University of Medicine and Pharmacy of Tîrgu Mureş Doctoral School

Abstract of the Ph.D. thesis: Oral manifestations in hematological disorders

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The disorders with the greatest impact on the oral cavity in both elderly and young adults, and most often in children, are hematological disorders. These give local oral-pharyngeal-dental injuries, sometimes being the starting point for the diagnosis thereof, but also general manifestations that may compromise oral-dental treatments or lead to serious accidents, sometimes fatal bleeding. It is known that oral mucosa is a mirror of general health, so it is important to evaluate both the incidence and the unique pattern of oral disorders that occur as a symptom or complication of hematologic disorders.

The increasing frequency of hemopathies of various causes and the increasing number of studies in this field fully motivate the approach from the perspective of the dentist, who, through contact with a large number of patients, can detect in the early stages some lesions characteristic of these disorders and the treatment of oral-dentation disorders may be timed or minimally invasive solutions adapted to the main hematological condition.

For this reason, before starting the specific treatment for which the patient has presented, it is imperative that any dentist to make a case history and a thorough examination of the oral cavity in which he may experience signs of benign or malignant hematologic conditions. These signs may be clinically important indicators in the early diagnosis of high-severity illnesses in apparently healthy patients.

The thesis is structured on several chapters. In the first part (**general part**), general notions of topographic anatomy of the oral cavity and a brief presentation of the most frequent hematological disorders with manifestations in the oral cavity are presented.

The motivation for the research is presented in the second part, "Personal Contributions", made up of three studies.

The first study entitled "Clinical statistical studies on oral manifestations in hematological disorders. Correlations between benign / malignant disorders and changes in laboratory parameters" is a retrospective clinical and statistical study in which we monitored the frequency of oral manifestations in hematological, benign and malignant conditions, the distribution thereof in different topographic areas of the oral cavity, and the correlation with other clinical and laboratory parameters.

Of the **hemorrhagic manifestations**, the most frequent were those with the location in the oral cavity. (gingival bleeding and purpura in the mouth mucosa) followed by skin purpura and hematuria. Oral hemorrhage manifestations correlate with changes in paraclinical parameters of hemostasis, especially with the degree of

thrombocytopenia, disseminated intravascular coagulation in all patients with benign or malignant, acute or chronic hematologic disorders.

The second study entitled: "Assessment of the stomatitis degree due to cytostatic treatment in patients with malignant lymphomas" shows correlations among the degree of stomatitis and the type and amount of cytostatic medication administered to the patient, with emphasis on the role of the dentist in the prevention and treatment of this complication, which, by the severity of the clinical manifestations, overlaps with a severe condition. Out of the total of 59 patients diagnosed with malignant lymphoma, 18 patients presented Hodgkin Lymphoma (HL) and 41 patients with non-Hodgkin Lymphoma (NHL).

In the studied group of patients treated based on plans of cytostatic medication, we found that the CVP+Rituximab plan causes more frequently $1^{\rm st}$ and $2^{\rm nd}$ degree stomatitis, without having any patient with $3^{\rm rd}$ and $4^{\rm th}$ degree stomatitis. In a total of 80 applications, the CHOP + Rituximab therapy plan presented $1^{\rm st}$ and $2^{\rm nd}$ degree stomatitis as complications, more frequently $1^{\rm st}$ degree stomatitis, without showing $2^{\rm nd}$ and $4^{\rm th}$ degree stomatitis. $3^{\rm rd}$ degree stomatitis occurs in two cases in CHOP-Bleo treatment.

Comparing the CVP + Rituximab versus CASC, DAHP treatment plans, there are significant differences in toxicity, more aggressive treatments leading to more serious complications.

The third study: "The incidence of malignant lymphomas with primary manifestations in the oral-maxillary-facial sphere", aspect less studied in the literature, and the clinical case rarely as the onset of palatine tonsils disorder is a suggestive example of the connections between the hemorrhagic and oral-facial structures. The guarded prognosis in cases of peripheral mature T-cell lymphoma located in the mouth involves the need of some clinical common protocols for assessment and the dental treatment planning allows the oral cavity to be repaired, decreasing the risk of complications and helping to improve the quality of life of these patients.

Processing the histopathological results from the Pathological Anatomy Service of the County Emergency Clinical Hospital for 3 years 2014-2016, we included in our study only LMNH that were diagnosed due to the first manifestations that occurred in the oral-maxillary-facial area and the immunohistopathological diagnosis was decided after processing the biopsy pieces collected from this area.

In our study, in 19 patients with LMNH, we found only one case of mature peripheral T-cell lymphoma, representing 5.26% of the total, the most common of which being 78.94% large cell diffuse lymphoma, our results being consistent with other researchers. The rarity of these cases may also be due to infection with the less common HTLV-1 virus in our country and more specific to Asian countries, which is also evidenced by the large number of studies in these countries.

As an example of the localization of malignant lymphomas in the oral-maxillary-facial area, we present an extremely rare case of a peripheral T-cell non Hodgkin malignant lymphoma that had the first manifestation located in the Waldeyer's tonsillar ring.

Key words: oral manifestations, hematologic diseases, oral bleeding, T-cell lymphoma, gingival bleeding, chemotherapy, immunohistochemistry.