Correlations of tumors of the oral cavity and diabetes mellitus

PhD Thesis

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Summary

The oral signs of diabetes mellitus are well known: gingivitis, parodontosis, and lesions of the oral mucosa (glossitis and candidiasis). However, the literature to date does not detail any connection between diabetes mellitus and tumors in the oral cavity.

The author has carried out epidemiological, clinical and histopathological studies on this topic.

The stomato-oncological screening of diabetics revealed that subjects with diabetes (and particularly that of type 2.) display an elevated incidence of inflammatory lesions, benign tissue growth and precancerous states. Diabetics who smoke are at high risk of the development of precancerous processes in the oral cavity.

A retrospective investigation of malignant tumors in the oral cavity demonstrated an enhanced frequency of diabetics (mainly of type 2.) among those with oral carcinoma.

The most frequent malignomas among diabetics are tumors of the gingiva and the lip.

It emerged from the clinical and histopathological studies that the progression of oral carcinomas is accelerated by diabetes: the tumors then form metastases more quickly, and death occurs earlier.

A new hypothesis is proposed as regards the correlation of tumors in the oral cavity and diabetes mellitus, study of which demands further detailed research work.
Aims

The research work was aimed at answering the following questions:

1. Can an epidemiological connection be found between diabetes mellitus and tumors of the oral cavity?
   a. What are the incidences of oral precancerosis and tumors of the oral cavity in diabetics?
   b. What is the incidence of diabetes among patients with malignant tumors of the oral cavity?

2. Is there a connection between the localization of malignant tumors of the oral cavity and the symptoms/complications of diabetes mellitus?

3. Does diabetes mellitus influence the progression of oral carcinomas?
Materials and methods

1. Epidemiological studies

The occurrence of precancerosis and tumors of the oral cavity among patients with diabetes mellitus

Between 1. March 2002. and 31. January 2003. stomato-oncological screening examinations were performed on 200 diabetic patients at the 1st and 2nd Departments of Medicine at Semmelweis University. Of these 200 patients, 82 had diabetes of type 1, and 118 had diabetes of type 2, 131 were females, and 69 were males. The average age overall was 458 years; in the type 1 group it was 55.3 years.

2. Clinical studies

1.1. The incidence of diabetes mellitus among patients with malignant tumors of the oral cavity

A retrospective study was carried out on patients with histologically confirmed malignant tumors of the oral cavity who were treated at the Department of Oral and Maxillofacial Surgery at Semmelweis University between 1. January 1998 and 30. June 2002.

Of the 610 patients studied, 435 were males, and 175 were females. 606 had histologically confirmed planocellular carcinoma, and 4 had adenocarcinoma. The average age of the patients was 56 years. The control group consisted of 5-74 adults who were tumor-free, who underwent dental surgical care; their average age was 51 years.

On the basis of the fasting blood sugar levels, the patients were divided into three groups:

1. a normal fasting blood sugar level (<6.1 mmol/l),
2. an elevated fasting blood sugar level (6.1-6.9 mmol/l), i.e. an impaired fasting glucose level, indicative of a disturbance of the carbohydrate metabolism,
3. diabetes mellitus (fasting blood sugar level >6.9 mmol/l),
Studies were made of the incidence of diabetes mellitus in the various tumor stages, and of the distributions of the malignomas of the oral cavity according to localization among the diabetic patients and the non-diabetic cases.

2.2. Study of the progression of malignant tumors of the oral cavity in diabetics

Retrospective, follow-up studies were carried out on patients with histologically confirmed malignant tumors of the oral cavity, treated at the Department of Oral and Maxillofacial Surgery at Semmelweis University between 1. January 1992 and 31. December 2002.

The criteria for inclusion in the study were as follows:

a. a gingival tumor (The most frequent malignant tumor in diabetes mellitus),
b. tumor stage T2−3N0M0,
c. identical surgical treatment: tumor extripation + functional cervical dissection,
d. no neoadjuvant treatment,
e. follow-up for 2 years postoperatively.

At the end of the 2-year follow-up period, a study was made of the TNM data, and hence the progression could be determined. Criteria for a diagnosis of progression:

a. local recurrence,
b. regional lymph node metastases,
c. distant metastases,
d. tumor-related death.

The different types of progression were surveyed in the diabetic group and the control group, and the results were compared and analysed statistically.
3. Histopathological studies

The surgical blocks of the patients with gingival tumors were assessed histologically from the aspect of progression in the diabetic and non-diabetic groups. The mode of invasion on the invasive front of the tumors was categorized in four grades:

1. the tumor was sharply delineated from its environment.,
2. the tumor was spreading in bundles, and was not sharply delineated.,
2. cell groups that had separated from the original tumor were invading the adjacent tissues.,
3. the spreading was diffuse, with the invasion of tumor cells and cell groups.

Immunohistochemical methods were used to evaluate the integrity of the basal membrane, and the expression of lamin-5 was studied.
4. Statistical methods

As we were searching for a correlation between two independent variables, we used the chi-squared test for the statistical analysis, with 2 degrees of freedom. The Student two-tailed $t$-test was employed in comparisons of histopathological samples and in studies of the differences in mean values. Significance examinations were made at a level of 5%. Statistical investigations were performed in the Department of Biophysics at Semmelweis University.

Results

1. The occurrence of precancerosis and tumors of the oral cavity among patients with diabetes mellitus

The lesions that were observed were classified into three groups:

a. inflammatory lesions (cheilitis and glossitis),
b. benign tissue growths,
c. precancerous lesions (leukoplakia and erythroplakia).

Malignant lesions were not found in the 200 patients examined.

Some form of lesion of the oral cavity was observed in 51.5% of the diabetic patients.

In both diabetic groups, the inflammatory lesions were most frequent, followed by the benign tissue growths and then the precancerous states.

The frequencies of all three types of lesion were higher among the patients with diabetes of type 2 than among those with diabetes of type 1: inflammatory lesions: 31.3% and 25.6%, benign tissue growths: 16.9% and 10.9%, and precancerosis: 11% and 3.6%, respectively.
2. The incidence of diabetes mellitus among patients malignant tumors of the oral cavity

The 610 patients with carcinoma of the oral cavity were found to include 89 diabetics (14.6%) and 59 cases (9.7%) with an elevated blood sugar level, 87 (97%) of the 89 diabetics had diabetes of type 2.

The control group included 32 diabetics (5.6%) and the same number of subjects with an elevated blood sugar level.

24.3% of those with malignant tumors of the oral cavity, and 11.2% of the control group exhibited irregularities of the glucose metabolism. The difference was significant (p<0.01). There was not a significant difference in incidence if diabetes in the different tumor stages.

The most frequent tumor of the oral cavity in the non-diabetic group was the sublingual carcinoma (146 cases, 28%), followed by lingual carcinoma (100 cases, 19%).

Among the diabetics, the gingival tumor was most frequent (26 cases, 29%), followed by carcinoma of the lip (21 cases, 24%).

The rates of tumors of the gingiva and of the lip were significantly higher (p<0.01) among the diabetics then in the non-diabetic tumor group.

3. Study of the progression of malignant tumors of the oral cavity in diabetics

3.1. Results of clinical studies

On the basis of the previously-listed criteria, 24 patients were classified into the diabetic group, and 52 into the non-diabetic group.

All of the diabetics had diabetes of type 2.

Among the 24 patients in the diabetic group, progression was observed in 15 cases (62.5%): 3 of the 15 progression cases involved local recurrence (20%), while the remaining 12 involved a combination of local recurrence and cervical lymph node metastases (80%). 12 of the 24 patients (50%) had died by the end of the 2-year follow-up period.
In the control group, 24 of the 52 cases (46%) displayed progression: 14 involved local recurrence (58%), and 10 (42%) the other form of progression. 6 of the 52 patients (11%) died.

In the diabetic group, there were significantly more cases involving metastases (p<0.05) and significantly more deaths (p<0.001) during the 2-year follow-up period.

3.2. Histopathological results

Among the patients in the diabetic group, tumor invasion of grade 3 or 4 occurred more frequently, whereas grade 1 or 2 was more characteristic in the control group.

The tumor invasion was significantly more aggressive in the diabetics (p<0.01).
New results presented in the theis

1. Significant epidemiological correlations were found between the incidences of precancerous states and tumors of the oral cavity and the occurrence of diabetes mellitus.

2. The rates of benign tissue growths and precancerous states were higher among diabetic patients than in the general population. Precancerous processes occurred more frequently among patients with diabetes of type 2.

3. Diabetes of type 2 was observed significantly more often among the patients with carcinoma of the oral cavity than in the tumor-free control group (p<0.01).

4. The most frequent malignomas of the oral cavity among the diabetic patients were tumors of the gingiva and the lip, while the most common types among the non-diabetics were sublingual and lingual carcinomas.

5. Both clinically and histopathologically, the progression of the carcinomas of the oral cavity was significantly more rapid among those with diabetes mellitus of type 2 than in the non-diabetic control group (p<0.001).
Publishing activity

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