oral diağnoz, histopatolojik değerlendirme

ABSTRACT

Squamous cell carcinoma of the gingiva: a case report and literature review

Squamous cell carcinoma (SCC) is the most frequent epithelial malignancy of the oral cavity which is characterized by variable clinical manifestations. It arises from dysplastic oral squamous epithelium. By considering the pathogenesis of SCC, the smooth and intact surface for this lesion is not usual. A 52-year-old female patient was referred to Marmara University, Faculty of Dentistry, Oral Diagnosis Clinic with a chief complaint of generalized swelling of the gingiva. There was neither significant medical and family history nor any history of medication. No bleeding was reported and submandibular lymphadenopathy (LAD) was noted. Buccal and a palatinal mucosal tissue of left maxillary first molar had a verrucous appearance. In addition to clinical examination, a smear biopsy and then incisional biopsy was performed and histopathological examination revealed the lesion had a malign characterization with a diagnosis of 'squamous epithelium carcinoma'. Consequently, the patient was referred to Ear, Nose and Throat (ENT) department where the lesion was treated by surgery.

Key words: Squamous cell carcinoma, oral diagnosis, histopathological examination

INTRODUCTION

Squamous cell carcinoma (SCC) is an invasive epithelial neoplasm, with variable degrees of squamous differentiation. This neoplasm can occur with or without keratinization. SCC originates at the level of the keratinized stratified squamous epithelium (skin) or non-keratinized (uterine exocervical, oral mucosa, esophageal) mucosa. The squamous metaplasia areas such as uterine endocervix or trachea-bronchial tree, are regions where SCC can also be involved. This neoplasm infiltrates the surrounding tissues creating rapid metastasis (1). It arises

from dysplastic oral squamous epithelium (2-6).

SCC of the oral cavity attributes for 4% of malignancies in men and 2% of malignancies in women, and is responsible for 3% of all cancer deaths (7). Epidemiologic studies portray an increasing incidence of SCC in young patients worldwide especially among young females, although this malignancy is generally more common in male than in female (8).

SCC may appear in endophytic, exophytic (verrucous or papillary), leukoplastic, ulcerated, erythroleukoplastic or erythroplastic forms (9,10). The most common sites of intraoral carcinoma are tongue, lip vermilion, soft palate,

gingiva, buccal mucosa, labial mucosa, and hard palate. Alveolar ridge carcinomas are usually considered as painless neoplasms and mostly arise from keratinized mucosa on the posterior mandibular region (11).

Invasive growth and squamous differentiation, which usually appear as keratinization with “pearl” formation, are the essential aspects of SCC histopathologically. Invasion is demonstrated by disruption of the basement membrane, and extension into the underlying tissue. Additional signs of malignancy in SCC are angiolymphatic and perineural invasion (1). A study investigated different stromal cells and tumor cells activities in SCC. The study reported that there is an association between cell proliferation markers in the basal lamina and connective tissue. Immunohistochemical markers which represent molecular events in the process of malignant transformation, proliferative markers (p53, Ki67, and HOXB7 HOXA1), tumor stroma myofibroblast markers (α -SMA) and basal membrane markers (COLIV) were also studied. It is found that HOXB7 was significantly associated with regional lymph nodes commitment and clinical stage in SCC (12).

Extrinsic and intrinsic factors may be responsible for the etiology of oral squamous cell carcinoma. External agents such as tobacco smoke, alcohol, syphilis, Human Papilloma Virus (HPV) and sunlight are extrinsic factors. Intrinsic factors consist of systemic conditions, such as general malnutrition or iron-deficiency anemia. All types of tobacco smoking have been associated with the cause of oral cancer (13,14). A published study from India reports that the mortality rate in tobacco chewers has increased by 5 times due to oral cancer, in sharp contrast to the non-chewers. In addition increased mortality rate due to cancer of the larynx, esophagus, stomach, pharynx and cervix were also reported among tobacco chewers (15).

World Health Organisation (WHO) considered cigarette smoking alone as the leading cause of cancer in the world. People who smoke have about three and a half times more chance of cancer of the oral cavity (16). The alcohol consumption has also been well accepted as an independent risk factor for SCC. It is reported that there is an increased risk of cancer of alcoholics when compared to non-alcoholic people (17). HPV infection is another important risk factor, especially the high-risk oncogenic

16 and 18 serotypes. The infection with these serotypes is associated with uterine cervical carcinoma and oral/laryngeal carcinoma (18).

The size and the site of the lesion, bone involvement, presence or absence of metastasis, and the stage of the disease play a determining role in the prognosis of SCC. Clinical stage of the disease is the most important indicator of prognosis (19). This paper presents the case of a female patient with a squamous cell carcinoma of the gingiva and literature review.

CASE REPORT

A 52-year-old female patient was referred to Marmara University, Faculty of Dentistry, Oral Diagnosis Clinic with a chief complaint of generalized swelling of the gingiva. There was neither significant medical and family history nor any history of medication. No bleeding was reported and submandibular lymphadenoma was noted. She had a habit of smoking for 25 years but she had quit smoking 4 years ago. She had been referred to our clinic by a general dentist.

Intra-oral examination revealed that palatinal and buccal gingival mucosal tissue of left maxillary first molar had a verrucous appearance at the surface with approximate size of 3 × 2 cm (Figure 1). Physical examination revealed no lymphadenopathy in submandibular or other neck triangles.

The Cone Beam Computed Tomography (CBCT) images on different planes showed a destruction of the



Figure 1: Palatinal mucosal tissue of first maxillary molar with a verrucous-erosive surface appearance with gingival swelling

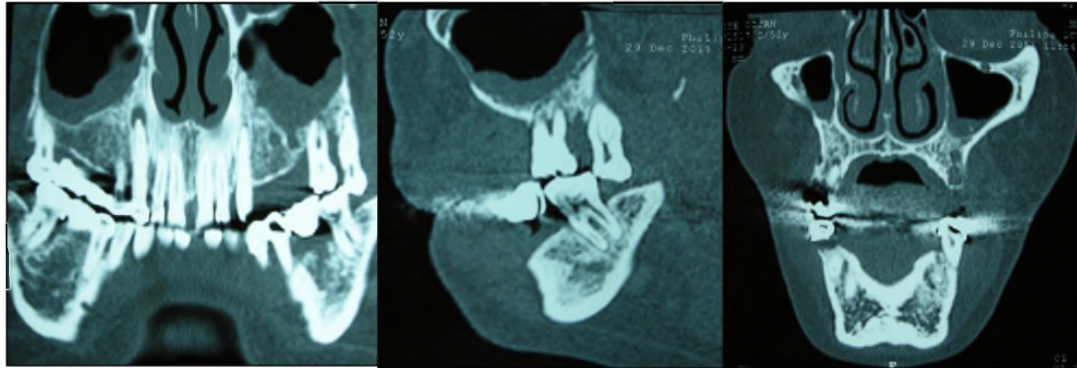


Figure 2a

Figure 2b

Figure 2c

Figure 2a-c: a) Panoramic, b) sagittal and c) coronal views of CT scan. Note the bone loss around the teeth in left maxillary molar region

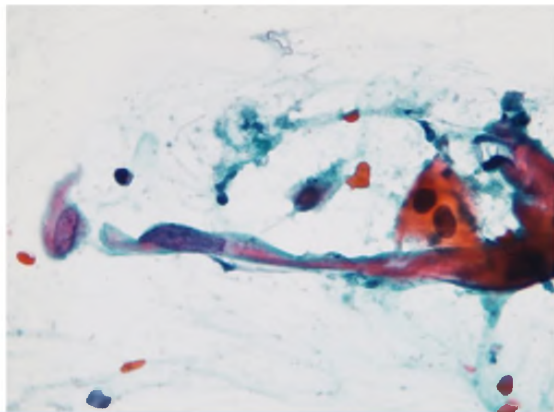


Figure 3: Cytopathologically, atypical squamous cells with hyperchromatic, abnormal nuclei and keratinized or basophilic cytoplasm are observed (Pap. x 1000)

alveolar bone around the teeth in left maxillary molar region (Figure 2a-c). First a smear biopsy was performed and pursuant to that cytopathologically, atypical squamous cells, with hyperchromatic, abnormal nuclei and keratinized or basophilic cytoplasm were reported (Figure 3). Following, a punch biopsy was performed on the palatal mucosa of the left maxillar posterior region under local anesthetic at the Department of Oral Diagnosis and Radiology. Histopathologic examination was performed at the Department of Oncologic Cytology and Tumor Pathology, Institute of Oncology, Istanbul University. The result of punch biopsy showed that the lesion was microinvasive squamous cell carcinoma. Histopathological analysis of the biopsy specimen revealed atypical squamous cells, which were proliferating towards the connective tissue nearby, forming small tumor groups (Figure 4, 5).

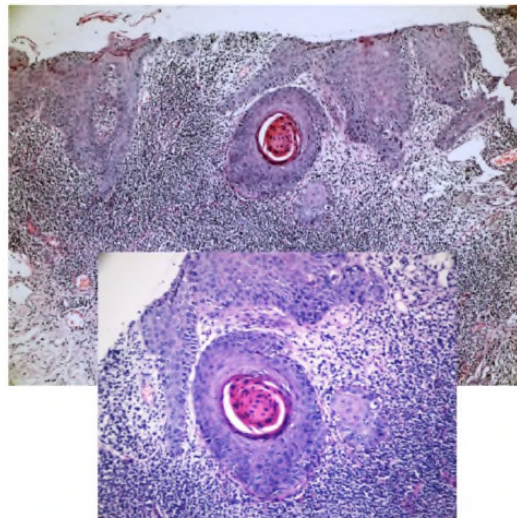


Figure 4: Microscopically atypical squamous cells, forming separate irregular tumor masses in the connective tissue, are seen (H.E. x100 and H.E. x200)

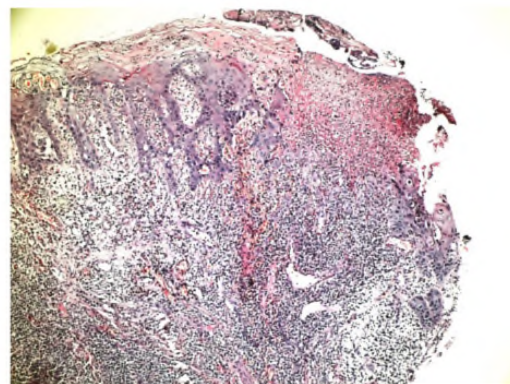


Figure 5: Microscopically surface epithelium is ulcerated and atypical squamous cells are proliferating towards the connective tissue nearby. On the other side, atypical squamous cells forming small tumor groups in the connective tissue are observed (H.E. x100)

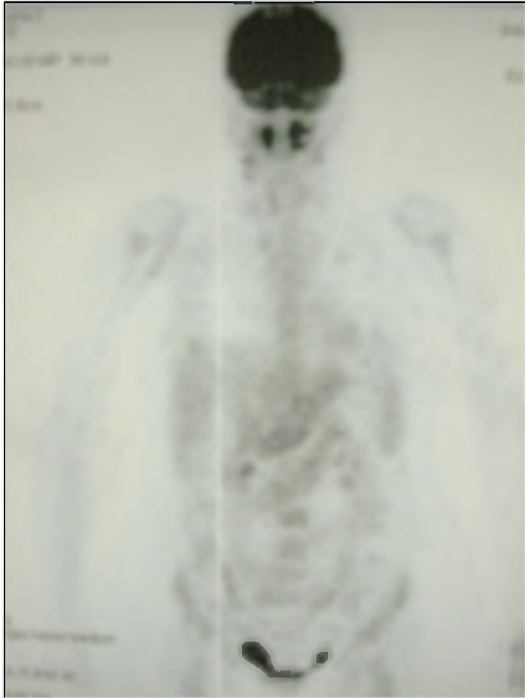


Figure 6: Maxillar bone involvement that was detected on FDG positron emission tomography (PET)

Moreover Positron Emission Tomography–Computed Tomography (PET-CT) revealed a hypermetabolic focus on maxilla (Figure 6). Eventually, the patient was referred to Ear, Nose and Throat (ENT) department and the lesion was treated by surgical operation.

DISCUSSION

It is reported that oral cancer is the sixth most common cancer worldwide and more than 90% of all oral cancers are squamous cell carcinoma (20-22). The incidence of OSCC portray large geographical variations (23,24). Oral SCC more frequently affects men than women (M:F= 1.5:1). Oral cancers mostly occur in patients over the age of 45 and a male predilection is reported. The incidence of OSCC increases until the age of 65 (25-27).

The two best known collaborative risk factors of SCC are tobacco and alcohol use, are predicted to be responsible for the cause of the disease (28-33). The association between tobacco use and squamous cell carcinoma of the entire head and neck region was investigated by a case control study. This study found that

risk of developing SCC among current tobacco users is 2.17 times higher than the others. This study also could not find any significant difference for the development of the disease between smoking and smokeless tobacco use (34). There is still controversy as to the recurrence rate of SCC but overall survival sounds more agreeable for patients with no history of risk factors in comparison with smokers and/or alcohol users, independent of age (35,36). Alcohol consumption is considered to play a role in cancer development (37).

The involvement of buccal mucosa, floor of mouth tongue, alveolar rim and the hard and soft palate is usually reported in SCC, which is the most common malignant neoplasm in the oral cavity (38). The less frequently involved regions of oral cavity are palate, retromolar area, gingivae and the buccal and labial mucosa (39).

Due to the fact that they are lined by thin non-keratinised epithelium, the ventral surface of the tongue and the floor of the mouth are the sites most commonly affected by SCC. Carcinogens easily penetrate this thin epithelium to reach the precursor cell compartment and tobacco products and alcohol in solution, constantly accumulate in the floor of the mouth and rinse the tissues of the floor of the mouth and the ventrum of tongue (39,40).

Various clinical forms of OSCC can be observed. These clinical forms may be leukoplakia, a verrucous leukoplakia, an erythroleukoplakia, or an erythroplakia. In addition, a necrotic ulcer with nonuniform borders may progress on these lesions, which portray an exophytic mass with a verrucous or smooth surface. Oral SCC bleeds easily when traumatized and usually a secondary infection is observed. When the tumor is secondarily infected, pain may occur. Normal speech, mastication or swallowing may be disturbed in larger lesions (21,41). Carcinomatous ulcers are generally chronic and have an irregular papillary surface, elevated borders and they are hard on palpation (42).

Depending on the grade which the tumor resembles the tissue of origin, SCC is divided into 3 stages histopathologically. The tumor is well-differentiated, moderately-differentiated or poorly-differentiated. Well-differentiated tumors closely resemble its tissue of origin. They grow and metastasize slowly. Contrarily, poorly

differentiated tumors which show more cellular and nuclear pleomorphism are considered as immature and do not resemble their tissue of origin. The tumor that lies between these two extremes is labeled as moderately-differentiated (43).

Our patient in present case was older than 50 years and had a complaint of a non-healing lesion, which continuously enlarges on the buccal and palatal mucosal tissue of left maxillary first molar. Similar with the studies reviewed in literature, she had a habit of smoking for 25 years.

The oral cavity is easily reachable for examination and biopsy, which leads to an early diagnosis. Thus a realistic and achievable goal in oral cancer control can be achieved. In the present case, due to the risk of the

disease, the patient was first diagnosed with histopathological examination and CBCT scans and screened with PET-CT. After mandibular resection and plastic surgery, the patient was followed up periodically.

CONCLUSION

Squamous cell carcinoma of the mandible is a condition in which chance of survival is higher specifically for early diagnosed and treated carcinomatous lesions. From this perspective, health care providers, and dentists in particular, play a crucial role in the early detection of oral squamous cell carcinoma and hence, in achievement of a better prognosis.

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