

Oral Tumors Having the Origins in Multiple Tissues, Non-differentiated or Differentiated

MIHAI CONSTANTIN¹, DORIANA AGOP FORNA^{1*}, CRISTIAN BUDACU^{1*}, AURELIANA CARAIANE², GHEORGHE RAFTU², NORINA CONSUELA FORNA¹

¹Grigore T. Popa University of Medicine and Pharmacy, Maxillofacial Surgery Department, 16 Universitatii Str., 700115, Iasi, Romania

²Ovidius University of Constanta, Faculty of Dental Medicine, 7 Ilarie Voronca Str., 900684, Constanta, Romania

The lesions in the oral cavity must be seen in the light of pathological and correlated system processes with systemic illnesses because systemic illnesses cause oral manifestations and inversely - oral affections (Alvin Gardner). Many times, when symptoms and signs occur, the disease is in an advanced phase, the interest of the oral cavity being the expression of a generalized illness. Extremely varied tumors in shape and evolution come from multiple tissues undifferentiated or differentiated, often in a complication of different structures, which imparts to them a histological polymorphism. They can be found and traced in their evolution during a dental examination, more easily than those developed at the organs. An early detection of precancerous states and neoplasia can be made, and clinical and paraclinical data are corroborated in the dynamics of the evolutionary process, with the observation that, in the presence of benign histological aspects, evolution may be serious due to functional turbulence lymphangioma of the tongue with muscle fiber atrophy, epithelial ulceration and superadded inflammation with oral phlegmon, haemorrhages (oral mucosal hemangioma). We studied 120 patients with oral tumors originating in multiple non-differentiated tissues or differentiated, over a 5-year period, January 2012-December 2016. Malignant ganglion involvement includes a broad pathology requiring rigorous, clinical, paraclinical, histological and immunohistochemical examination to achieve effective therapeutic management. The degree of malignancy should be specified in all cases where this is possible with the help of available systems as it is of prognostic and predictive importance.

Keywords: oral tumors, undifferentiated tissues, differentiated tissues, histological polymorphism, functional disorders, precancerous states.

All benign and malignant tumors have two basic components: the proliferating neoplastic cells constituting their parenchyma and the supporting stroma formed by connective tissue and blood vessels. Although cell parenchyma represents the proliferative compartment of neoplasms and consequently determines pathological behavior, growth and tumor progression is critically dependent on their stroma.

The oral cavity - the incipient segment of the digestive tract can exhibit lesions marked in many general diseases due to the disorders present in these diseases.

Irritating oral mucosa by eliminating endogenous toxic products from saliva (urea, uric acid, creatinine, ammonia, ammonium carbonate) contribute to the formation of these lesions, too.

Saliva flow disorders (hyposalia, asialia, xerostomy etc.) and salivary pH changes are favorable conditions for increasing microbial virulence as well as the biological balance of the oral environment. These lead to increased oro-dental lesions as well as the occurrence of nearby or distant complications.

As precancerous states we can mention both inflammatory processes with dysplasias and some dezinembrioplastic tumors with varying degrees of malignant potential, with particular importance being given to preinvasive cancer. The first category includes actinic cheilitis, Paget and Bowen's disease, planar lichen and leucoplasias with their various etiopathogenic forms and, to a certain extent, epilepsy.

Actinic cheilitis is an inflammation of the lips due to the action of sun rays, the red lips being a photosensitizer; it

appears as a diffuse thickening of the injured region with bleeding cracks and painful ulcers. Microscopic: ortho- and hyperparakeratosis, basophilic degeneration of the papillary and lymphoplasmocytic infiltrate.

Long-term progression: it can malignize (epidermoid carcinoma, usually spinocellular).

Bowen disease is a precancerous dermatosis; develops on the skin and the mucous membranes

malpighiense; is an anaplastic dysplasia, considered by some authors to be *in situ* carcinoma; evolves to an epidermoid carcinoma.

Paget's disease of the lips: parakeratosis diskertatosis, segregation by desmolise, balloon degeneration of the epithelial cells and lymphoplasmocyt infiltration; it can become malign (spinocellular carcinoma). There are also some oral signs, namely: the sign of *galos*. If it is affected and the facial massif is particularly interested in the mandible, taking the look of *rubber shoe* with bone hypertrophy and dental alveolar widening, leading to spontaneous fall of teeth.

Another sign is the *too small hat sign* which consists in increasing the volume of the skull (too small a hat, *Le signe du chapeau*) in aesthetic disagreement with the facial massif.

Planched lichen, which is especially a dermatological condition, may also have an oral localization under the three main forms (non-erosive, bullous and ulcerated); malignancy is possible, turning into epidermoid carcinoma, which is not the case in dermatological locations.

Oral planal lichen appears most commonly on the inside of the cheeks, but can also affect the tongue, lips, gums.

* e-mail : dr.doriana.forna@gmail.com; cristibudacu@yahoo.com

Typical oral planar lichen appears in the form of white spots and dots that do not usually cause symptoms. Dentists often discover them during routine dental examinations. Strong oral forms of lichen can cause painful injuries and ulcers in the oral cavity. Diagnosis may require a biopsy to be confirmed.

Occasionally, the tissue taken should be studied by a special technique, and blood tests may also be required to exclude other diseases. There are cases of lichen plan as an allergic reaction to dental materials, but they are very rare. Allergenic tests may be required to identify allergy; in this case removal of the dental material is recommended.

Leukoplazia is an important condition of the oral mucosa through its frequency and possibility of malignancy; microscopic: hypertrophy of the epithelium as a whole, with an exaggeration of the sinuosities produced by the interpenetration of the papillae and the interpapillary buds, the surface covered by a thick layer of corn blades, with numerous keratohaline and eleidine granules; divided into four groups: the last group presents a disorganization of tissue architecture as well as carotid artery, as it is an intraepithelial carcinoma [1-3].

Oral leukoplasia means white or gray spots located in the oral cavity (on the tongue, under the tongue, or inside the cheeks). The word *leucoplasia* derives from the Greek word *leukoplakia*, which means *white spot* or *white form* (euko = white + plakos = stain). This condition can also be found under other names: leukocheatosis, idiopathic leucoplasia and idiopathic keratosis, or idiopathic white plaque. The disorder is manifested by covering with keratosis or adherent plaque of large areas of the oral cavity, respectively the mucous membrane of the mouth. For this reason, when leucoplasia occurs not only on teeth but also on other surfaces of the mouth, the correct name is oral leukoplasia.

Epulis: can be pseudotumor (peripheral granuloma), but myeloplax and papillomatous giant cell form represent true tumors of mesenchymal or epithelial origin, with the potential for sarcoma malignancy or epidermoid carcinoma (especially spinocellular), having an invasive character of the alveolar bone (osteoclast). Under the term epulide are described the proliferative, tumoral, slow-moving formations located on the gum. Masson considers the epulise as a hyperplastic tumor that develops on the verge of inflammation, due not to the cell itself but to the local extracellular irritation. Some general disorders may favor pseudotumoral proliferation, such as:

Dechaume blood discrasias, hypertrophic parathyroid gland (Abrikosov), neuro-vegetative instability, hormonal disorders (Trauner and Cooke), pregnancy, etc.

They are found at all ages, predominantly in young adults aged 20-40, are more common in women and especially during pregnancy, when tumors develop much more rapidly, suffering a post-natal stasis, which pleads for the role of endocrine factors in epileptic genesis [4-7].

It develops in both arches, predominantly in frontal teeth and premolars (Hesse, Partsch).

It is represented by six histological forms: - Simple granulomatous epulis in which there is the proliferation of connective tissue granulation and mild epithelial hyperplasia with rich vascularization;

Fibrous epulis-composed by fibroblast-fibrous connective tract, low-graft tissue and poor vascularization;

Osteogenic epulis - formed of various conjunctival hyperplastic elements with young fibroblasts impregnated with lime salts, leading to the formation of an osteoid and even bone, lamellar bones and osteoblast cells; Teleangiectatic epulis (angiogranuloma) in which multiple

dilated neoformation vessels predominate, with thin walls in the mass of fleshy buds, sometimes forming true blood vessels;

Mixomatous epulis is rarely encountered. In the mass of the granulation tissue there are gelatinous areas and star-like cells with extensions that are anastomosis between them; Giant cell epulis (epulis with myeloplaxis) is a tumor with a gingival onset, unlike the tumor with myeloplaxis, which starts in the depth of the bone and which only then turns out; the proliferative buds are formed from connective granulation tissue in which mass is located giant cells with central nuclei (such myeloplaxis): abnormal vasculature.

Epulis usually starts in the form of a proliferative gingivitis, located in the interdental papilla, around a dental rest or a cell after extraction; In the condition period, the tumor differs in clinical terms from its anatomopathological structure. The evolution of epulids is slow, progressive, without affecting the general condition. They can complicate by suprainfection or excretion, resorption and bone demineralization may favor pathological fractures.

Dizembrioplastic tumors include:

Hamartoma benign tumor or malignant hamartoblastoma arise as a consequence of defects in embryonic development, with the formation of epithelial and mesenchymal tissue combinations, with a rise in their own oral localization: thyroid follicles in the tongue, lymphoid follicular tissue in the extra-ganglion region.

Coristom: an embryonic tumor with a development of the cortises (embryonic fragments), observing the existence of tissues that normally do not exist in the oral cavity (sebaceous glands in the lamina of the oral mucosa - Fordyce-cartilage granules in the adult mandible body, or nebaby cells); questionable malignancy.

Branch cyst, usually with localization in the anterior part of the sterno cleidomastoidian muscle; the delineation of the cyst is made by squamous epithelial cells, having connective tissue and lymphoid follicular structures; may have leftovers of the pharyngeal bags, or result from a cystic degeneration of embryonic epithelial inclusions in the lymph nodes; malignancy possible on the epithelial line.

Papillary chistadenolymphoma: a particular tumor of the salivary glands; usually benign; histopathy is confusing (after Harris would be heterotypic salivary glands included in *lymphatic islands* Microscopic is an association of epithelial tissue with acins and cystic dilations with papillary proliferation with lymphoid tissue with follicular structures may be malpighian metaplasia areas Malignancy is possible on both lines.

Pleomorphic adenoma: main salivary gland tumor and accessory (80% in parotid). Slow growth as well defined single or multiple nodules. The histological map is complex, polymorphous and specific to this tumor; a tubular structure characterized by a uniform distribution of cubic cells with vacuoles and prominent nuclei (such as normal gland myoepithelial cells) or similar to ductal cells (eosinophilic granulocyte eosinophilic cells) or mucoid resembling stromal fibroenomas (cilindromatos), mixoid, condroid osteoid, the glandular epithelium level can be noticed and areas of epidermoid metaplasia, also.

Recurrent potential and malignant degeneration on the epithelial line with atypical anaplasia and mitosis (adenocarcinoma, rarer epidermoid carcinoma with ortho- and parakeratosis pearls). The lymph node metastases are common; remote metastases may appear in the lungs, bones, and so on.

Oncocytoma: Salivary gland tumor (parotid) characteristic of older age is benign and rare, may be pluricentric, but this does not indicate any malignancy.

Microscopic: large and clear cells (Hamperl), distinguished by enzinoophil adenoma.

The inflammation of the oncoytes is not clear (they are found in both the acini and the canal). Cell proliferation is slow.

Follicular cyst: a benign tumor of the jaw, with a series of theories on pathogenesis (Broca's follicular theory, representing a teratological development disorder, Malassez's gubernacular theory, tooth invasion included in a temporary teeth cyst, Bloch, Jürghensen) : there was no unity of points of view.

Generally, the Broca-Magiot hypothesis is accepted, after which the cyst originates from the degeneration of the adamantin follicle of the remaining tooth. This category includes the anterior and posterior marginal cysts that develop in relation to the inferior incisor teeth included.

Microscopically: a cystic membrane composed of a malpighian epithelial layer, bounded by a variable density connective tissue. Carcinomatous malignancy is exceptional and occurs after relapses[8-10].

It develops in relation to the remaining teeth embedded in the jaw thickness, more often in connection with the inclusion of the superior canines.

Ameloblastoma represents a jaw heterotopia (Broca, 1868); the term adamantinoma was introduced by Malassez (1885); approximately 1% oral tumors (80%) in the mandible. Grows slowly, with minor symptoms, or even asymptomatic, can be discovered at a routine dental exam; but sometimes leads to deformation of the bone, the radiological examination showing a lysis of the bone, mono- or polychistic tissue.

Microscopic may have follicular aspects with cystic dilatations or compact forms in the form of epithelial cell tracts in a more or less dense stroma; there are mixed forms.

The histological pathogen is pathognomonic due to the existence of small cells and tachycromatic cells and clear large cells, arranged palisadically. Serious malignancies occur to an epidermoid carcinoma[11,12].

As malignant tumors we mention in the order of the frequency of the cancer of the lip (especially at the lower lip); is usually spinocellular epidermoid carcinoma; metastasis is submandibular lymphangiopathy; may be bilateral, due to the crossing of the lymphatic lymphatic channels, the cancer of the tongue, also on the epithelial line with very serious evolution, the malignant melanoma of the lips, the parotid adenocarcinoma in its schiogenic form, the facial nerve invasion and consecutive paralysis and lymph ganglionic metastases (gougerot) and metastasis on its sanguine (pulmonus etc.) or the periosteal osteofibrosarcoma and the association with the cartilage by making the chondrosarcoma, under the different types of osteoarthritis, the osteosarcoma of the jaws, usually the osteolytic form, with the invasion of the periosteum, its hyaline or fibrous forms, and a vascularisation that represents, besides cellular affections, a feature of the malignancy of the tumor process[13-15].

The Ewing tumor, which occurs rarely in the jaws, especially in the young people, with predominant mandibular localization. Microscopically, the tumor consists of small, round, uniform tumor cell plates with a low cytoplasm containing PAS-positive glycoprotein. The cells have a round nucleus with obvious nucleolus, and cellular boundaries are indistinct.

The tumor exhibits areas of necrosis and haemorrhage. Rare muscular tumors (tongue, masseter): myoblastoma (Abrikosov) with possibility of malignancy.

Apart from lymphatic and haematogenic metastasis, we should mention the direct (mechanical) pathway in the gastrointestinal and respiratory tract; of the gastrointestinal tract to reach the liver through the portal vein.

In connection with the rich network of lymphatic lymph nodes, limfoganglion tumors, such as Hodgkin's and non-Hodgkin's malignant lymphomas, with frequent localizations; and include adenopathies in leukemias when even early gingival localizations of leukosis infiltrates are found, sometimes in the masseter muscle, clinically occurring a tumoral aspect in that region.

We recall malignant hemangiopericytoma with local invasion and metastasis proper on the line of the vessels concerned; the same for the hemangiosarcoma, with extremely serious evolution, interested in soft or hard parts. The complications that occur for any of these tumors are very numerous, depending on their shape and location, with eating difficulties, phonation. Metastasis that may occur in the oral region, with primary neoplasms (in the mandible, or soft parts), will also be reported. On the mandible, these metastatic nodules can become necrosis, making chists with spontaneous fractures.

Experimental part

Material and method

In the present paper, we studied 120 patients with oral tumors, which originated in undifferentiated or differentiated multiple tissues, who had histological examination at the University Emergency Hospital, oro-maxilo-facial department, Iasi.

Of the 120 patients, 79 were men (65.83%) and 41 women (34.16%). All the patients examined in the study presented an observation sheet that we used in the present paper. The methodology of examining patients with oral tumors originating in undifferentiated or differentiated multiple tissues is of great importance and is necessary to establish the diagnosis of disease and its stage of development in order to develop an effective treatment and follow-up strategy in time of the results. The algorithm of evaluating a patient with oral tumors originating in multiple undifferentiated or differentiated tissues involved several steps: anamnesis, clinical examination of the cervical region, complementary examinations, radiological examinations, imaging investigations.

For the determination of the diagnosis of certainty, we used the ganglionic record accompanied by the histopathological examination of the extirpated ganglia as the latter guided the undertaking of the surgical, radiotherapy, chemotherapeutic treatment.

Results and discussions

The diagnosis of oral tumors originating in undifferentiated or differentiated multiple tissues is regarded by most patients as a *fatality*, being historically associated with the death verdict, a verdict that is difficult to admit and accept, which produces strong emotional reactions. In general, malignant neoplastic processes with the location in the oral cavity adversely affect the quality of life of the patient in the new conditions due to the mutilating effect of sequelae that occur frequently postoperatively.

Patients with oral tumors originating in undifferentiated or differentiated multiple tissues most often benefit from a favorable prognosis if the tumors are differentiated and have a previous location. For histologically undifferentiated

tumors with posterior localization the prognosis is reserved, unfavorable[16-18,].

To make reasonable estimates of a tumor in terms of prognosis and treatment, it is necessary to consider both the location of the lesion and the degree of histological differentiation of the tumor, in addition to the conventional TNM criteria. Among the five criteria considered, the most important in establishing the prognosis are the absence / presence of lymph nodes (N) and distant metastases (M). For these patients, other malignancy-related diseases as well as the development of secondary neoplastic processes are major risk factors that can influence both the survival of the patient and the possible relapse of the primary neoplastic process[19-22].

Conclusions

The location of the tumor must be accurately recorded; the size of the tumor and its depth (depending on the superficial fascia) should be noted, as these data have prognostic value along with the degree of malignancy. Survival prognosis depends on several factors, including the presence of untreated necrosis and hemorrhage and the heterogeneity of treatment-emergent changes. Multidisciplinary assessment, including the anatomical pathologist and radiologist, is recommended. The anatomopathological diagnosis is based on the morphological and immunohistochemical aspect. Patients in the early stages of the disease generally have no symptoms; the first symptoms occur when tumor growth results in inflammation and pain.

References

- 1.EID A, LI S, GARZA R, WONG ME. Chemotherapy for oral and maxillofacial tumors: an update. *Oral Maxillofac Surg Clin North Am.* 2014 May;26(2):163-9.
- 2.KLEIN NULENT TJW, NOORLAG R, VAN CANN EM, PAMEIJER FA, WILLEMS SM, YESURATNAM A, ROSENBERG AJWP, DE BREE R, VAN ES RJJ. Intraoral ultrasonography to measure tumor thickness of oral cancer: A systematic review and meta-analysis. *Oral Oncol.* 2018 Feb;77:29-36.
- 3.MANOR E, TETRO S, BRENNAN PA, BODNER L. Cytogenetic findings in benign and malignant oral tumors - the role of autologous human plasma. *Br J Oral Maxillofac Surg.* 2012 Oct;50(7):606-10.
- 4.ETTINGER KS, YETZER JG. Controversies in Oral and Maxillofacial Oncology. *Oral Maxillofac Surg Clin North Am.* 2017 Nov;29(4):487-501.
- 5.BEIL CM, KEBERLE M. Oral and oropharyngeal tumors. *Eur J Radiol.* 2008 Jun;66(3):448-59.
- 6.TURI K, BARABAS P, CSURGAY K, LEHNER GY, LORINCZ A, NEMETH ZS. An analysis of the epidemiological and etiological factors of oral tumors of young adults in a Central-Eastern European population. *Pathol Oncol Res.* 2013 Jul;19(3):353-63.

- 7.MACOVEI L.A., BIRSAN, M., TEODOR, V.I., CRISTOFOR, A.C., IOANID, N., REZUS, E. On the role of chemical and molecular biology in inflammation research. *Rev.Chim.(Bucharest)*, **68**,no.4, 2017,p. 786-788
- 8.TUFFAHA M.S.A., GUSKI H., KRISTIANSEN G. (2018) Markers and Immunoprofile of Tumors of the Oral Cavity and Salivary Gland Tumors. In: *Immunohistochemistry in Tumor Diagnostics*. Springer, Cham. pp. 43-47.
- 9.RIVERA C. Essentials of oral cancer. *Int J Clin Exp Pathol.* 2015 Sep1;8(9):11884-94.
- 10.KESHAVERZIM, DARIJANIM, MOMENI F, MORADI P, EBRAHIMNEJAD H, MASOUDIFAR A, MIRZAEI H. Molecular Imaging and Oral Cancer Diagnosis and Therapy. *J Cell Biochem.* 2017 Oct;118(10):3055-3060.
- 11.MCGURK M, SCOTT SE. The reality of identifying early oral cancer in the general dental practice. *Br Dent J.* 2010 Apr 24;208(8):347-51.
- 12.HODGSON TA, BUCHANAN JA, GARG A, ILYAS SE, Porter SR. An audit of the UK national cancer referral guidelines for suspected oral mucosal malignancy. *Br Dent J.* 2006 Nov 25;201(10):643-7.
- 13.ANCUTA, C., ANCUTA, E., CHIRIEAC, R., ANTOHE, M., IORDACHE, C., Anti-Tumor Necrosis Factor Alpha Therapy and Periodontal Inflammation in Rheumatoid Arthritis A clinical and biochemical approach, *Rev.Chim.(Bucharest)*, **68**,no.2, 2017,p. 369-372
- 14.GURAU G., DINU C.A., EARAR, K., et al, Diagnostic Value of chemical and hematological markers in children acute abdominal pain, *revista de chimie*, 67(3), 2016 ,p:507-511
- 15.STOIAN, A., EARAR, K., BUDACU, C. et al., No association between antioxidant enzyme gene polymorphism and Albuminuria in Type 2 Diabetes Mellitus Cases, *Rev.Chim.(Bucharest)*, **67**,no.11, 2016,p. 2016
- 16.BARBINTA, C.A., EARAR, K., CRIMU, C.I., In vitro evaluation of the cytotoxicity of some new titanium alloys, *Bioceramics*, Vol25, Book series: Key Engineering Materials, Vol 587, 2014, 303
- 17.EARAR, K., CERGHIZAN, D., SANDU, A.V., MATEI, M.N., LEATA, R., SANDU, I.G., BEJINARIU, C., COMAN, M., The Role of Functional Polymers in the Optimization of the Acrylic Biomaterials Used in Removable Prosthetic Restoration - II. Assessment of traction test and antifungal activity. *Mat.Plast.*, **52**, no.4, 2015,p.487-493
- 18.CALIN, A.M., DEBITA, M., DRAGOMIR, R., et al. Treatment methods conditioned by the gravity of drug-induced gingival hyperplasias, *Rev.Chim.(Bucharest)*, **68**, no.11, 2017,p.2618-2622
- 19.GRADINARU I., ANTOHE, M.E., IOANID, N., Contemporary therapeutic decisions in the treatment of various types of edentation, *Romanian Journal of Oral Rehabilitation*, 8(2), 2016, p:44
- 20.IONESCU, C.A., VLADAREANU, S., PLES, L., Synchronous bilateral primary ovarian carcinoma-case presentation, *Romanian Journal of Morphology and embryology*, 58(1), 2017, pg.219-223
- 21.GRIGORE, A.M., BUSILA, C., CHESARU, I.B., et al., Biological features of tumors results of experimental studies, *Rev.Chim.(Bucharest)*, **68**, no.3, 2017,p. 594-598
- 22.BALAN, G., GRIGORE, A.C., BUDACU, C.C. et al, Antisepsis, disinfection sterilization-methods used in dentistry, *Rev.Chim.(Bucharest)*, **68**, no.1, 2017, pg.186-191.

Manuscript received: 21.01.2018