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Original research article

Role of extended histological examination in the assessment of local recurrence of tongue and floor of the mouth cancer

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ABSTRACT

Aim: The aim is to find out why the rate of recurrence of tongue and floor of the mouth cancer is so high despite radical surgical treatment combined with radiochemotherapy.
Background: Oropharyngeal cancer is the second most common head and neck cancer in Poland. Tongue cancers account for 40% of all oral cavity tumours. A frequent reason for a failure in treatment of tongue and floor of the mouth cancers is local recurrence. Based on that examination, cancer treatment can be precisely planned.
Materials and methods: The study comprised a group of 56 tongue and floor of the mouth cancer patients. 9 patients who showed local recurrence were given an extended histopathological examination. The infiltration of the vessels, nerves and muscles was examined. The examination also checked the largest dimension of the tumour, the greatest depth of invasion from the mucous membrane, invasive front of the cancer, vessel embolisms, intra- and perineural infiltrations in the cancer invasive front. Tumour aggressiveness was assessed according to M. Brandwein-Gensler.
Results: In five patients, primary tumours were found to be histologically aggressive as indicated by the infiltration of the vessels, nerves and muscles. Tumours which penetrate these structures were characterized with peri- and intraneural infiltration and were correlated with the depth of invasion from the mucous membrane, the occurrence of embolisms, and a high risk assessment as proposed by M. Brandwein-Gensler.
Conclusion: The progression of cancer depends strongly on histopathological traits. The incidence of penetration of the vessels, nerves and muscles correlates with aggressiveness of the tumour front.

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1. Background

Oropharyngeal cancer is the second most prevalent head and neck malignancy in Poland following laryngeal carcinoma. Tongue cancers account for 40% of all oral cavity malignancies.[1] The incidence of cancers in this location is ever increasing. In 2007, according to the National Cancer Institute, it amounted to 2.9 cases per 100,000 population for the tongue and 0.5 per 100,000 population for the floor of the mouth. Tongue cancer in men is approximately 2.5 times more prevalent (4.2 per 100,000) than in women (1.7 per 100,000). The increase in tongue malignancies is also confirmed by WHO (World Health Organization) and IARC (International Agency for Research on Cancer) statistics. The risk of oral cavity cancer increases 6–7-fold with individuals overusing tobacco or alcohol and as much as 15-fold with those who both smoke and drink alcohol.[2] Other risk factors include: age, race, poor oral cavity hygiene, irritation of mucous membrane (e.g. by ill fitted dentures or untreated inflammations), pre-neoplastic conditions (leukoplakia, erythroplakia). There are also more and more reports confirming the relationship between oral cavity cancer and HPV infection or sexual behaviours.[3]

Local recurrence tends to be a frequent cause of failure in treatment of oral malignancies. The frequency of local recurrence ranges from 19%[4] to 28%.[5]

A routine basic histopathological examination provides information on a histopathological type of the cancer and its degree of differentiation (G). A vital role in the identification of squamous cell carcinomas, in particular tongue and floor of the mouth tumours, is played by an extended histopathological examination that involves assessment of several parameters, including: the largest dimension of the tumour, the greatest depth of invasion, invasive front of the cancer, vascular embolisms, intra- and perineural infiltration, bone infiltration, diameter of the largest metastasis. The examination is very time-consuming and must be performed by an experienced pathologist. It would be useful to identify such traits that are most correlative to high aggressiveness of tumours, thus indicating a high risk of local relapse. By taking due account of the results of extended histopathological examinations and patient's clinical status, oncology treatment can be precisely planned and the chance for full recovery increased.

1.1. *Aim of the study*

The aim of the study is to find out why the rate of recurrence of tongue and floor of the mouth cancer remains so high, despite radical surgical treatment combined with radiochemotherapy.

2. Materials and methods

The study comprised a group of 56 tongue and floor of the mouth cancer patients treated surgically at the Laryngological Oncology Department, Greater Poland Oncology Centre, Poznań, in the years 2007–2009. To determine a clinical stage of cancer, imaging techniques were used, apart from physical examination, including transcutaneous and intraoral sonography, CT and MRI. All the patients had underwent surgical treatment. Those treated with prior radiotherapy or chemotherapy was excluded from the group. Excluded from the study were also tumours that could not be treated with radical surgery due to an advanced stage of cancer. Local recurrence was differentiated from second primary tumour using the Warren and Gates criteria.[6,4] Qualified as local recurrence were lesions histologically resembling the primary tumour, occurring within 3 years of the primary tumour diagnosis and located less than 2 cm away from the primary focus.

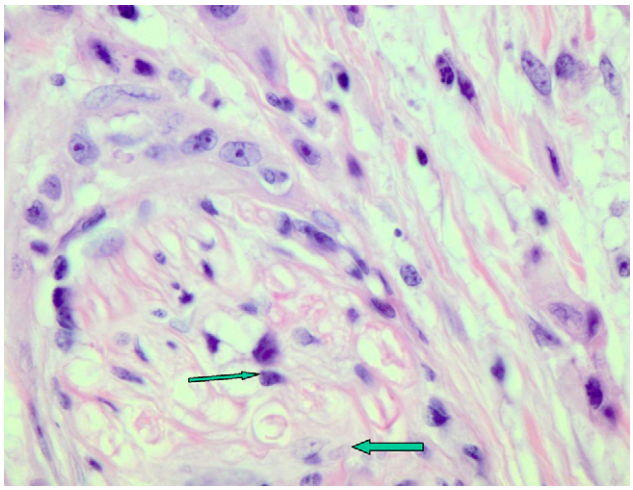

Fig. 1 – Intraneural infiltration.

Nine patients with local recurrence were subjected to an extended histological examination based on post-operative samples held by the Pathology Department of the Greater Poland Cancer Centre in the form of paraffin blocks and routinely stained specimens (H + E). The specimens were analysed in keeping to the guidelines of the Royal College of Pathologists. Apart from the routine identification of a cancer type and degree of differentiation (G), the examination also checked the degree of infiltration for the vessels, nerves and muscles. The extended histopathological examination involved the assessment of the largest dimension of the tumour, the greatest depth of invasion into the mucous membrane, invasive front of the cancer, vascular embolisms caused by cancerous cells, intra- and perineural infiltrations in the cancer invasive front, bone infiltration, and the diameter of the largest metastasis.

3. Results

Of the nine patients who had been diagnosed with local recurrence, 78% were male and 22% female. In five cases keratinizing squamous cell carcinoma G2 was found and in three cases G3. Nonkeratinizing squamous cell carcinoma G3 was recognized in one patient. In five patients, primary tumours were found to be histologically aggressive as indicated by the infiltration of the vessels, nerves and muscles. In two cases, cancer penetrated either vessels and nerves or vessels and muscles, and in two other cases, just one of those structures (Figs. 1–5).

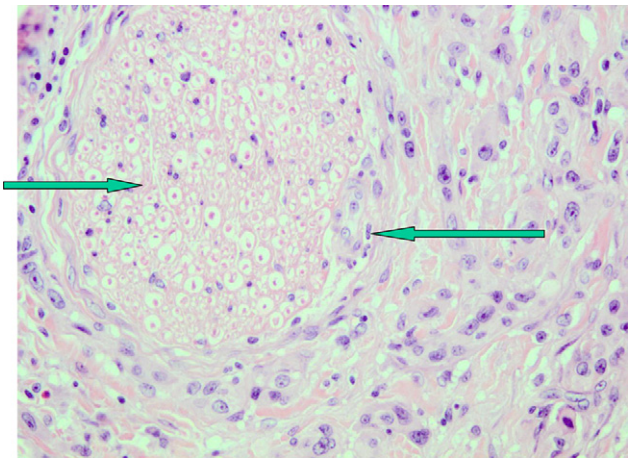

Fig. 2 – Perineural infiltration.

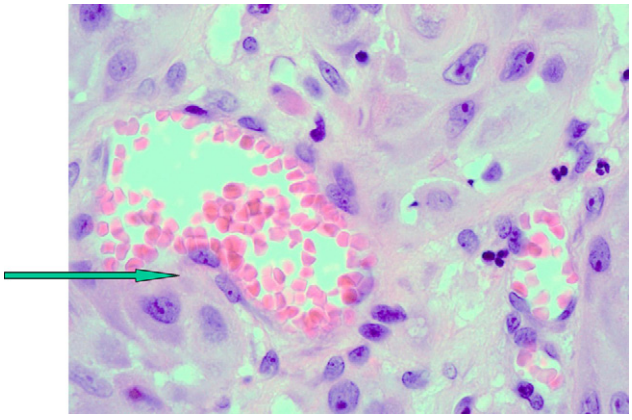

Fig. 3 – Vessel infiltration.

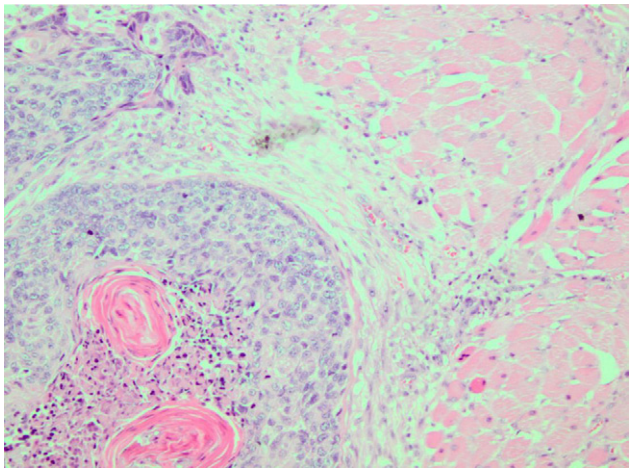

Fig. 4 – Level I of tumour aggressiveness according to Margaret Brandwein-Gensler et al.

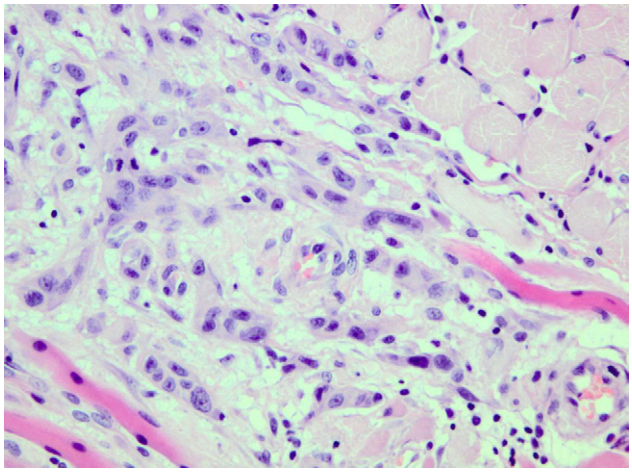

Fig. 5 – Level IV of tumour aggressiveness according to Margaret Brandwein-Gensler et al.

The TNM classification was used to assess the stage of both the primary lesion and local recurrence. The stage of the primary cancer was mostly (in seven cases) classified as T2, the other two cases were T1 and T4. Pathological augmentation of lymph nodes accompanying the primary tumour was found in eight patients. The histological examination confirmed metastasis to neck lymph nodes in five cases (N1 in 3, N2 in 2 cases) (Table 1).

The rT4 stage of tumour recurrence was found in six patients. Such a high stage of local recurrence was in to a certain extent due to patients' failing to make regular follow-up visits with their doctors. In seven cases, the local recurrence was accompanied by metastatic neck lymph nodes. N1 stage was recorded in one case, N2 in two, N3 in one, and Nx in three. Metastasis to distant organs (lung, bones) concomitant with local recurrence occurred in two cases.

The time to local recurrence ranged between 2 and 14 months, 8 months on average.

The histological examination revealed keratinizing squamous cell carcinoma G2 in three cases and G3 in one case. Nonkeratinizing squamous cell carcinoma G3 was found in two patients. Two patients, due two scarce biopsy material, were diagnosed with squamous cell carcinoma, and one with squamous cell carcinoma G1.

Another trait reported to correlate with the prevalence of infiltration was the depth of invasion into the mucous

Table 1 – Routine and extended histopathological examination.

Histopathological type of cancer	Routine histopathological examination
Degree of differentiation (G)	
Largest dimension of tumour	Extended histopathological examination
Greatest depth of invasion	
Invasive cancer front	
Vascular embolisms	
Peri- and intraneural infiltration	
Bone infiltration	
Diameter of the largest metastasis	

membrane. The deepest penetration of 1.65 cm was found in the patients who had their vessels, nerves and muscles invaded, medium depth of 1.45 cm was found in those with two structures involved and 0.55 cm in those with only one structure affected.

Both the system proposed by M. Brendwein-Gensler et al. and the assessment of the infiltration of vessels, nerves and muscles permit prediction of high tumour aggressiveness.

4. Discussion

Local recurrence in head and neck surgery is a frequent problem. This is confirmed by numerous articles widely discussing the subject. A. Eckardt[5] showed that recurrence of tumours of the oral cavity is 28%, while R. Gonzales,[4] respectively lower: 19% among men and 18.7% among women. In our material, local recurrence after radical surgery followed by radiation therapy was 16.1% with 9 cases of 56 operated patients. Causes of local recurrence in a selected group of patients have been evaluated by the infiltration of nerves, blood vessels and nerves. Kurtz[7] demonstrated that there is no evident correlation between vascular, perineural and lymphatic spread and survival in patients with oral cancer. However, Spiro[8] showed an increase in the incidence of local recurrence in patients with involved margins; but this did not affect overall survival. An alternative option of treatment for patients with local recurrence, who have already used radiation therapy, is the HDR brachytherapy. However, the risk of nodal recurrences is substantial – L. Tucek et al.[9] A greater chance of cure is given by radical surgery.

In the present study, infiltration of these three structures was compared with the British Pathologists Consensus guidelines (Royal College of Pathologists). It revealed a high correlation to such features as greatest depth of invasion, the invasive front of cancer, vascular embolisms, intra- and perineural infiltrations in the cancer invasive front.

The occurrence of vascular embolisms in the tumour front was found in 75% of the patients who had their muscles, vessels and nerves invaded. Those with two of the structures involved were less affected (50%), while those with only one structure penetrated (muscles) did not show any vascular embolism.

Tumours which were found to penetrate the vessels, nerves and muscles were also characterized with peri- and intraneural infiltration in the tumour front. Whereas those which penetrated two of the examined structures were marked with perineural infiltration only, with no cancerous cells detected inside the nerves.

Similarly, high correlation was found between the frequency of infiltration in the structures we evaluated, and the depth of invasion under the mucosa. The deepest penetration of 1.65 cm was found in the patients who had their vessels, nerves and muscles invaded, medium depth of 1.45 cm was found in those with two structures involved and 0.55 cm in those with only one structure affected.

Tumour aggressiveness was assessed according to Margaret Bredwein-Gensler et al. by means of a five-level score of cancer invasion. Level I tumour is distinguished with a compact surface with a clear blunt boundary. Levels IV and V are in turn characterized by a poorly outlined tumour front with long appendages with the width of one cell and nests of 15 cancerous cells. It was established that the patients who had their vessels, nerves and muscles penetrated were marked with the very aggressive level IV invasion, whereas those with only two structures affected scored also II and III. Both the system proposed by M. Brendwein-Gensler and the assessment of the infiltration of vessels, nerves and muscles permit prediction of high tumour aggressiveness.

Extended histopathological examination including: the British Pathologists Consensus guidelines and tumour invasion model by M. Brandwein-Gensler is very time consuming, requires high experience from the pathologist and is not a standard test panel. Invasion of blood vessels, nerves and muscles pointing to the high aggressiveness of cancer invasion is unfavourable risk factor for local recurrence and may have a decisive influence on the choice of adjuvant therapy in the form of radio- and/or chemotherapy.

5. Conclusion

The progression of cancer depends strongly on histopathological traits.

The incidence of penetration of vessels, nerves and muscles correlates with aggressiveness of the tumour front.

A detailed histological examination, taking account of the penetration of the vessels, nerves and muscles, permits to assess the risk of local occurrence and may be decisive in the selection of adjuvant treatment involving radiotherapy and/or chemotherapy.

Conflict of interests

None declared.

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