Morphological features of tongue squamous cell carcinoma diagnosed in Dolj County population between 2012–2014

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Abstract

Tongue squamous carcinoma can be found in many forms, having a lot of risk factors, and whose morphological characteristics can be used as a prognostic. The purpose of this study was to histologically characterize a number of 54 patients diagnosed between 2012–2014, with tongue squamous carcinoma. Surgical resection specimens of tongue tumors were processed by paraffin inclusion technique. The diagnose samples were reevaluated according to the World Health Organization (WHO) criteria for head and neck tumors diagnosis, by screening the Hematoxylin–Eosin staining sections. The most common histopathological variety of tongue carcinoma observed in our cases was the non-keratinized form, the basaloid and sarcomatoid types of carcinoma being ranked on the last places. The study outlined the prevalence of non-keratinized forms of tongue squamous carcinoma and all types of tumoral invasion patterns have been observed in different percentages.

Keywords: lingual squamous carcinoma, invasive tumor process, histopathological classification.

Introduction

Oral cancer develops as consequence of an individual genetic predisposition and by the accumulation of a series of genetic alteration due to chronic exposure to environmental carcinogen factors [1, 2].

In a report of the International Agency for Research on Cancer (IARC), there were listed a series of carcinogenic risk factors, such as: tobacco, alcohol, infections, radiations, professional exposure and medication [3]. More on this, World Cancer Research Fund and the American Institute for Cancer Research also added diet, overweight, obesity and sedentarism [4].

According to the most recent data in the literature, even though the general tendency is that of the incidence reduction in oral squamous carcinoma, the incidence of the tongue carcinoma seems to be growing especially amongst the youngsters of the white race [5].

Specialty studies show that most frequently the tongue tumors develop on the edges of the tongue and less on its dorsal part [6]. Other studies show that the anterior 2/3 of the tongue are more interested in developing a tumor than the posterior 1/3 [7]. On the other side, the posterior 1/3 of the tongue, if affected, has a bad prognosis, because of the quicker metastasis to the locoregional lymph nodes in comparison to the ones that develop in the anterior 2/3 [8].

Different morphological features have been suggested as predictive for the prognosis of oral squamous cell carcinoma (OSCC) and different histological grading systems of malignancy have been developed [9–10].

The latest tendency is to group squamous carcinoma into three main categories: (1) non-keratinized, that have an etiopathology in human papillomavirus (HPV) infections and are usually located in the oropharynx; (2) keratinized, not linked to a HPV infection, and (3) keratinized with squamous differentiation, the keratinized areas covering 10% of the tumor and not necessarily linked to a HPV infection [11].

Aim

The purpose of our study was to investigate, from the histopathological (HP) and statistic point of view, a number of 54 patients diagnosed with tongue squamous carcinoma over a period of three years, between 2012–2014.

Materials and Methods

The HP study consisted in 54 fragments of tongue tumors (surgical resection specimens) that have been processed through the paraffin inclusion technique. The study was performed between 2012–2014 by reviewing the paraffin blocks archived in the Laboratory of Pathology at the Emergency County Hospital, Craiova, Romania. From the pathology register of the enrolled casuistry,
there was collected data about the HP diagnostic of the lesions. The archived Hematoxylin–Eosin (HE)-stained sections were reevaluated by the World Health Organization (WHO) criteria of diagnosis of head and neck tumors (2005). Also, the HP study has investigated the main morphological microscopic characteristics of tongue squamous carcinoma, considering that in the literature were described the various types of tongue squamous carcinoma, the degree of histological differentiation, the existence of vascular invasion, or perineural and/or muscular invasion, and also the tumoral invasion pattern, and the existence tumoral invasion at the edges of surgical resection and the existence or not of lymph nodes dissemination.

Results

The 54 cases were grouped in order to comply with the WHO criteria (2005) of classifying head and neck tumors [12] in the following variants: keratinized squamous cell carcinoma (SCC) (20 cases, 37.1%), non-keratinized SCC (24 cases, 44.4%), acantholytic SCC (seven cases, 12.9%), basaloid SCC (two cases, 3.7%), sarcomatoid SCC (one case, 1.86%) (Table 1).

The analysis of the data presented in the table shows that the most frequent variety of tongue SCC was the non-keratinized form, on the last places being the basaloid form with 3.7% and the sarcomatoid form, representing 1.86% of the cases.

<table>
<thead>
<tr>
<th>Histopathological variety</th>
<th>Keratinized</th>
<th>Non-keratinized</th>
<th>Acantholytic</th>
<th>Basaloid</th>
<th>Sarcomatoid</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>20</td>
<td>24</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>54</td>
</tr>
<tr>
<td>Percentage</td>
<td>37.1%</td>
<td>44.4%</td>
<td>12.9%</td>
<td>3.7%</td>
<td>1.86%</td>
<td>100%</td>
</tr>
</tbody>
</table>

All the non-keratinized tongue SCC was made of a proliferation of carcinomatous cells, relatively uniform, tightly packed with a relatively syncytial aspect, with round-enveloped nucleus, vesicular and frequent atypical mitosis.

Rarely, the process of keratinized has been highlighted during the proliferation process with a unicellular keratinization (Figure 1a). Generally, the growing tumor pattern was cord type or nest type, most usually distinct from the inflammatory infiltrate. The tumor stroma was by default reduced, being a vascular connective tissue type infiltrated by inflammatory cells, especially with lymphocytes and plasmocytes.

The keratinized SCC of the tongue reproduced the morphology of the squamous stratified epithelium, therefore is made of Malpighian-like cells, in a polygonal form, with distinct limits, visible intercellular bridges, nucleus with variable dimensions and an eosinophilic cytoplasm with varied degrees of keratinization.

The most frequently observed tumoral growth pattern was a trabecular and floating island infiltrative pattern with a predominant fibrous stroma (Figure 1b).

Often, amongst the carcinomatosis islands there have been observed keratin pearls with a concentric arrangement leading to an eosinophilic sheets area. The tumoral stroma presented an inflammatory infiltrate of variable aspect, made of lymphocytes and plasmocytes sometimes shaped as an inflammatory granulomatous reaction to a foreign body (Figure 1c).

The acantholytic SCC of the tongue was made of areas of moderately non-keratinized squamous carcinoma but also presented the tumoral islands with acantholysis, thus leading to the glandular differentiation aspect. In the middle of some of the tumoral islands after the acantholysis of the neoplastic cells, there can be seen an aspect of false glandular differentiation or pseudolumina. In the newly formed pseudolumina there are acantholytic and dyskeratotic cells or cellular detritus (Figure 1d). The tumoral stroma presented a desmoplastic aspect with a varied lymphoplasmacytic infiltrate.

The basaloid SCC of the tongue was made of small cells with hyperchromatic nucleus and a small amount of cytoplasm that did not contain nucleoli, the arrangement being mostly lobular with a palisading pattern at the periphery. The tumoral growth pattern was in the form of nest and cords of variable dimensions and the tumoral islands of a larger size presented aspects of “comedo-type” necrosis (Figure 2a). In association with these proliferations, we managed to identify a component of keratinized or non-keratinized conventional squamous carcinoma. The stroma was generally quantitatively reduced and with hyaline or myxoid aspects.

Sarcomatoid squamous cell tongue carcinoma presented carcinomatous cells with a predominant fusiform morphology disposed in variable thickness bundles. The tumoral growth pattern was mostly fascicular with proliferations that interceded in angles that gave a sarcomatoid aspect (Figure 2b). Moreover, within the tumor, there were typical areas of non-keratinized squamous carcinoma.

The vascular invasion has been studied by examining the microscopic samples stained with HE. There were revealed vascular micrometastasis in almost a third of the investigated cases (28%) (Figure 3). Small groups of carcinomatous cells, that invaded the perineural spaces, were also highlight (Figure 4).

Muscular invasion was present in 34 cases, representing 62.96% of the investigated cases. In these cases, there was observed the presence of cohesive/discohesive carcinomatous cells that infiltrated the striated muscular fiber bundles and some of them being destroyed (Figure 5, a and b).

In more than 68% of the investigated cases, we did not record the presence of the microscopic invasion in the surgical resection limits but in approximately 28% of the cases, we observed the presence of dysplastic lesions with a malignancy potential. In 15 of the cases associated with dysplasia, the microscopic investigation recorded the presence of a high-degree dysplasia with cytological and architectural abnormalities (Figure 6a), including more than 2/3 of the thickness of the tongue coating epithelium in four of the cases.

Of all the studied cases, the locoregional lymph node metastasis was present in 13 (27.78%) cases. In all of these cases with lymph node dissemination, the HP exam
outlined the partial deletion of lymph nodes architecture that was replaced by the malignant tumoral proliferation, which has also presented various grades of differentiation (Figure 6b).

**Discussions**

Most of the tongue squamous carcinoma investigated in our study corresponded to the non-keratinized form (44.44%) closely followed by the keratinized form (37%) and to a certain distance we diagnosed the basaloid form (3.7%) and the sarcomatoid form (1.86%).

The acantholytic SCC with oral localization is a rare tumor, its maximum incidence being in the sixth or seventh life decade [13]. This type of cancer is characterized by a high degree of intercellular discohesion that leads to the formation of false glandular or vascular lumens and it often leads to differential diagnosis problems with adenocarcinoma, adenosquamous carcinoma and angiosarcoma. Regarding the prognosis of such lesions, the data are contradictory; some of the authors claim the aggressive character of these squamous carcinomas [14], while others challenge their metastatic and relapsing ability [15].

![Figure 1](image1.png)

**Figure 1** – Tongue squamous carcinoma: (a) Non-keratinized form, unicellular carcinomatous keratinization; (b) Keratinized form, island-type growth pattern; (c) Keratinized form, inflammatory lymphoplasmacytic infiltrate and gigantic foreign body cells; (d) Acantholytic form, in their pseudolumen there are isolated carcinoma cells present, along with cellular debris. HE staining: (b and c) ×40; (a and d) ×100.

![Figure 2](image2.png)

**Figure 2** – Tongue squamous carcinoma: (a) Basaloid form, carcinomatous island with central “comedo-like” necrosis; (b) Sarcomatoid form, pattern of fascicular growth that intersects in different angles. HE staining: (a) ×40; (b) ×100.
According to the latest WHO HP classification (2005) of head and neck tumors, the basaloid cell squamous carcinoma is a tumor which has in its composition variable proportions of squamous and basaloid elements the latter consisting of small monomorphic cells with a lobular disposition and often with “comedo-like” central necrosis [12]. Most studies indicate that such a tumor develops in the tongue or oral floor area, mainly in men and clinically it has a rather aggressive behavior more than half of the cases presenting loco-regional metastasis.
and approximately 50% of the patients are dying [16].
However, data on the survival rate of these patients are controversial, some authors claiming there is no difference between the conventional oral squamous carcinoma and this HP type [17].
The sarcomatoid SCC is rarely encountered in the oral cavity (<2%) and it consists of a conventional squamous carcinoma compound associated to a fusiform epithelial malignant proliferation [18]. Usually, this type of squamous carcinoma is predominant in men in the seventh or eighth life decade that have consumed alcohol, tobacco or have been exposed to ionizing radiation [18, 19]. The clinical behavior of this type of carcinoma is apparently more aggressive than the conventional one because of its way of relapsing easily and because it frequently develops metastasis especially regional ones [20, 21]. The surviving rate of the patients with this type of carcinoma is much lower compared to patients with common forms of squamous carcinoma [22].
Regarding the vascular invasion, Hoşal et al. [1998] noticed that the lymphovascular invasion is correlated to the regional extension of the disease but not to the surviving rate of the patients with tongue SCC [23]. However, Myers et al. showed that patients with tongue cancer younger than 40 years old that presented a lymphovascular invasion had a lower survival rate [24].
The perineural invasion within the investigated cases was reported in a third of the cases. Generally, in the literature studies that indicated the existence of a prognosis correlation of the tongue squamous carcinoma with lymphovascular invasion also reported a similar correlation to perineural invasion [24–26]. More on these, there are studies indicating that such a correlation is superior to the lymphovascular invasion.
Regarding the tumor invasion in the intrinsic tongue muscules, from our study we noticed that this aspect has been noticed in more than half of the cases (62.96%). Literature data indicate the muscular invasion as a morphological aspect quite frequently observed in oral squamous carcinoma. Sharma et al. indicated a percent of 85% of invasive tumors in the tongue intrinsic musculature, this aspect being present in 91% of the relapses [27]. Moreover, another study indicates that in tongue squamous carcinoma, the invasion of its intrinsic muscular structure was associated with an intrinsic predictive value of the lymph nodes occult metastasis in 23.3% of the cases [28]. The same authors also showed that the rate of prediction of local relapses was superior within the investigation of this morphological parameter in comparison to the depth of the invasion.
In the present study, we observed the presence of positive edges (tumor invaded) in approximately 1/3 of the cases (31.48%). Literature data established for the “clean” resection edges the limit of 5 mm and even more for the invasive form of carcinoma, a distance of 1–5 mm is considered to be positive/closed, while a distance smaller than 1 mm is considered to be invaded [29]. The general consensus is that the presence of clear resection edges is an important factor of prognosis but there is still a controversial matter about what is the true meaning of an adequate resection edge. Some researchers recommended as adequate edges those who had up to 2 cm, while others have suggested 3 mm as being sufficient [30] although the actual tendency is that a three-dimensional 1 cm is considered an adequate edge [31].
Regarding the lymph nodes dissemination, our study outlined the presence of loco-regional lymph nodes metastasis at the time of diagnosis in 27.78% of the cases. Literature data indicate that more than 50% of the patients with advanced local cancers from head and neck develop loco-regional or distance relapses, which are usually detected in the first two years from the surgical treatment. When the lymph nodes are affected, it is considered to be the first sign of cancer dissemination and an important prognosis factor in head and neck cancers [32]. Strictly, in the tongue localization there has been proved that the tumors that develop in the mobile area have a reserved prognosis caused by the high rate of dissemination in the loco-regional lymph nodes area [33]. This morphological parameter is considered to be one of the most important prognosis factors of tongue cancer [34]. More on these, some authors consider there is a correlation between the presence of metastasis and the degree of tumor differentiation [35, 36], respectively with the vascular density and the lymphatic invasion [36].

Conclusions

HP study outlined the prevalence of non-keratinized form of tongue squamous carcinoma followed in descending order by the keratinized form, the acantholytic form, the basalioid and sarcomatoid form. The tumors belonged to all the differentiation degrees. The tumor invasion in the host tissue was realized in most of the cases with an aspect of third pattern, peculiar in the form of small cellular groups or cellular cords of infiltrative tumoral cells. The vascular and perineural invasion were both observed in a third of the studied cases, most of them in association with the muscular invasion.

Conflict of interests

The authors declare that they have no conflict of interests.

References

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