

Head and neck, and orofacial tumours prospect and future

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ABSTRACT

Head and neck, and orofacial tumours are not uncommon diseases in clinical practice. It represents about 8 % of the total incidence of cancer in human beings. The anatomical sites of this speciality is very diverse; each site has its own predilection towards certain types of cancer. Each tumour has its own prevalence, behaviour, and response to treatment. The traditional treatment was based mainly on surgery. In addition to the use of some chemotherapeutic agents and deep X ray therapy. Surgery is very aggressive involving neck dissection with removing of muscles and other tissues in an attempt to remove any lymph nodes that may be involved in the cancerous process. However, this way of treatment was not free of dreadful complications.

Over the last few years, the trend for treatment of these kind of tumours has witnessed dramatic changes that are going to replace the traditional way. The core of these advances are based on better identification of lymph nodes involved and the use of new chemotherapeutic agents; agents that are not only going to kill the tumour cells, as the case in the old agents, but also to change the susceptibility of tumour cells for killing and affect their apoptosis.

Key words: Head, neck and orofacial tumour, cancer, apoptosis, flap surgery

Head and Neck cancers represent nearly 12% of the total malignancies in the USA and about 7 % in the UK. They represent 8% of the total incidence of cancer in human being. Cancer of the tongue, the mouth, or its floor are fatal diseases due to early metastasis to cervical lymph nodes.

Smoking and drinking of alcohol are strong predisposing factors, in addition to consumption of spicy chillies. Keratinizing lesions like leukoplakia, erythroplakia, and infected lesions like chronic hyperplastic candidiasis, human papillomavirus infection, and syphilitic leukoplakia are also other recognized predisposing factors.

All modalities for Treatment of cancer have been used including radical surgery, chemotherapy and deep X- ray therapy (DXT).

In Iraq, Head and neck cancers become more prevalent and more aggressive probably due to genetic mutation by effect of radiation

from depleted uranium and pollution from wars since 30 years and spread of oncogenic viruses.

Head and Neck cancers include cancers of the orofacial region, pharynx, parotid glands, salivary glands, orbit, jaw, sinuses and other parts of the face including the skin. These anatomical sites might be affected by variety of histopathological types of cancer such as basal cell carcinoma, squamous cell carcinoma, fibrosarcoma, osteogenic sarcoma, jaw lymphoma, Hodgkin's and non-Hodgkin's lymphoma.

Jaw lymphoma is very peculiar and interesting tumour affecting jaws of children. The author described this fatal disease in children in 1978, in addition to other malignant tumours of the oral cavity and the face including periorbital and orbital tumours.

Jaw lymphoma is quite different from Burkitt's lymphoma in its clinical features, aeti-

ology, treatment and behaviour. Jaw lymphoma has a very rapid onset with a fast spread to internal organs including central nervous system, while Burkitt's lymphoma is a slowly growing tumour. Treatment of these tumours depends on their nature and stage. Few courses of cyclophosphamide (40 mg/m^2) may be enough for the treatment of Burkitt's lymphoma, while we need more complicated regimens for treatment of stage I and II of jaw lymphoma such as CHOP which consists of eight doses of Vincristine (1.5 mg/m^2), Adriamycin (50 mg/m^2), Cyclophosphamide (1000 mg/m^2), Methotrexate (10 mg/m^2) and Prednisolone (50 mg/m^2) given over 24 weeks.

Squamous cell carcinoma of the oral cavity forms about 95% of oral cancers. It features as a fissure, exophytic growth or ulcer with or without leukoplakia. The most common site is the lateral side of the tongue and floor of the mouth. **Melanoma** is a rare, aggressive tumour that has early metastasis and very poor survival rate. **Adenocarcinoma of the oral cavity** is a less common, slowly growing tumour with fewer tendencies for cervical lymph nodes deposit.

Cancer of paranasal sinuses is an aggressive type of malignancies with tendency to invade the orbit and the base of the skull; perforating the palate in the maxillary sinus of the upper jaw. The most common tumour of the sinuses is squamous cell carcinoma rather than adenocarcinoma. This is due to cellular metaplasia of respiratory columnar type of epithelium to squamous type. Recurrence of infection and other irritating agents are the predisposing factors for this metaplastic change. Both types of tumour are metastasized to the cervical lymph nodes including the deep chain (supra clavicular lymph nodes). The managements of these tumours are by three modalities of surgery, chemotherapy and DXT. Other modalities may be useful in early lesions such as cryosurgery and radical CO₂ Laser therapy.

Surgery, chemotherapy and DXT have been used for treating these tumours. Other modalities may be useful in early lesions such as cryosurgery and radical CO₂ Laser therapy. Frozen sections are required for safety margins and for assessment of complete eradication of the tumour.

The use of Gamma Knife (Cobalt 60) in the managements of brain tumours and intra ocu-

lar malignancies without evisceration of the eye balls is convincing. The advances of surgical managements of orofacial tumours are based on advances of flap surgery. Pedicle flaps (forehead flap, tapes dorsalis flap, lateral cervical flaps, deltoid-pectoral flap and trapezius flaps), free flaps like forearm flap and latissimus dorsi flap require microsurgical vascular anastomosis for reconstruction of the defect after radical cancer surgery.

The traditional use of radical neck dissection for treatment of cervical lymph nodes deposit by radical excision of the sterno-mastoid-muscle, accessory nerve and deep cervical fascia, in addition to ligation of internal jugular vein have not often been used and became less popular due to creation of obvious vertical bands of scars over the lateral side of the neck with dropping of shoulder and superficial exposure of the carotid contents and its obvious effect on venous drains of the brain. This technique was replaced by selective neck dissection and supra-omohyoid neck dissection.

The advancement of different diagnostic tools for detection of cervical metastasis by application of ultra-sonography, Magnetic resonance (MRI) and computed tomography (CT) scans with protocol for managements of cervical lymph nodes metastasis is the basis for managements of lymph nodes deposit.

Basal cell carcinoma is the most common tumour affecting the face of white people because of less melanin pigment in their skin and continuous exposure to sun light. It is slowly growing tumour with a tendency to invade deep structures of the orbit, so it requires radical surgery with reconstruction by flap. This tumour does not metastasise to cervical lymph nodes.

Adenocarcinoma is less common in the oral cavity, affects minor salivary glands, more common in the maxilla. In contrast to that of the gastrointestinal tract, adenocarcinoma of the oral cavity is a slowly growing, less aggressive and rarely metastasise to cervical lymph nodes.

Recent advances and prospect for the future:

Nowadays, Advances in Chemotherapy and DXT have played an important role in the management of orofacial and head and neck cancers. These modalities of treatment have

become more specific and more precise in targeting cancerous cells. One of these new drugs is Gemzar (Gemcitabine) which is used for the treatment of adenocarcinoma. It interferes with growth and spread of cancer cells by affecting their metabolism and inducing apoptosis. It is usually used with Carboplatin. Gemzar shows promising results even when it is used for the treatment of stage IV adenocarcinoma of the pancreas.

Biological agents like Cetuximab have been used effectively in the managements of squamous cell carcinoma of head and neck especially in conjunction with other established treatment modalities.

There are two major intrinsic pathways for inducing apoptosis in cell. The first begins with ligation of cell surface death receptors and the second involves mitochondrial release of cytochrome C. Recent reports have suggested that anticancer drugs kill susceptible cells by inducing expression of death receptor ligands, especially Fas Ligand (FasL), while other researches have indicated that chemotherapeutic agents trigger apoptosis by inducing release of cytochrome C from mitochondria.

Current cancer researches are focused on understanding the response and resistance to treatment and apoptosis.

Recently In the USA, two new chemotherapeutic agents are approved by FDA; Opdivo and Keytruda. They are considered a breakthrough in the management of cancer. Both target the same pathway which is PD-1. PD-1 is an internal block which has the ability to prevent the immune system from attacking the self cells. Its function would also lead to prevent the immune system from attacking the emerged cancerous cells as well. So by disrupting this pathway these new drugs would kill the tumour cells. Recent clinical trials have approved the effectiveness of these drugs in treating patients with melanoma; a tumour which has exhausted other options. Clinical trials have showed that Opdivo has a response rate of about 32 % of patients while Keytruda has 24 % response rate. It's really hard to make a comparison between trials since they may have enrolled patients with different severities of their diseases.

Management of cancer depends not only on cellular damages as achieved by chemotherapy

and DXT, but on the ability of the malignant cell to respond to damages by inducing apoptotic changes and mutation in apoptotic pathways to end with resistant to chemotherapy and DXT.

Mitochondria and cell surface receptors have a major role in the pathway of cell apoptosis. This pathway is mediated by Bcl-2 family proteins. Setting of this pathway on will lead to release of cytochrome C from the mitochondria which trigger caspase cascade to induce apoptosis. Most of chemotherapeutic drugs modulate apoptotic inducers for treatment of malignancies.

The future might be promising for controlling cervical lymph nodes metastasis by using different methods for accessing neck dissection as well as recent application of Robot surgery (the Da Vinci surgical robot system), this system has emerged as potentially useful tool in microsurgery with improvement of multiple domains of performance with reputation of robotic microsurgical task and widely used in eradication of tumours and flap reconstruction.

Whether surgery has been used or not, the role of chemotherapy and DXT are expanding nowadays as a first line therapy for head and neck, and orofacial tumours aiming at achieving cure without the need for performing a radical neck dissection.

We hope to give our colleagues some ideas about the prospect and future managements of Head and Neck, and Orofacial tumours.

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