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Oral squamous cell carcinoma (OSCC) an overview

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ABSTRACT

Oral Squamous Cell Carcinoma (OSCC) represents more than 90% of all oral cancer cases. It is considered one of the most frequent oral malignancies worldwide with a yearly prevalence of more than 500,000 new cases. OSCC may be found in various anatomical structures in the oral cavity, but usually appears on the lateral border of the tongue, the floor of the mouth and the lower lip. OSCC starts as a complicated process that depends on multiple risk factors such as excessive consumption of alcohol and long-term use of tobacco. During this process, epithelial cells are influenced by genetic mutations which eventually leads to the development of several neoplastic sites all over the oral cavity or in most the cases, will promote an already existed precancerous lesions to keep on growing. The TNM classification which is a famous method of oral cancer staging assists healthcare practitioners in diagnosis the stage of cancer in addition to the regular clinical evaluation. This classification also provides important data regarding the required way of treatment, which may be noninvasive, such as radiotherapy or invasive, such as surgery, which is usually the first option of treatment. OSCC rates of mortality among the general population cannot be completely vanished, but can definitely be reduced by few steps such as lifestyle changes and broad educational programs.

Keywords: Oral squamous cell carcinoma, Oral neoplasms, OSCC risk factors, Non-invasive and invasive detection technique.

Abbreviations

Oral squamous cell carcinoma (OSCC), World Health Organization (WHO), Potentially malignant disorders (PMDs), The International Agency for Research on Cancer (IARC), South-East Asia (SEARO), Europe region (EURO), Human papilloma virus (HPV), Ultraviolet radiation (UV), Epstein-barr virus (EBV), Magnetic resonance imaging (MRI), Single-photon emission computed tomography (SPECT), Toluidine blue (TB), Orthopantomogram (OPG), computed tomography perfusion (CTP), Ultrasonography (USG).

Introduction

Oral squamous cell carcinoma (OSCC) is rated among the 6th most frequent oral malignancies, with a yearly prevalence of more than 500,000 cases [1]. OSCC alone considered as responsible for more than 90% of oral cancers cases and have the highest rate of mortality globally [2, 3, 4]. World Health Organization (WHO) reports that the highest prevalence and mortality of OSCC is divided to different regions worldwide, such as South-East Asia (SEARO) and Europe region (EURO). SEARO includes countries such as Sri Lanka, India, Pakistan and Taiwan while EURO includes countries such as France, Hungary, Slovakia and Slovenia [4]. OSCC may affect numerous anatomical structures such as the lips, tongue, upper and lower gingiva, retromolar triangle, alveolar mucosa, floor and roof (palate) of the mouth, buccal mucosa, oropharynx and the salivary glands [2, 7]. OSCC usually appears on the

lateral border of the tongue 40%, followed by the floor of the mouth 30% and the lower lip [4, 7].

In 2005, WHO had advised to change the term of “precancerous lesions” to the term “potentially malignant disorders” (PMDs) followed the fact that most of the OSCC cases were a result of a previous precancerous lesions. The PMDs include leukoplakia, erythroplakia, oral lichen planus, oral submucous fibrosis, actinic keratosis, discoid lupus erythematosus and palatal lesions which may have been developed due to smoking. Those disorders have a much higher probability to become malignant compared to other oral pathologies [3].

The ongoing researches and the development of a new therapies, have not yielded any significant improvement survival rate for the patients and continue to be a challenging topic for the medical community [4]. Accordingly, an early diagnosis of oral PMDs will able practitioners to supervise, diagnose and treat those disorders at the initial stages of dysplasia or even carcinoma in situ [3].

The aim of this article is to present a general review of the literature regarding OSCC for the general population and for the healthcare practitioners.

Definition and risk factors

Oral cancer is a malignant neoplasm which grows within the oral cavity. Approximately 90% of the oral cancers have a histological origin of squamous cells and as a result, this type of

cancer is typically defined as OSCC. The OSCC has few levels of differentiation and a tendency for regional lymph node metastasis [4].

The oral cavity is very accessible during every clinical evaluation, but even to that fact, most of the OSCC are been diagnosed at a very critical and late stages. The main reasons for this situation are the lack of knowledge from the patient's side and of course from the doctor side who did not diagnose the condition properly. The late diagnosis drastically reduces the rate of survival although the broad possible methods of treatment [4].

The most significant risk factors for OSCC, with a rate of over 90% are the long term over consumption of alcohol and use of tobacco [4, 2].

Tobacco

Smoke of tobacco contains 3 groups of chemicals such as nitrosamines, benzopyrenes and aromatic amines which promotes cancer. Smokers have a 3 times higher risk for developing an OSCC compared to nonsmokers. In case of nonsmokers, the involuntary smoking as a result from the surrounding environment may increase the chance of developing OSCC in 87% compared to those who have not been in that environment. In addition, smoking not only reduce the immunity of the oral cavity, it also promotes gingivitis, periodontitis and of course OSCC [4].

Alcohol

Is known as Ethanol and has a negative effect on the organism. This effect acts on the local level by allowing higher permeability into the oral

mucosa, dissolving lipid particles of the epithelium and leading to epithelial atrophy in general. On the systemic level, it has a mutagenic effect which leads to a smaller salivary flow, decreased liver competence to deal with carcinogenic chemicals and eventually lead to impairment of the immunity system. This impairment results an increased risk for infections and new abnormal growth of tissue [4].

Other risk factors

Less common but still possible risk factors may be insufficient dental hygiene, genetic tendency, chronic mechanical trauma by a sharp object such as a tooth or a denture, chewing of areca nut which occurs mostly in indo-asian populations, human papilloma virus (HPV) which according to the International Agency for Research on Cancer (IARC) the HPV16 is responsible for the cancers of the tonsils, pharynx and oral cavity while HPV18 is responsible for oral cancer [4, 9]. In addition, ultraviolet radiation (UV) which is mostly related to lip cancer, other viruses such as hepatitis C and Epstein-barr virus (EBV) may be also related to OSCC [4, 5].

Carcinogenesis

Oral carcinogenesis is a very complicated process which depends on multiple factors. During this process, epithelial cells are influenced by genetic mutations which eventually lead to a several neoplastic sites all over the oral cavity, those sites may develop over the years to the form of OSCC. As a guideline, if an oral mucosal lesion does not improve after three weeks, it must be considered as a highly threatening condition which will require biopsy and further histopathological investigation [4].

Tnm stage classification

The most significant and predictive factor which will determine the survival rate is the stage of the tumor during the diagnosis [1]. The TNM classification is a worldwide known method of oral cancers staging which is used by healthcare practitioners such as doctors, researchers and cancer registration facilities [7, 10]. The initials, T stands for tumor, N for lymph nodes and M for metastases, are based on the measurements of the disease prior to treatment [4]. The main role is to provide an anatomical classification and to properly describe the development of the cancer. Specific description is the key for the selection of a correct method of treatment, the possible outcome and limitation for certain activities [10].

Table. TNM definitions for oral cancer [4].

Primary tumor (T)			
TX	Cannot be assessed		
T0	No evidence of primary tumor		
Tis	Carcinoma in situ (CIS)		
T1	Tumor 2 cm or less in greatest dimension		
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension		
T3	Tumor more than 4 cm in greatest dimension		
T4a	Moderately advanced local disease. Lip: Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (chin or nose). Oral cavity: Tumor invades through cortical bone, into deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus, or skin of face.		
T4b	Very advanced local disease. Lip and oral cavity: Tumor invades masticator space, pterygoid plates, or skull base; or encases internal carotid artery		
Regional lymph nodes (N)			
NX	Cannot be assessed		
N0	No regional lymph node metastasis		
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension		
N2	Metastasis as specified in N2a, 2b, 2c (see below)		
N2a	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension		
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension		
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension		
N3	Metastasis in a lymph node more than 6 cm in greatest dimension		
Distant metastasis (M)			
MX	Distant metastasis cannot be assessed		
M0	No distant metastasis		
Clinical stages (T+N+M)			
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T3 (enough alone), T2 or T1	N1	M0
IV A	T4a	N0 or N1	M0
	T1, T2 or T3	N2	M0
IV B	any T	N3	M0
	T4b	any N	M0
IV C	any T	any N	M1

Diagnostic methods

Diagnosis of a doubtful lesion most often begin with the conventional oral examination, which includes clinical evaluation and palpation of the mucosa of the oral cavity under the lighting of the dental chair [1]. The ability to make a diagnosis at an early stage of OSCC is very important in order to reduce the high rate of sickness and death among the patients [6]. The most common methods used for diagnosis of PMDs and OSCC in an early stage are listed below [5].

Vital Staining

Methods such as Toluidine blue (TB), Methylene blue staining, Rose bengal staining, Lugol's iodine staining. Staining with TB is a known method for the identification of premalignant and malignant lesions, which is recommended to be as part of the clinical evaluation of oral mucosal tissues, especially in high-risk patients. Those methods are not expensive, quite easy to apply and effective [3]. The staining implemented by various types of dyes over the mucosa in order to mark the neoplastic cells, cells with a high reproductive activity and to indicate the specific areas for examination and biopsy [5].

Light-based detection

In order to identify oral PMDs and OSCC in their initial stage, several light-based devices have been developed [3]. Those specific devices can emit certain light which will reflect the abnormal tissue and improve the clinical evaluation [5].

Histological methods

Incisional and/or excisional biopsy are the most accurate diagnostic methods and together with the histopathological tests, remains as the most reliable methods for OSCC diagnosis [5, 6]. Before the procedure of excisional biopsy, it is important that the margins and depth of the tissue will be verified of being a disease-free. Epithelial dysplasia is known as the most prognostic sign of any malignancy. WHO have defined that dysplasia may be classified as mild, moderate and severe [5].

Cytological methods

Those are methods that use a microscope in order to evaluate the cells which were obtained from smears, scraping and needle aspiration over various depths of the mucosa [5]. The common findings are a typical mucosal lesion which at first sight looks normal, but the prepared specimen will present atypical cells. The cytological tests which have been taken from the oral cavity may help to identify and diagnose tissues with a high-risk or even malignancy [5].

Imaging diagnostic methods

Those methods include local dental radiographs, orthopantomogram (OPG), magnetic resonance imaging (MRI), computed tomography perfusion (CTP), C-arm CT, nuclear medicine such as single-photon emission computed tomography (SPECT), ultrasonography and combination of few methods such as PET, CT/ MRI and SPECT/CT [5, 7].

Management

The most common treatment methods for oral cancer can be noninvasive, such as radiotherapy in most of the cases or can be invasive, such as surgery, which is usually the first option of treatment despite the fact that radiotherapy survival rate and control of the anatomical site are similar [8, 9]. Those methods can be provided separately or as a combination [8].

Radiotherapy may be provided separately or as a combination with chemotherapy in order to treat the initial tumor. It may be provided as neoadjuvant therapy, which will decrease the tumor size before the initial surgery. Radiotherapy may also be provided as adjuvant therapy, which will improve the efficiency of the initial therapy and by doing so will prolong the survival rate, decrease the change of possible recurrence and even improve the symptoms of a late stage oral cancer [8]. Radiotherapy has some major drawbacks such as xerostomia, osteoradionecrosis, mucositis and long duration of treatment which in cases of proximity to the bone and/or young patients are not preferable [9].

The treatment methods for oral cancer such as surgery, radiotherapy and chemotherapy have a major effect on the patient's quality of life and considered as very harsh due to the location and the obtrusive ways of treatment [7, 8]. The aim of OSCC treatment methods is to treat the initial tumor and to preserve as much as possible the shape and function with a proper restoration [9].

Prevention

In order to reduce the OSCC mortality among the general population, few steps should be promoted. First, in case of patients with high risk, the mortality may be reduced by promoting lifestyle changes and apply clinical evaluation as a part of a broad diagnostic program among the population. Second, an educational program with the basic knowledge regarding the OSCC should be embedded in the population while a frequent professional diagnostic and pathologic knowledge should be provided to the healthcare practitioners. Third, the ongoing and future researches regarding the OSCC must continue in order to define the particular etiological factors and biomarkers of the disease [4].

Conclusion

In conclusion, the scientific literature contains an enormous number of researches regarding the OSCC and its comprehensive information such as diagnostic methods, various treatments and known risk factors. However, the researches have not yielded any significant benefit as the prevalence and rate of mortality of the OSCC remains high.

Disclosure of conflict of interest

The authors declare no conflict of interest.

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