The Role of Chemical Factors in Oro-Maxi-Facial Surgery

The effiency of surgical act in lower lip cancer

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Oro-facial soft parts may be the site of benign or malignant tumors, which, although presenting histological similarities, aspects and clinical development vary depending on the affected region. An upper lip lesion that does not heal in a few days could be a big health problem. Also, the presence of chronic inflammation, thickening, or whitish appearance in the lip are all alarm signals. Lip cancer is manifested by the presence of the upper or lower lip tumor, which may be solitary or multiple, ulcers that do not heal for more than three weeks, haemorrhages in the tumor. Sometimes it is considered as being a trenant/delayed herpes, the spinocellular carcinoma of the lip is the most common form of localized cancer in the head and neck level. The lip cancer occurs predominantly in men between 50 and 70 years of age but cases have been identified in young patients aged 20-30 years, too. The study includes 95 patients with lower lip cancer studied in 2016-2017. A good collaboration between ablative surgeon and restorer surgeon gives the patient the best opportunity for complete resection and restoration of the shape and function of the involved structures; the ablative surgeon can remove the tumor without compromising the excision due to a specific reconstruction plan. Reconstruction possibilities from the lower lip were adapted to each patient, depending on the size of the tumor and the properties of the facial tissues.

Key words: maxillofacial area, lip cancer, tumor, lower lip.

The cancer of the maxillofacial region (Ackerman and the Regate) is located at 85-98% at the lower lip (Cernea). It almost exclusively evolves in men, the proportion of men and women being 1 to 14 (Bernier, Clark)[1,2].

Cancers located at the upper lip usually have a faster progression and a reserved prognosis.

Lip cancer usually occurs after the age of 45, but the appearance at earlier ages is exceptional.

Cancer disease is the expression of changes in cellular genetics and involves two aspects: the fundamental alteration of cell metabolic processes and the action of a carcinogenic factor in the body. It presents two main steps: the stage of primitive cancer (the period from first contact with carcinogenic factors to the appearance of the first cancer cells); the stage of secondary cancer (ranging from the appearance of the first malignant cells to malignant transformation). Prior to the onset of the secondary stage of cancer, epithelial neoplasia is a true reversible intermediate stage, particularly important for cancer prophylaxis[3-5].

There are incriminated in the etiology of lip cancer: mechanical, chemical, prolonged thermal irritation, smoking, alcohol. Among the diseases predisposing to the occurrence of lip cancer are leucoplasia, chronic glandula cheilitis and Plummer-Vinson syndrome. It seems that long exposure to the sun as well as lack of oral hygiene would favor the appearance of lip cancer[6-8].

The carcinogenic effect of ionizing radiation is well known and documented; skin cancer being among the first cancers induced by X-rays.

As chemical agents, various chemicals (aromatic hydrocarbons, asphalt, paraffin waxes), alcohol, and non-specific microbial agents, specific microbial agents, genetic factors, aging as biological factors are taken into consideration.

Tabagism is the main risk factor in the genesis of lip cancer; in cigarette smoke next to nicotine, carbon monoxide, nitrosamines, polycyclic aromatic hydrocarbons whose carcinogenic effect has been demonstrated experimentally have been identified. The carcinogenic risk of smoking is directly proportional to the number of cigarettes smoked[9-11].

Tobacco and concentrated alcohol correlate with a high percentage of oral cancer. In general, big drinkers are also big smokers that leads to a difficult separation of the contribution of one or both the two components.

These risk factors interact at the chromosome level, producing alterations of the suppressor p53 gene. Tobacco is a source of mutagenic agent and it causes damage to cellular DNA, and alcohol reduces the effectiveness of DNA repair mechanisms. Not all individuals who smoke and consume distilled alcoholic drinks make lip cancer because there is an intrinsic susceptibility factor in people who make tumors[12-14].

Viral agents may contribute to the etiopathogeny of lip cancer, taking into account the oncogenic properties of different strains of the virus human papilloma and herpes simplex viruses. These viruses are ubiquitous and frequently transmitted through the mouth through oral, cutaneous, oral and genital and oral-anal contact, and cause

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lesions with warts, condylomas that are associated with a high degree of cancer, diskeratoses causing changes in the epithelium until apparent dysplasia. At young age, oral squamous cell (spinocellular) cancer occurs more frequently in HIV-infected homosexual men[15-17]

Environmental factors explain the presence of lip cancer in some geographical areas, the climate, the profession, or some food deficiencies. By external environment one may understand external factors: atmospheric conditions, climate, light, sound, electrical phenomena, pathogens of infections, food character. The influence of these factors on man is reflected by the social environment. The social conditions in which man lives and work determines the action of other factors[18-20].

Therefore, a fair conception of the causes and mechanisms of occurrence of different diseases in man can only be made taking into account the importance of social existence of man. Meteorological factors can explain the increased frequency of lip cancer in regions with high temperature variations and strong winds, areas where the cheilitis are frequently encountered, which led Rains and Capper to introduce the notion of *the countryman's lip*. The vitamin A profile is in many cases a factor favoring the occurrence of carcinomas, and its derivatives can stimulate the immune system to become more active against carcinogenic factors. They can be criticized as risk factors and anti-tumor-surgical, radiotherapeutic, chemotherapeutic treatments that themselves contribute to the development of cancer by diminishing the patient's natural immunity and thus increasing the chances of multiplying malignant cells residual or of tumor metastases[21-23].

Chemicals causing various diseases are in general a subject of study in pharmacology and toxicology. Chemical substances can exert different actions and often cause disease.

The evolution of pathological processes due to the action of chemicals depends on their dose, their solubility in biological humor by their way of administration, and the resistance of the body. One and the same chemical exerts, depending on the dose, a curative action, a toxic effect and even a deadly intoxication.

Toxic substances include toxins of inorganic and organic origin. Of the chemical factors to consider various chemicals (aromatic hydrocarbons, asphalt, paraffin waxes), alcohol, can contribute to the etiopathogenesis of lip cancer[24,25].

The result of the action of a toxin depends not only on its properties but also on the condition in which the body is located. The throttling of the liver's antitoxic function decreases the body's resistance to the action of poisonous substances. The solubility of toxins and chemicals, the mode of administration is of considerable importance[26,27].

The mechanism of action of chemical agents determines the degree of intoxication caused by them; it is not irrelevant whether the substance acts when it enters, maintains or removes it from the body. One role in elucidating the origin of the tumor has been the discovery of a series of new facts about agents that are capable of causing tumor growth, including carcinogenic substances well known from of chemical sight. Based on this theory, the modern (chemical) carcinogenic theory of tumor origin has emerged[28,29].

According to this theory, the transformation of normal cells into blastoma cells is caused by carcinogenic substances that enter the body outside or formed in the body due to changes in metabolism.

The number of carcinogens capable to cause increased tumor growth at present is larger. These substances include whole groups of organic compounds, and some relationships between the chemical composition and the carcinogenic action are found.

The mechanism of action of these substances would be able to disrupt the synthesis of proteins in the body, which leads to the appearance of malignant tumors are so-called cancerous proteins. A particularly important role in the mechanism of tumor appearance is the state of the whole organism, the disturbance of complex regulatory mechanisms and primarily the function of the nervous system, which establishes the unity of the organism with external environment.

Industrial chemical processes are recognized or suspected as having an etiological role in developing cancers. The occupational factor would account for about 2-4% of all cancer deaths. These factors have been identified due to the close association between some cancers and exposure to occupational factors or industrial poisons.

A risk factor is defined as *a well-defined event or a feature that has been associated with increased rates of onset of a subsequent disease* thus, the term is limited to patients who do not have a disease. Chemicals (aromatic hydrocarbons) are incriminated in the etiology of lipid cancer[30].

The frequency of cancer is increasing, and in this general context, oro-facial cancer is no exception. Disease has a serious impact on patients and sufferers, either through the infirmity created by the disease or its treatment, and by the often mutilation of sequelae.

It is caused by the morphological type, different from previous precancerous tumors and diseases.

The most common changes prior to malignant neoplastic process are cheilitis, benign tumors, traumatic or post-combustive ulcers, keratopathies, and post-traumatic scars.

Other premalignant lesions that can be mentioned are chemical cheilitis, cheilitis post-radiotherapy, post-traumatic ulcerations, scars especially post-postural and tuberculous lupus.

The ebb can be interstitial (nodular), but most frequently superficially. as a blunky, thickened area, which is either a verticus appearance or the appearance of ulcerative hoarseness, which covers hemorrhagic crusts without a tendency to healing.

An element that helps diagnosis is the paramedic location of the tumor. In the static period, malignant tumors at this level may have a ulcero-destructive or ulcero-vegetative form (in relief).

In the elderly, some forms may develop slowly and may significantly expand with interest in neighboring structures.

The surrounding tissues react by lymphatic-histiocytar mobilization. The reaction of the stroma together with the tumor infiltration forms a unique mass of firm consistency; prognosis is more severe.

In the multiple localized form, the lip lesion also coexists with facial injuries. It can also encounter double-localized cancer located in opposition, the so-called *opposition* cancer.

The remote bone metastases are very rare, but the neighboring bone interests are particularly encountered when the lip is overcome by the tumor process or when the process develops on the mucous membrane of the lip[31].

The bone damage is: the path of the mandibular canal and the vascular-nerve elements it contains, the indirect

pathway, represented by the secondary adenopathy fixed to the mandible and comprising successively the periostum and the bone in the neighborhood; the mixed pathway on two or all of the pathways mentioned.

The evolution is slow however, adenopathy (inflammation and ganglionary involvement) occurs locally, proximal bone disease or metastasis (in advanced stages).

The general stage of the patient is affected late in the advanced stages of the disease. The malignant tumors of the lip extend to the genian soft parts, the buccal vestibule, or the bone marrow arch. The lymph node metastasis appears late. Within 1-2 years, the vast majority of patients have cervical metastases.

The perineural invasion of malignant cells has been recognized as a distinct entity for tumor progression for many years. It has been shown that this occurs via the virtual spaces that connect the peripheral nervous system and the subarachnoid space of the central nervous system.

The growth and progression of the tumor along the nerve fibers can be both centriped and centrifuged from the site of the cancer invasion.

The tumor may be present in the small peripheral nerves surrounding the tumor or it may extend into larger branches of the nervous trunk. The pathophysiological invasion is explained by the ultrastructure of the perineural lining consisting of several concentrically arranged cell layers lacking a thick basal membrane with a very thin outer laminar both resembling the basal membrane of epithelial tissue.

The occurrence of recurrences depends on the time course of the primary tumor, the expansion of the tumor, the quality of the therapeutic act, the histological type of the tumor. After the appearance of the first objective clinical or subjective signs, the early diagnosis can be established because the detection of genetic abnormalities suggesting the malignant tumor does not indicate where the tumor will appear.

During the clinical examination, long-term lesions advocate for a benign pathological process, whereas those with rapid evolution suggest malignancy, but there are also patients who complain about recent symptoms, extensive clinical lesions not extended by the patients.

The clinical examination includes careful inspection and palpation of all areas in the oral cavity and areas of the oropharynx. Palpation follows, by controlling all areas of oral casualty. From an anatomo-pathologic point of view, it is located initially on the red part of the lip or at the limit of the cutaneous mucosa, halfway between the median line and the oral commissoma, and later it can expand, invading the soft labiomentogenic parts, the lower vestibule and the mandible. The lymph node metastases appear quite early, being localized submandibular and submandibular bilaterally, due to the lymphatic vessels crossing.

As a 90% histological figure (Valerian Popescu) spinocellular epithelioma is encountered, otherwise epitheliomas are found undifferentiated cellular or glandular. Spinocellular carcinoma acantolytic (pseudoglandular) usually arises in acantolytic keratosis lesions. Acantholy is the loss of normal intercellular contact. The cells are separated from each other giving the pseudoglandular appearance. The cytoplasm is pink and opaque, the intercellular bridges are prominent and the appearance of epidermal origin usually leads to a precise diagnosis.

The anatomopathological result can confirm or refute the clinical presumption. If this does not correspond to the clinical data, in collaboration with the morphopathologist, it is decided to repeat the harvesting and examining a new preparation. The well differentiated spinocellular carcinoma exhibits prominent desmosomes and tonofibres. They are in a small amount in poorly differentiated spinocellular carcinomas.

In immunohistochemical analysis, squamocellular carcinoma contains low and high weight cytokeratin molecules.

Keratinocytic differentiation markers, including involucrin and filagrin, are present in well-differentiated tumors and are much less common in poorly differentiated tumors. Among malignant oro-maxillo-facial tumors, malignant tumors of the lip (25-30%), being localized predominantly in the inferior lip. In the malignant pathology of the lower lip, the loco-regional lymph nodes are affected relatively early, adenopathy being reported at the first consultation in 10-15% of the cases, with frequent involvement of sub-submandibular and latero-cervical nodal ganglia. The differential diagnosis is usually done with keratoacanthoma, botryomychomoma, adenocarcinoma, angiosarcoma or malignant melanoma.

Staging systems are all clinical and are based on a best estimation of the extent of the disease before the treatment.

The tumor should be histologically confirmed included and all pathological data obtained from the biopsy. The normal lymphatic drainage will also be carefully examined by palpation. The information provided by the imaging diagnosis can be used in staging (orthopantomography). Magnetic resonance offers several advantages over computer tomography in terms of detection and the localization of the tumor and in distinguishing lymph nodes from the blood vessels. Preoperative radiotherapy has the greatest advantages contributing to tumor resorption, inhibits its bioactivity, blocks lymph flow and contributes to the creation of ablation conditions for surgery.

The principles of treatment are: chemotherapy, immunotherapy, surgery and radiotherapy. The radical cancer of the lips, has the advantage of radiotherapy that it avoids the formation of ulcerations and, furthermore, we can ensure by histological examination the quality of the excision.

A combined treatment is accepted by many people, the order of different used methods are also widely discussed. There are three situations: radiotherapy applied preoperatively, radiotherapy applied postoperatively, radiotherapy preceding and following the medical act. Surgery removes all or a large part of the tumor, radiotherapy complements the exertion; using for healthy tissue coverage, surgery avoids suppurations and so a large source of radio resistivity is eliminated.

The factors to be taken into account in the restorative treatment are: the field, the extension of the excetion, the efficiency of the surgical act, the anatomical elements upon which it intervenes; the opportunity to make the plaster, the quality of tissues necessary to escape of restoration.

In front of different groups of patients, surgical treatment generally comprises three important stages: surgical treatment of primary lesion; of lymph nodes; and of associated or secondary bone lesions.

In the choice of treatment, the magnitude of the lesion is a decisive factor, the location and histological differentiation being of secondary importance. As the lesion size increases, the amount of radiation and surgical treatment decreases, but the value of the first decreases suddenly. The difference between the results of radiation and surgical treatment is more evident in the middle lesions, being much lower in the case of small and large lesions.

Experimental part

The study includes 95 patients with lower lip cancer studied in 2016-2017. Of these, 22 cases (23.15%) are women, and 73 cases (76.85%) are males. Of these, 74 cases (77.89%) were from the rural area, the remaining 21 cases (22.10%) being urban.

Regardless of its location, cancer is a serious condition requiring a diagnosis as early as possible, treatment that can make a difference between a prolongation of life or healing. It should also be forgotten that malignant tumors as frequency occupy the second place after heart disease and the fact that it is the most common cause of death in developping countries.

Results and discussions

Malignant tumors are a class of diseases characterized by an uncontrolled cell division and invasion of neighboring tissues as well as the ability to metastasize regionally or remotely.

The problem of lip cancer is dominant on the one hand by its increasing frequency, and on the other hand, the need for early diagnosis and effective therapy. It appears on the backdrop of long-lasting pathological processes that have been systematized and described as precancerous states, or simply precancer. This disease has been the focus of specialist oncology in recent years, with the disease continuing to increase morbidity (fig.1).

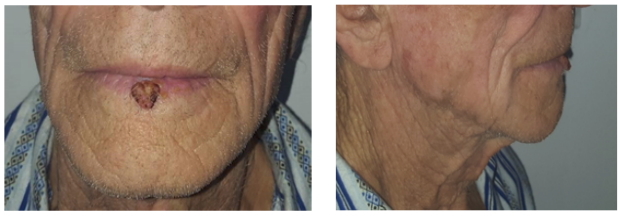

Fig.1 Aspects of clinical case

Of the 95 cases, 69 cases (72.63%) were smokers and 26 cases (27.36%) were non-smokers. The age of the patients was between 35 and 79 years.

Taking into account the tumor size: (T1 = 13 patients (13.68%); T2 = 48 patients (50.52%) T3 = 25 patients (26.31%) and the rest in T4 = 9 patients (9.47%), and ganglion status, surgical treatment consisted in: extirpation of the tumor with defect plaster in 69 cases (72.63%), extirpation of the tumor followed by defect plaster and lymph node recording in 17 cases 17.89%), extirpation of the formation (6.31%), and in 3 other cases (3.15%), tumor biopsy was performed because the patients were inoperable either due to the size of the tumor or due to the poor general condition which did not allow surgery.

The lymph node of patients with inferior lip carcinomas showed concomitant adenopathy with the tumor, adenopathy occurred after primary tumor extirpation, and without metastatic adenopathy.

The surgical treatment included tumor biopsy, tumor extirpation followed by lymph node, tumor extirpation + lymph node, reconstructive plastid of postoperative defect with restoration of the physiognomy and lip function, conduction to cervical lymph nodules.

In 15 patients (15.78%), anatomopatologically the lymph node metastases were exhibited, recommended to perform radiotherapy but only 9 cases (9.47%).

Surgical treatment was associated with chemotherapy and radiotherapy. In the multimodal treatment, the surgical step often raises problems in the area of postoperative defects, given that some patients present themselves in the advanced stage of the disease (T3, T4), most often with detectable clinic adenopathies.

Whenever possible, the site of the postoperative defect is immediately performed; performing it in the second stage involves a number of consequences, which consist of incontinence of the oral cavity with eating difficulties, phonetic dysfunctions and marked impairment of the physiognomy, which implies a poor social reintegration marked by important psychiatric disorders with a decrease in the quality of life .

The reconstruction of the lip will take into account its normal parameters, namely: intercommissional distance, maximum opening of the mouth (measured at the soft part), depth of the vestibular trench, lip sensitivity and tonicity of the perioral muscles.

The reconstruction of the defect will follow the restoration oral dental arcade, obtaining an acceptable physiognomy and phonation, and a functional opening of the oral cavity. In the case of a malignant tumor at the stage of the onset of red lips, vermillonectomy is used, followed by translation mucous membrane to the outside, to cover the defect, liposuction will occur at the lip level, thus the distance between two distinctly perceived sensitivity points will be 6-12 mm versus 3-8 mm.

To minimize sensitivity, it is necessary to carefully delineate the mucosal flap in a plan located between the submucosa and the orbicular muscle of the lips, gradually reducing the depth of the dissection as the flap is laterally mobilized.

The disadvantage of this technique is the fact that in these cases thin lips are produced. Depending on the method used, the extent of the tumor and the certainty or the uncertainty of complete exhaustion as well as the psychosocial consequences of the operative act, the restorative intervention has indications of immediate achievement, secondary or delayed.

The different processes are derived from the three general methods of autoplasty: the Italian flap translation method, the French flap sliding method, the Indian method of torsion of the flaps.Although a multitude of methods of reconstruction postoperative defects were be proposed for the lower lip, often it is used a number of successfully applied techniques in today's tumors.

In the lip tumors with bone invasion, mantlegenic soft parts and the buccal floor it is possible to carry out extensive resection of the whole tumor block (labiogenomandibular resections) with subsequent plaster, resulting in a rust surviving over 10 years.

In order to increase survival, an aggressive attitude is achieved through a tumor extirpation within wide limits of oncological safety. If the patient presents lymph node metastases or if they occur after removal of the primary tumor, it is necessary to perform some radical cervical lymph nodes associated with radiotherapy or chemotherapeutic complementary treatments.Having in mind the relatively low rate of lymph node metastasis, no prophylactic lymph node prophylaxis is required in all patients with inferior lip carcinoma, but only to those whom an effective dispensarization is possible.

As the rate of lymph node metastasis is maximal in the first year, it is very important that the follow-up of the patient be performed monthly, so that from the second postoperative year the dispensarization frequency will gradually decrease. After the removal of the tumor, the functions and the aesthetics must be preserved. The functions are oral consistency, lower lip mobility for participation in phonation as well as facial expression, maintaining adequate access to the oral cavity.

Oral consistency is critical for food intake and their mixture with saliva in the oral cavity. Lips are essential for the formation of sounds, especially letters B, F, M, P and V (Salasche). The microstromy that can result from some reconstructive processes can influence the phonance of these consonants and should therefore be avoided whenever possible. Keeping sensitivity in the lower lip has a social and functional role because their absence leads to the frequent occurrence of traumatic lesions.

Modern reconstructive surgery techniques, however, allow the placement of defects that can not be restored by using classical techniques so that the existence of tumor formations can be treated even if they are of a very large size or are extended to the mandible bone.

Conclusions

The risk of developing cancer of the lip is increased by smoking, chronic exposure to sun radiation, poor oral hygiene, chronic oral infections, chronic local trauma.

The appearance of spinocellular carcinoma may be preceded by precancerous lesions, and the tumor may develop as a nodule, harder area, or lip erosion.

The spinocellular lip carcinoma has a more aggressive evolution than forms with other localizations, generating faster metastases, therefore, in the case of suspected lip lesions, it is necessary to perform a dermatological consultation.

Surgical treatment should be adapted to the size of the tumor formation; there are several surgical techniques in this regard, and they are addressed to both primary tumor and eventual lymph node metastases .

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