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Conservative treatment in head and neck cancer

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The incidence of head and neck cancer in Slovenia is increasing, especially in male population. Late diagnosis, in advanced stages of disease, influences not only the treatment results but also the treatment strategies and modalities: aggressive surgery combined with radiotherapy and reconstructive procedures and chemotherapy in inoperable tumors is therefore indicated too frequently instead of organ sparing treatment. Early detection should be improved, especially in the target population, and all up-to-date diagnostic technology should be employed in centralized multidisciplinary pre-treatment assessment. Good co-operation between surgeons, radio and chemotherapists in planning, performing as well as in evaluating the treatment is also a basic condition for better implementation of organ sparing approaches in head and neck cancer.

Key words: head and neck neoplasms; combined modality therapy

Epidemiological data as introduction

According to data from the Cancer Registry of Slovenia, the incidence of cancer of the mouth, oropharynx, hypopharynx, and throat (besides colon) was increasing most steeply among all types of male cancer during the period 1978-1987.[1] In the year 1991 head and neck cancer (including lip and regional skin carcinoma) comprised 19% of all cancer localizations in male and 9% in female population.[2] The incidence and its increasing rate are among the highest in Europe in the male population, comparing the data from 22 European states.[2]

The result of five-year survival rate for the patients with the oral, oropharyngeal and hypopharyngeal cancer has not improved; for patients from the period 1973-1976 it was 13% and for those diagnosed in 1981-1984 period it was 14%. The proportion of localized stage even decreased in the last mentioned period (20% in the period 1973-1976, 14% in the years 1981-1984).[1]

Incidence of laryngeal carcinoma is increasing more moderately as it was established for previously mentioned localizations. The extent of disease at the time of diagnosis was more favorable in the last time period (about 50% of localized stages). The relative one- and three- year survival rates increased in the last periods while the five-year rates dropped in the last observed period after previous significant increase.[3]

In Slovenia, 102 patients with malignant tumors of the nasal cavity and paranasal sinuses were treated from 1985 to 1993. Overall projected survival rate at 9 years was 29% (44% in patients treated with surgery and 12% in non-surgical group). Among 46 patients with carcinoma of the maxillary sinus 30 were in T4 stage at the time of diagnosis and 19 of 20 patients with carcinoma of ethmoid.[4]

In the context of these epidemiological data, comparable to those reported from other countries, the problems of early diagnosis and the place and role of organ sparing treatment (and its modalities) of cancer in head and neck region should be discussed.

Problems of early detection and staging

Early diagnosis is only possible if the patient seeks advice immediately on noticing symptoms. According to our data[5] and to other reports[6] the delay in diagnosis is still often very long also in patients

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with evident symptoms as in vocal cord carcinoma, where the late diagnosis results in one of the most mutilating surgical procedures - laryngectomy. The factors, defining the population at risk for oral cavity, pharyngeal and laryngeal cancer are well known: male sex, increasing incidence with age, alcohol consumption and cigarette smoking, either alone or even more in combination. Consequently, the ideal target group is well defined but the screening in this population is connected with several difficulties:

- the target population consists of subjects who are not health conscious and do not seek preventive care;
- acceptance of primary preventive behavior such as smoking cessation is generally low;
- acceptance of secondary preventive behavior (willingness to undergo examinations) is not so infrequently missing.

Much more should be done in the field of a public health education, using all modern methods of propaganda. The role of general practitioners is crucial.

Early diagnosis is also possible only if the physician thinks of a possibility of tumor, if he performs basic investigation, or, at least, if he immediately sends the patient to otorhinolaryngologist. Due to improved medical education the situation has been improved in this field in the last decade.

The third level, crucial for improvement of recruiting of candidates for organ sparing treatment in carcinoma of the head and neck is the level of specialist. On this level, the employment of all up to date examinations is mandatory to discover precancerous lesions and early cancers and to delineate their localization and extent.

Besides laryngomicroscopy, endoscopies using various types of rigid telescopes and flexible fiberoptic endoscopes, fluorescence pharyngo-laryngoscopy was developed at the University Department of Otorhinolaryngology and Cervicofacial Surgery in Ljubljana. It is based on the detection of fluorescence induced by helium-cadmium laser, without photodynamic drugs, where the reduction or even absence of fluorescence reveals the cancerous tissue. The experience from our work shows that autofluorescence endoscopy is a useful complementary method in detecting laryngeal and pharyngeal malignancies.[7,8]

The current role of diagnostic imaging is to offer more accurate information on the standard clinical and endoscopic staging of the primary tumor, its regional lymph node spread and distant metastases.

Computer tomography is indispensable in choosing the treatment modalities and planning the extent of surgery in cancer of the nose and paranasal cavities, and it is useful in selected cases of laryngeal carcinoma, determining the possible invasion of laryngeal cartilage which can divert the therapeutical strategy from conservation treatment towards radical surgery.

Magnetic resonance has proved to be sometimes of decisive importance in tongue and floor of the mouth carcinoma.

Ultrasound scanning is used in our department in the first place for detecting lymph node metastases and estimating the operability of nodal disease. Ultrasound guided fine needle biopsy is not used routinely but in selected cases, for instance, in diagnosis of possible contralateral neck metastasis and in local and regional recurrences.[9]

We are starting with video-laryngostroboscopy for detecting early glottic cancer, estimating the extent of subepithelial cancer invasion, evaluating the treatment results and detecting early reccurrences following radiotherapy.

No technology can replace experiences in diagnostics, especially when decision upon conservation treatment is made. Therefore it is crucial that patients with head and neck carcinomas are centralized in institutions where besides technology a high experienced and specialized team is available.

Standard and the changing role of conservation surgery in head and neck region

Standard in the head and neck conservation surgery is without doubt conservation surgery of the larynx. It has developed for more than hundred years and appeared almost simultaneously with laryngectomy. The reason is obvious: the voice is the most cherished possession and despite its replacement by artificial means there is no substitute for the natural voice - even one which is impaired. Nothing especially revolutionary has happened in this surgical field in the last decades: basic goal (to preserve voice and natural way of breathing) and basic oncologic principles (radical excision) have remained unchanged. Frozen-section diagnosis in the operating room is the basic condition for this surgery. Our results showed that the reliability of this histologic method was very high in comparison with the diagnosis from specimens embedded in paraffin but it depends mainly upon the thorough knowledge and

experience of the pathologist, upon the experience and also the professional integrity of surgeon, good cooperation between the surgeon and pathologist as well as upon the adequate organisation of work.[10]

The conservation principle in surgery of some oral cavity, especially tongue tumors, is the same. The surgeon should excise just "enough" and verify the excisional margins of properly orientated specimens by frozen section technique. Some recipes and sketches in surgical atlases are sometimes misleading or, better, leading to unnecessary extent of excision, but, on the other hand, basic principles of frozen section technique are sometimes not strictly applied. The conservation of function in T1 and T2 lesions is usually not a problem and depends mainly on surgeon's skill and experience in using local recontructional techniques.

Besides the larynx, the mandible is perhaps the second most important site of conservation treatment attempts. In recent decades the opinion has begun to dominate, as regards planning surgeries for floor of the mouth cancer, that it is safe enough to excise tumor as local treatment so long as the tumor does not directly involve the periosteum. Our study, comparing the 3-year survival rate of patients with floor of the mouth cancer in terms of spread of the disease and form of treatment showed us that survival after segmental intervention or hemimandibulectomy, despite the late stage of the disease (III. and IV.), was 50%, whereas the overall survival was only 21%, primarily because of local tumor recurrence, in patients with limited tumors (stage II.) where only excision was performed as local surgical treatment. Other therapeutic parameters were the same in both groups. Lightmicroscopic and immunohistochemical methods were used to prove the link between the lymphatic vessels of the floor of the mouth and the mandibular periosteum as well as the lymphatic tumour embolization of the periosteum of the lower jaw. More aggressive surgical treatment has been adopted in the last years at our department in spite of cosmetic and functional sequelae following partial mandibulectomies.[11]

It is well known that the histopathological presence and the extent of lymph node metastasis in the neck is the most important prognostic factor, not only in terms of loco-regional reccurence, but also of distant metastases. The chance of survival in patients with regional metastases is half of those with tumors confined to the primary site. Elective neck dissection and elective radiation give comparable results for the N0 neck. The problem is that despite a thorough pre-treatment assessment staging errors are not infrequent. "Wait and see" policy is therefore too hazardous in our opinion, but the same is true for elective radiotherapy as "probabilistic" approach. Modified neck dissections have been used at our department in the last 15 years (supraomohyoid, anterolateral - depending on the site of primary tumor) as staging surgical procedures. This type of surgery should not be rigid, and staging operation should be continued as classical functional dissection if positive nodes are found and verified during surgery. The similar principle is applied to patients with smaller and mobile palpable nodes. Despite controversial opinions we believe that funcional neck dissection is a safe procedure and follows the idea of organ sparing surgery of Suarez. The Argentinian Suarez, who in 1962 introduced this operation, stated that "the extent of a radical approach should be conceived against cancer, not against neck". In the case of positive nodes at the periphery of dissection or extracapsular spread established on histopathologic study of in paraffin embedded surgical specimens, postoperative radiation therapy is used as well as in doubtful cases. We must admit with humility that the principle "the more the better", despite its questionableness, is applied in these cases.[12,13]

On the other hand, the surgeon should respect the classical radical neck dissection and perform it is cases of larger metastases or evident regionally disseminated disease despite its mutilating consequences.

Radiation therapy as organ sparing treatment

Knowing the basic principles of radiotherapy, the radiation therapy with curative intent is used in early and superficial head and neck cancer where no evidence of nodal disease exists or its probability is very low. The organs and their function are spared, but we are facing the constant problem of the possibility of understaging. Surgical approach in the cases where the extent of disease could be questionable and where surgery does not leave any relevant sequels is in our opinion a better choice.

The role of definitive radiation therapy for laryngeal cancer in the context of organ sparing treatment is specific. The principle is that initial radiotherapy of laryngeal carcinoma has the capability of being curative or final treatment, and can be

followed, if necessary, by salvage surgery. On the occasion of every meeting when surgeons and radiotherapists are brought together, the same statement, that radiotherapy and surgery must not be considered as competitive methods but rather as partners is repeated. In reality, as usual, the situation is different and the philosophy of initial approach is varying from one to another institution, country or region. It is known that radiotherapy is preferred as initial treatment in Scandinavia, United Kingdom, Canada, and surgery in Germany, Latin countries.

The rationale for the definitive radiation therapy are the reported treatment results which demonstrate an overall five-year cure rate for glottic cancer from 87% to 98% in T1, from 80% to92% in T2 and from 57% to 75 % in T3 stage and also larynx preservation in about 50% of cases of T3 glottic carcinoma.[14]

While T1 supraglottic tumors are uncommon and could be suitable for radiotherapy in T2 N0 category the success rate lies between 51% and 77%. In spite of these results, mainly because of the unpredictable nodal disease and well established surgical techniques, the surgical management is generally preferred.[15]

Comparison of treatment results of the two therapeutic modalities in early laryngeal cancer usually shows very similar results. The problem is that the studies are retrospective, nonrandomized, and that factors influencing treatment outcome are very numerous. Reports are based on TNM system, which unfortunately carries a high proportion of incorrectly classified cases and even each T category represents a wide spectrum of cancers ranging from those that are so small that they can be removed by biopsy to others large enough to be almost the next T stage. A deficiency of radiotherapy is that it consists of more or less standard schemes and dosage regimens which are not adapted to the volume of tumor. On the other side surgical procedures are tailored. The problem is that the exact limits of the tumor cannot be always defined prior the surgery and being aware of the fact that radiation therapy is not a substitute for free margins a planned and attempted conservation procedure may be finished as laryngectomy.

Obviously, in many cases, there is no treatment of choice but choice of treatment. The initial treatment of patients with head and neck carcinoma in Slovenia is therefore always planned by a standard team of surgeons and radiotherapist from the University Department of Otorhinolaryngology and Cervicofacial Surgery and from the Institute of Oncology in Ljubljana. Our treatment results show that in T1 and T2 glottic carcinomas, suitable for voice preservation surgery, no significant difference between the groups of primarily irradiated and primarily operated patients exists. The patient should be therefore fully informed of the advantages and disadvantages of each treatment and must take his part in decision making.[16]

We hope that improved therapeutic schemes using chemotherapy in combination with radiotherapy will improve organ sparing treatment of the head and neck, especially of laryngeal carcinoma. While our approach to inoperable head and neck cancer showed significantly better results in patients, where radiotherapy was combined with concomittant chemotherapy[17] and was introduced as standard therapy we still watch with guarded optimism the results of studies using neoadjuvant chemotherapy combined with radiotherapy in responders with T3 laryngeal carcinoma.[18] The goal of these clinical trials - larynx preservation, could be evidently applied also to organ sparing treatment in the head and neck cancer in general.

Organ reconstruction

Due to the high percentage of advanced tumors in head and neck carcinomas at the time of diagnosis the treatment success is greatly dependent on the extent of surgical excision with convincing safety margins. Therefore, the operability of these patients is primarily influenced by the possibility of related defect reconstruction. The microvascular free tissue transfer most closely complies with the basic requirements of reconstruction: the method should be a reliable and final one and it should offer a wide range of possibilities to achieve the optimum functional and cosmetic results, so very important in our specific anatomical region.

In the last two decades, several different microvascular flaps have been introduced at our institution, selected with respect to the tissue to be substituted (e.g. the skin or mucosa alone, or deeper defects including a missing bone). This technique has shown so many advantages over pedicled flaps that it is now regarded as the method of choice particularly in recurrences after previous unsuccessful treatment, where an extremely well vascularized flap is needed. Double-team approach using

highly qualified head and neck surgeon and a micro-vascular surgeon who handles free-flap transfers routinely, has minimized the rate of complications and shortened the duration of surgery.[19]

In 1991, free jejunum flap was introduced at our department, mainly for reconstruction of defects after total pharyngolaryngectomies. 20 reconstructions have been performed with an overall technical success rate of 90%. Three patients also required additional reconstruction of soft tissues of the neck by free radial forearm flaps and in last cases a voice prosthesis was implanted additionally to improve the functional success. The functional results and low complication rate of the free vascularized jejunum transfer has led to abandoning of classical techniques of reconstruction.[20]

Conclusions

Some guidelines should be drawn from this discussion regarding the place and role of organ sparing treatment in head and neck carcinoma.

Early detection is generally inadequate and should be improved as basic condition for conservation surgery and definitive radiation therapy.

Multidisciplinary pre-treatment assessment, selectively including all up-to-date technology, is mandatory for proper selection of conservation treatment modalities.

Choice of treatment modalities must be performed by a standard and highly qualified team, including surgeons of different specialities, radiotherapists, chemotherapists, pathologists and radiologists. In cases in which there is no "treatment of choice" available, a fully informed patient must take his part in deciding upon the treatment modality.

The role of chemotherapy, not only in patients with advanced or progressive locoregional disease but also in the frame of organ sparing treatment should be defined.

For the time when we are dealing with aggressive surgery in combination with radiotherapy, in advanced tumors the term "organ sparing" could be replaced with the term "organ reconstructing".

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