749

State of the art in pre- and post treatment imaging

Abstract not received.

750

Combined chemo-radiotherapy

A. Alimonti[1], E.M. Ruggeri[1], F. Cognetti[1,2]. [1]*Regina Elena Cancer Institute, Oncologia Medica A, Rome, Italy;* [2]*Regina Elena Cancer Institute, Scientific Director, Rome, Italy*

Traditional therapy for loco-regionally advanced laryngeal cancer has consisted of radical surgery and postoperative radiotherapy (RT). In spite of it, the rate of relapse-free survival is generally 25%, and most patients die from complications of progressive local disease. Additionally,the frequently aggressive surgical procedures, result in a significant long-term anatomic functional and psychological sequelae in the surviving patient. In light of these data in recent years organ-preserving treatment strategies have increased and several clinical trials exploring chemotherapy(CT), hyper-fractionated radiation-therapy, radiation sensitizers, or particle-beam radiation therapy are at the moment under clinical evaluation. During the past 20 years,systemic CT has been tested in the management of laryngeal cancer, and many chemotherapeutic agents have showed an effective antineoplastic activity. At the moment the combination of two drugs, fluorouracil (FU) and cisplatin (DDP)is considered the most active. As the matter of fact, several phases III clinical trials and meta-analyses have successfully showed both a survival and loco-regional control benefit for concurrent radiation and CT regimens based on FU and DDP when compared with RT alone. Another promising approach to locally advanced laryngeal cancer it has been the introduction in clinical practice of hyper-fractionated irradiation in order to increase the probability of a loco-regional control reducing the risk of tumor repopulation. To date we have reached some improvements in tumor response, especially in the rate of loco-regional control of disease and relapse free-survival although these advances have come at the cost of increased toxicity respect to conventional daily fractionation.Fundamentally, in these years authors have studied two different approaches: induction with combination chemotherapy followed by definitive RT or CT administered concomitantly with RT. Up to date a concomitant combined modality approach seems to be superior to both RT alone and the sequential multimodality therapy. Laryngectomy can be reserved for patients with less than 50% response to chemotherapy or who have persistent disease following radiation. Finally, several single and multi-institutional trials have reported both a survival and loco-regional control benefit from more aggressive concurrent radiation and new multiagent CT regimens,including carboplatin and Paclitaxel or Paclitaxel, FU and Hydroxyurea.

751

Larynx preservation: What is new in radiotherapy?

J. Bourhis. *Institut Gustave Roussy, Radiothérapie, Villejuif, France*

Larynx preservation can be achieved in a high proportion of patients with T1-T2 larynx/hypopharynx carcinoma when using partial laryngectomy or partial pharyngo laryngectomy. Radiotherapy may be a good alternative when the patient is not amenable to partial surgery and may be also in some cases the treatment of choice (T1N0 glottic cancer). For more advanced cases such as T3 disease, induction chemotherapy followed by radiotherapy in good responders or by surgery with total laryngectomy in poor responders has been shown to be a valid alternative to initial total laryngectomy. However we have shown in a recent meta-analysis of 3 randomized trials (Veterans, Gettec, EORTC trials, that this approach has to be used with caution since a 6% difference at 5 years in DFS and overall survival was observed in favor of the initial surgery arm. More recently a novel approach has used concomitant induction RT-CT showing promizing results (RTOG 91-11: randomized trial). Modified fractionated radiotherapy is also a possible alternative to conventional radiotherapy as suggested in a recent meta-analysis.

In T4 disease and/or invasion of the subglottic area, total laryngectomy is most often necessary, with little possibility for larynx preservation.

752

There is still a place for surgery

J.L. Lefebvre. *Centre Oscar Lambret, Department of Head and Neck Surgery, Lille, France*

The first reported treatment of a laryngeal cancer was a total laryngectomy performed by Theodore Billroth on December 31st 1873. Five years later the same surgeon performed an hemilaryngectomy. In 1903 the first treatment of a larynx cancer with irradiation was published. This was the beginning of an intensive clinical research for the improvement of both partial surgery and definitive irradiation. Unfortunately neither partial nor radical surgery have been compared to definitive radiation therapy in randomized trials (i.e. in comparable populations of patients with comparable diseases). This missing prerequisite compromises subsequent discussions on the respective places of either surgery or irradiation. In 1986, the Veterans Administration in the US initiated a randomized trial on larynx preservation in larynx cancer patients thanks to an upfront chemotherapy that concluded that this approach 1) did not compromise disease control nor survival and 2) allowed to preserve two thirds of the larynx. At about the same time a French similar trial but carried out on more advanced cases showed opposite data. As a result the discussion about the remaining place of surgery remains debatable. As far as partial surgery is concerned, there are 8 different procedures for the supraglottic larynx and 9 for the glottic larynx. This remarkable panel of surgical procedures allows the surgeons to adapt the resection to each clinical situation. When properly selected and performed this surgery gets local control rates as high as at least 90% (supraglottic cancer) to at least 95% (glottic cancer). But it requires a thorough selection of patients (in particular for the largest procedures due to the risk of transient postoperative aspiration). Anyhow these results cannot be neglected. As far as total laryngectomy is concerned, it seems that very infiltrative tumors, transglottic cancers and tumors destructing the cartilage are better controlled with surgery (control above clavicles = 85%) and are not good candidates for larynx preserving strategies. To sum up there is still a place for larynx surgery as the first treatment that must be discussed in parallel with radiation therapy or chemotherapy based protocols according to patients characteristics (age, occupation, pulmonary function, wishes), tumors characteristics (extension, infiltration, necrosis) and local expertise and resources.

753

Chemokines, chemokine receptors and selectin ligands expression by tumour cells: involvement in extravasation and metastasis

I.P. Witz. *Tel Aviv University/Faculty of Life Sciences, Department of cell research and immunology, Tel Aviv, Israel*

In order for cancer cells to form metastases at specific organ sites, pre metastatic cells must exit the vasculature, migrate into these sites and be able to survive and proliferate there. Molecules involved in transendothelial and in directional migration are therefore key players in metastasis formation.

The molecular basis of cancer cell extravasation and of site-specific metastasis is poorly understood. A comprehensive and thorough understanding of the mechanisms underlying these processes is an absolute requirement for the development of therapeutic modalities aimed to block or retard metastasis.

This presentation is focused on mechanisms regulating the extravasation of cancer cells as well as their directional migration to specific organ sites.

The FX enzyme plays a key role in the biosynthesis of fucosylated selectin ligands. These ligands initiate the interaction between extravasating cells and endothelium via their binding to endothelial selectins. Indeed we demonstrate that the fucose-generating FX enzyme controls the expression of selectin ligands on colorectal cancer cells and their adhesion to endothelial cells or to E selectin.

To elucidate the mechanisms involved in the ability of cancer cells to form site-specific metastases, we focus on the role of chemokine-chemokine-receptor-mediated interactions in this process. The role played by mammary tumor-derived MCP-1 and its interaction with monocytes as well as that of the CXCR4 and CXCR3 chemokine receptors expressed by human neuroblastoma cells in the progression of these tumors will be discussed. †