

Epidemiological, Clinical and Histopathological Studies Regarding the Positive and Differential Diagnosis of the Most Frequent Potentially Malignant Disorders of the Oral Mucosa

Abstract

Introduction. Despite of important progress achieved in surgery, radio- and chemotherapy, clinical and histopathological findings of the last two decades show an increased frequency of malignant tumours of the oral cavity. Therefore, besides early diagnosis and adequate treatment of malignant tumours, the importance of prevention in oncogenesis is more and more emphasized.

In the complex process of carcinogenesis – in which two distinct steps are mentioned by some authors – potentially malignant disorders play an incontestable role. Leukoplakia and lichen planus are the most frequently seen potentially malignant disorders of the oral mucosa, but data regarding the incidence and malignant transformation rates of these affections vary in the literature, according to different authors.

Many times, the treatment of oral leukoplakia and lichen planus can show a series of difficulties, especially in extended or disseminated forms.

Another essential aspect is represented by the fact that routine histopathology cannot predict reliably the malignant transformation of these disorders, therefore additional examinations are needed. Despite of numerous histopathological and immunohistochemical studies carried out by different authors, there is yet no single prognostic marker regarding the studied affections.

In this thesis we included epidemiological, clinical, respectively histopathological and immunohistochemical studies of the most frequent potentially malignant disorders of the oral mucosa, in order to bring some important contributions to the complex problem represented by these affections.

The thesis is structured in two parts: I. The General Part and II. The Practical Part, containing several chapters.

I. The General Part consists of two chapters, the first of them presenting the normal structure and functions of the oral mucosa, while the second one the potentially malignant disorders of the oral mucosa.

1. Generalities regarding the normal structure and functions of the oral mucosa. This first chapter describes the clinical anatomy of the oral cavity, the histological structure, the physiology and the protecting mechanisms of the oral mucosa. Changes in the aspect of the

mucosa – without any pathological importance, but role in the differential diagnosis – are also presented. Knowing these aspects is essential in understanding the etiology and pathogenesis of the potentially malignant disorders arising in the oral cavity, as well for the correct positive and differential diagnosis, treatment plan and follow-up of the lesions.

2. Generalities regarding the potentially malignant disorders of the oral mucosa. This chapter presents the classification, epidemiology, etiology, clinical and histopathological aspects, evolution and treatment of potentially malignant disorders of the oral mucosa.

II. The Practical Part consists of four chapters, the first three containing the epidemiological, clinical and histopathological studies carried out by us, and the last one summarizes the general conclusions of the thesis.

3. Epidemiological studies regarding the most frequent potentially malignant disorders of the oral mucosa. In this chapter a retrospective study was carried out, for a period of 12 years (between 2000-2011), based on the patients of the Oral and Maxillofacial Surgery Clinic from Târgu Mureș, analyzing especially leukoplakia and lichen planus – the most frequent potentially malignant disorders of the oral mucosa. The most important aspects of our results can be summarized as it follows:

- We found that the incidence of leukoplakia as well of the lichen planus (0,48% and 0,42%) was near the lower limit of the values published in the literature (0,4-11,7%; 0,2-3%).

- Leukoplakia affected almost equally the two genders, with a slightly higher percent in male patients (54,73%), while lichen planus was seen predominantly in female patients (74,24% in case of ambulatory and 88,89% in case of internated patients).

- As it regards the age, both of the affections appeared mainly in the group of 50-59 and 60-69 years, but the great majority (above 70%) of leukoplakias in young patients (under 40 years) affected the females.

- No malignant transformation was found in the group of lichen planus, while 6,08% of leukoplakias showed malignant transformation, this value being at the upper limit of data published in the Romanian literature, but in the international literature we found also higher malignization rates.

4. Clinical studies regarding the most frequent potentially malignant disorders of the oral mucosa. The fourth chapter – based on several representative clinical cases – demonstrates the treatment difficulties of the studied disorders, and the advantages of the use of LASER-s in this treatment, which helps to eliminate a great part of the mentioned difficulties.

5. Histopathological and immunohistochemical studies regarding the most frequent potentially malignant disorders of the oral mucosa. This chapter contains two studies.

The first one is a histopathological study, using the results of histopathological analysis of the specimens obtained from the patients of our clinic, for a period of 12 years (between 2000-2011). We followed the incidence of different clinical and histopathological forms of leukoplakia, localization of the lesions and the concordance between clinical and histopathological diagnosis. The histopathological analysis revealed „in situ”, microinvasive or even invasive carcinoma in 8,82% of cases diagnosed clinically as leukoplakia. As for lichen planus, the routine histopathological analysis was able to confirm the diagnosis in only 63,16% of the cases.

The second study included in this chapter is an immunohistochemical analysis of expression of three markers (Cyclin D1, Ki67 and p53) in case of the most frequent potentially malignant disorders of the oral mucosa, in comparison with normal mucosa, benign and malignant tumours (in total 99 cases). Cyclin D1 and Ki67 showed a similar pattern of expression. We found statistically significant increase in the expression of these two markers in parallel with increasing severity of leukoplakias, both from the clinical and histopathological point of view. The differences were also significant between leukoplakias and normal mucosa, leukoplakias and benign tumours, leukoplakias and lichen planus and finally between leukoplakias and oral squamous cell carcinomas. In case of p53 although the oral squamous cell carcinomas showed a significantly higher expression rate than leukoplakias, no correlation was found with any of the clinical or histopathological features of leukoplakias.

6. General conclusions. The last chapter summarizes the general conclusions of the thesis:

- According to our results, of the studied potentially malignant disorders of the oral mucosa, leukoplakia has a major importance in the complex process of carcinogenesis, with a 6,08% malignant transformation rate.
- The use of LASER-s represents important advantages and benefits in the treatment of the studied disorders.
- Of the analysed immunohistochemical markers Cyclin D1 and Ki67 may have prognostic value in oral leukoplakia, while p53 has less importance in this matter.

References. The list of references used for the elaboration of the thesis consists of 177 titles.

Annexes: In extenso articles published as a result of the thesis.