REVIEW

Management of oral cancer

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Oral cancer is a serious disease that is on the increase. The most pressing need is early recognition and referral for specialist treatment. Too many cases present with advanced tumours. Radiotherapy and surgery remain the primary modalities of curative treatment, but understanding of tumour pathology and developments in surgical and radiotherapeutic technique have combined to produce a rational approach to management. In many instances ‘radical’ methods of surgical access can be combined with a more ‘conservative’ resection of the mandible or cervical lymph nodes. One-stage reconstructive procedures, often incorporating osteotomy techniques, miniature bone plating and free tissue transfer, have minimised the morbidity and functional deficit so often seen after earlier operations. All surgeons involved in the modern management of oral cancer should have expertise in these techniques or be part of a team which can provide them.

In global terms, oral cancer is the sixth most common malignancy, but it remains relatively rare in the UK, accounting for only 1–2% of all malignant tumours. Nevertheless, there is concern that the incidence is increasing, particularly in younger patients and women (1,2). The male to female ratio is less than 2:1 and the gap is closing steadily (3). Overall there are about 2000 new cases per year registered in the UK, but there is possibly an element of under-reporting.

The main aetiological risk factors are recognised as tobacco habits and a high alcohol intake, with a strong synergistic relationship between the two which increases the risk considerably (1). There are a number of other risk factors which have been postulated, including chronic candidal infection, and nutritional and vitamin deficiencies. The level of risk with these other factors remains unproven in most cases and is certainly small compared with tobacco and alcohol. In younger patients in particular it is often difficult to find any obvious predisposing factors. There are also certain well-recognised premalignant lesions such as erythroplakia, leukoplakia and arguably erosive lichen planus. The management of these lesions is a matter for debate. The increased risk is difficult to quantify but factors such as site, histology and length of time the lesion has been present are all important.

Oral cancer is still a lethal disease, with a 5-year survival of less than 50%. The annual mortality figures are actually of the same order of magnitude as malignant melanoma or cervical cancer (4), both of which are subject to intense media interest, educational campaigns and screening programmes. It is interesting to ask why there appears to be less interest in oral cancer despite the emotional, functional and aesthetic importance of the face and mouth. Unfortunately, many patients still present with advanced disease, and the importance of patient education and regular screening by dentists and doctors needs to be emphasised. The message to all health professionals must be ‘If in doubt—refer early’.

Basic principles of management

Oral cancer is a heterogeneous condition with a predilection for certain sites within the mouth, notably the anterior tongue, floor of mouth, retromolar trigone, buccal mucosa and palate. The vast majority (>85%) are primary mucosal squamous cell carcinomas with minor salivary gland neoplasms as the next most common. The remainder will be lymphomas, malignant melanomas, sarcomas, secondary tumours, etc. In assessing the outcome of treatment, the large number of patients needed to obtain a statistically significant result, and the problem in obtaining true informed consent, make the
satisfactory construction and execution of randomised controlled trials extremely difficult if not impossible. Most of our understanding of the behaviour of the disease comes from retrospective analyses of large series treated by a variety of methods. There are problems in interpreting these results which stem from such factors as lack of accuracy in defining the primary site, lack of accuracy in staging, variations in treatment protocols or inclusion of sites that some consider not strictly part of the oral cavity, such as lip, posterior tongue and oropharynx.

Death from oral cancer often results from uncontrolled disease at the primary site or in the neck. Up to 20% of patients with controlled local disease will subsequently develop further primary carcinomas in the upper aerodigestive tract. Death owing to distant metastases, once considered to be a rare feature, is now more common as a result of better locoregional control (5). However, even if local disease control is better it is still too early to say whether the survival figures will eventually improve. There is little evidence to date that cure rates have increased over the past four decades, although the changing pattern of disease, with a decrease in lip cancer and a rise in tongue cancer, for example, may actually mask a relative improvement in outcome.

Treatment is directed at the elimination of the primary tumour and any neck nodal metastases, with the minimum morbidity to the patient. The principal modalities of therapy remain radiotherapy and surgery, often in combination. Other modalities, including chemotherapy, have been tried not only as palliative treatment but also as induction therapy or as an adjuvant to surgery or radiotherapy with curative intent. Despite encouraging early reports of tumour response no significant survival benefit has been shown (6,7) and the increased morbidity of treatment is often unacceptable. The same applies to trials of fast neutron therapy.

The difficulty in achieving the ideal aims of treatment relates in part to the complex nature of the anatomical area in which the disease presents. Radiotherapy may cause functional impairment as a result of short-term problems such as xerostomia and stomatitis, or long-term problems such as osteoradionecrosis. Surgery often requires the loss of important functional units such as the tongue, lips or mandible. Wide excision may be compromised by the proximity of vital structures such as the internal carotid artery, and tumour extension to inaccessible areas may preclude resection despite recent advances in methods of surgical access.

It can be appreciated that the management of oral cancer presents a considerable challenge to the multidisciplinary team which should be involved in treatment. Added to the patient’s fear of the disease and the possible morbidity of effective treatment is the fear of disfigurement, loss of speech and impairment of swallowing. All patients will need a thorough evaluation of their condition, comprehensive treatment planning, a co-ordination of the appropriate therapeutic modalities, careful reconstruction and rehabilitation and continued psychological and social support. There have been great advances in most of these areas of management over the past decade and it is vital that all the clinicians involved, in both the medical and support specialties, liaise fully as part of a head and neck oncology team. The establishment of cancer units and cancer centres in the UK, as proposed by A Policy Framework for Commissioning Cancer Services (8), should reflect the need for such close collaboration in specialist centres. As recommended in this consultative document, any surgeons involved should be specialists in the anatomical area in question.

Investigations and surgical pathology of the primary tumour

Accurate assessment of the extent of disease is the prelude to treatment planning. This will include a biopsy of the primary tumour, often combined with an examination under general anaesthesia to allow accurate measurement of the tumour dimensions, although tumour thickness, which is probably the most important dimension, is difficult to assess on palpation alone. Endoscopic inspection of the rest of the upper aerodigestive tract is advisable in order to exclude synchronous tumours and, if medium- or long-term problems with swallowing are anticipated, this is an ideal opportunity to carry out a percutaneous gastrostomy, since this method of enteral nutrition is far superior to prolonged nasogastric tube feeding (9).

Primary intraosseous carcinomas are rare, but spread of soft tissue tumours to involve the mandible or maxilla is more common and has an obvious bearing on treatment. Standard plain radiographs such as the orthopantomogram are reasonably sensitive in detecting mandibular invasion, but this should be confirmed in doubtful cases using other imaging techniques (10). CT and MRI have been shown to have equal specificity (false-positive 0%) but MRI is more sensitive (false-negative 6% compared with 28% for CT). CT scans are advised for accurate assessment of maxillary sinus involvement or spread to the posterior maxilla and pterygoid region. Both imaging modalities, particularly MRI, have a role in assessing soft tissue tumour thickness, especially in the tongue.

Bone involvement in oral cancer is almost certainly an indication for primary surgery, although current views on how tumours invade the mandible may allow for a more conservative resection in some cases than was previously considered necessary. The preferential pathway for invasion of the non-irradiated edentulous mandible is via deficiencies in the cortical bone of the resorbed alveolar crest (11). In the dentate mandible, the tumour probably enters through the periodontal ligament, but it has also been suggested that direct spread through the keratinised attached gingiva is important (12). Once the inferior alveolar nerve canal is breached, anterior and posterior perineural extension takes place in both the edentulous and dentate mandible. The practical consequences of this pattern of spread are discussed later under surgical advances.
Cervical lymph node staging

One of the most important factors, with a major influence on treatment and outcome, is the involvement or otherwise of the cervical lymph nodes. Our understanding of metastatic spread to the neck from oral cancer has improved in recent years as a result of anatomical, clinical and pathological studies. Investigations have shown that lymph node metastasis in the untreated neck occurs as a result of embolic spread, rather than permeation through the lymphatic channels (13). This calls into question the concept of the so-called en bloc resection of primary tumour and regional node-bearing tissue. A stepwise spread occurs through the lymphatic chain with involvement of first level nodes before spread to the next level. Thus, if there is no evidence of macroscopically involved nodes in the upper neck then microscopic involvement lower down is most unlikely. Furthermore, it is now recognised that the lower deep cervical nodes and nodes in the posterior triangle are rarely affected in mouth cancer (14), and from what has been said it can be seen that other nodal areas such as the submandibular triangle or upper deep cervical chain would almost invariably be involved in the rare event of such inferior or posterior spread. The practical implications of this pattern of lymph node metastasis are discussed below.

The limitations of palpation as a means of assessing possible lymph node metastasis are self-evident. The skill level of the examiner, anatomical factors and inflammatory enlargement can all combine to mitigate against accurate staging. In an effort to improve this situation investigations have been carried out to compare various imaging modalities as a means of determining pathological spread (15). A comparison of palpation, ultrasound, ultrasound-guided fine-needle aspiration cytology (FNAC), CT and MRI (16) showed that palpation was the least accurate, CT and MRI were equally sensitive and specific and that ultrasound-guided FNAC was the most accurate (sensitivity 90%, specificity 100%). However, the latter is also dependent on the skill level of the investigator and pathologist.

What is the significance of positive cervical nodes in oral cancer? Most retrospective series confirm that neck involvement is one of the major predictive factors in outcome (17). The likelihood of lymph node metastasis depends on the size, site and histological type of the primary tumour. As a general rule the larger the tumour, the more posterior the lesion in the mouth and the less the degree of differentiation, the more likely it is that lymph node metastasis will have occurred. In addition, there are other factors which will affect outcome, such as fixity of the nodes (which is evidence of extracapsular spread), large nodes, bilateral node involvement, and nodes at the lower end of the internal jugular chain or in the posterior triangle (18). It might also be thought that the total number of nodes involved would be important, but this remains controversial apart from the factors already mentioned.

At a histological level, in addition to evidence of microscopic extracapsular spread, the immunomorphology of the nodes also has some prognostic significance. Germinal centre predominance or lymphocyte predominance represents a B-cell or T-cell response to the tumour while the opposite, namely a lymphocyte-depleted node with few germinal centres, suggests a poor response. This difference is reflected in the 5-year survival figures with lymphocyte predominant patterns carrying a much better prognosis (19).

Primary treatment—radiotherapy or surgery?

The basic decision to be made in the curative treatment of oral cancer is between radical radiotherapy and elective surgery. Preferences for one or the other vary considerably between treatment centres, as do the radiotherapy regimens and probably the types of surgical procedures performed, but the two forms of treatment which have a curative role in oral cancer should be regarded as complementary. Generally speaking, if radical radiotherapy, either external beam or interstitial therapy, is chosen as the primary treatment, surgery will be reserved for 'salvage', i.e. for biopsy-proven recurrent or residual disease. Conversely, if surgery is chosen, radiotherapy may be used in an adjuvant manner, either pre- or postoperatively, but the operation should still be planned as the fundamental definitive curative procedure. Two other points are worthy of note. Radiotherapy rarely cures a patient who develops recurrence after initial surgery. Conversely, surgery can sometimes rescue a radiotherapy failure, but the complication rates of 'salvage' procedures are greater than those of primary elective surgery.

Having made these general comments there are a number of factors which may favour radiotherapy or surgery as the primary modality. Occasionally a patient will be unfit for any form of surgical operation under general anaesthesia, but this is rarely the major factor in the decision making. The factors which normally influence treatment policy are the site of the primary tumour, the stage of the disease, whether there has been previous irradiation in the area, and personal and social considerations. Some tumours are relatively inaccessible for primary surgery, although recent advances in methods of surgical access (see below) make this less of a factor. Small, well-localised tumours generally do well with either modality, but if surgery is unlikely to produce significant deformity or functional morbidity it may be preferred, for example in lip cancers. If the tumour is large, or if there is evidence of the bone invasion and/or cervical lymph node metastasis, then surgery is usually considered the most appropriate treatment, usually with adjuvant radiotherapy. The areas of possible controversy centre on the intermediate group (i.e. larger T1; most T2 and early exophytic T3 tumours), since elective surgery or radical radiotherapy would appear to produce similar survival rates (20). In this situation the likely morbidity of treatment and functional outcome of each method needs to be considered. Radiotherapy may be considered
without advantageous since it is an outpatient procedure, but it is not without immediate and delayed morbidity. Surgery may create extensive defects, but modern reconstructive methods can restore form and function to a considerable degree. The decision as to what is best for an individual patient will depend on their own wishes, medical and social factors, and on the expertise available at the treatment centre. It is here that there is an obvious requirement for combined planning by clinicians who respect and understand the strengths and weaknesses of each treatment modality.

Advances in surgical treatment

Resection of the primary tumour

Two areas for consideration are methods of surgical access for tumour excision and the approaches to mandibular resection.

Understanding of the blood supply to the facial bones has led to the development of a number of safe ostetomy procedures which are often used for the correction of skeletal facial deformity. This has been accompanied in turn by the development of small power saws for accurate division of the bone and miniature titanium plates for relocation of the segments with rigid internal fixation. These techniques are also applicable to cancer surgery and it is now relatively commonplace to perform a mandibulotomy as part of the surgical procedure if access to the posterior part of the oral cavity is required (21). Surgeons with expertise in this area can safely divide the mandible between the roots of the standing teeth if necessary. This simplifies surgery to the posterior tongue, retromolar trigone, or soft palate region, for example. Excision of the primary tumour with a margin of normal tissue in all dimensions can be carried out under direct vision with protection of vital anatomical structures and safe haemostasis. Although it is a more difficult procedure, osteotomy of the maxilla, with the segment pedicled on a cheek flap, can also be performed to allow access to the posterior aspect of the palate or the retromaxillary region (22).

In the past there was often an unthinking radical removal of complete segments of the mandible as part of the primary resection. Recent investigations into the methods of tumour invasion already discussed have prompted interest in the concept of a more conservative approach. The periosseum itself is relatively resistant to tumour spread and close proximity of the tumour with no evidence of mandibular invasion does not normally mean that extensive jaw resection is necessary. In this situation subperiosteal stripping of the specimen from the bone, or possibly a marginal resection, is all that is needed (21). The place of this type of partial resection when there is definite evidence of bone involvement is more debatable and it is usually not feasible in the thin edentulous jaw. However, since invasion from oral tumours is from the superior aspect, preservation of the inferior border of the mandible may be possible in selected cases where there is sufficient bone bulk. If such a procedure is considered anatomically and oncologically safe care should be taken to extend any resection in the body of the mandible to include the nerve canal from the lingula to the mental foramen, in view of the predilection for tumour spread by this route.

Neck dissection

For many years the only operation considered appropriate for removal of the cervical lymph nodes was a radical neck dissection. Recognition of the morbidity associated with the loss of important structures such as the spinal accessory nerve and the problems of carotid exposure consequent on the removal of the sternocleidomastoid muscle have resulted in the development of so-called 'functional' neck dissections. These aim to preserve various anatomical structures while removing the node-bearing tissue within an envelope of deep fascia. This concept has been combined with the realisation that metastases from oral cancer are normally limited to the submandibular triangle, upper third and middle third of the deep cervical chain (14). The terminology of neck dissection is not yet standardised and is often confused by eponyms. A recent classification proposed by the American Academy of Otolaryngology and Head and Neck Surgery deserves wider acceptance (23):

1 Radical neck dissection.
2 Modified radical neck dissection (ie aiming for the same radicality of node removal but preserving certain key anatomical structures such as the internal jugular vein, sternocleidomastoid muscle or spinal accessory nerve. So-called 'functional' neck dissections fall within this group).
3 Selective neck dissection:
   a Supraomohyoid.
   b Posterolateral.
   c Lateral.
   d Anterior compartment.
4 Extended radical neck dissection (ie where more than a radical neck dissection is performed, eg including removal of parotid, preauricular or occipital nodes).

The need to remove the node-bearing tissue from all areas of the neck as in the classical radical neck dissection has been questioned in the management of oral cancer even in the presence of positive nodes (24). The supraomohyoid dissection covers the nodal sites most often affected and may be used electively as a sampling procedure in node-negative necks. Any patients with more than one involved node or extracapsular spread should undergo radical postoperative radiotherapy. Some surgeons would still advocate a supraomohyoid dissection even if there is a single small mobile node (N1) in the upper neck, but others would wish to exclude microscopic spread to lower levels and would perform a modified radical dissection. In oral cancer the classical radical neck dissection should probably be reserved for extensive neck disease, ie large or multiple nodes (N2, N3), fixed nodes, nodes in the lower third of the deep cervical chain, nodes in the posterior triangle and recurrence in the neck after radiotherapy (18).
Reconstruction

Many of the problems previously associated with the surgical management of oral cancer related to the limited methods of reconstruction available. Staged procedures using pedicled flaps were often required and the cosmetic result was sometimes less than ideal (eg with the forehead flap.) The development of myocutaneous flaps has allowed one-stage reconstruction in many instances, but the use of free tissue transfer with microsurgical anastomosis has undoubtedly been the greatest advance (25). It is now possible to carry out complex replacement of soft tissue and bone as a primary procedure at the same time as tumour resection (26,27). The importation of vascularised tissue aids healing in compromised situations and facilitates early postoperative radiotherapy if indicated. If bone is required, the donor site can be selected to provide sufficient bulk to allow complete rehabilitation with an implant-retained dental prosthesis at a later date (28,29).

References


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