Clinical review

Fortnightly review

Oral cancer

Joanna M Zakrzewska

The survival of patients with oral cancer remains poor despite recent surgical advances. About 30-40% of patients with intra-oral cancers will survive five years; the short survival time is caused, largely, by late detection.[1] Public awareness of oral cancer as compared with other cancers is low and this contributes to delays in diagnosis.[2] However, the mouth can be examined by healthcare professionals with much greater ease and accuracy than many other parts of the body. All healthcare workers need to be aware that a patient with an ulcer or white patch that persists beyond three weeks should be referred for further evaluation to an oral physician or to an oral and maxillofacial surgeon. Tobacco use is a major cause of oral cancer, and doctors and other health professionals can contribute to primary prevention by making patients aware that tobacco, in all forms, predisposes them to oral cancer.

Summary points

- The incidence of squamous cell carcinoma of the oral cavity is increasing
- The use of tobacco, in all forms, is major risk factor for squamous cell carcinoma; tobacco acts synergistically with alcohol
- Squamous cell carcinoma presents intra-orally as a non-healing ulcer, or a white or red patch
- A biopsy done under local anaesthesia is the single most important investigation in diagnosing oral cancer
- Five year survival rates for cancer of the lip are good but are low for other forms of mouth cancers, especially if the lesions are large at the time of diagnosis

Department of Oral Medicine, St Bartholomew's and the Royal London School of Medicine and Dentistry, London E1 2AD

Joanna M Zakrzewska, *head*

j.m.zak@mds.qmw.ac.uk

BMJ 1999;318:1051–4

Methods

The majority of references in this article were obtained from a personal collection built during 10 years of work in this subject and during a study of screening for oral cancer. A Medline search of articles published between 1966 and 1998 using the terms "mouth" and "neoplasms" yielded 20 664 articles. Adding the keywords "systematic" and "review" did not identify any systematic reviews. The Cochrane database does not list any protocols or completed systematic reviews of randomised controlled trials of head and neck surgery.[3] Searching the Cochrane Controlled Trials Register identified 11 randomised controlled trials, mainly on the use of chemotherapy. The American College of Physicians Journal Club and Evidence-Based Medicine database (1991-1997) lists no articles relating to mouth neoplasms.[4]

Main types of oral cancers

- **Epithelial**
  - Squamous cell
    - Verrucous
    - Spindle cell
    - Adenoid squamous
  - Basal cell
  - Malignant melanoma
- **Odontogenic**
- **Primary bone tumours**
- **Salivary gland tumours**
  - Mucoepidermoid
  - Acinic cell
  - Adenocarcinoma
- **Haemopoietic**
- **Lymphoreticular**
- **Metastases from other sites**

Definition and classification

Neoplasms of the mouth are defined as neoplasms involving the oral cavity, which begins at the lips and ends at the anterior pillar of the fauces. The most common intra-oral malignancy is squamous cell carcinoma. Tumours of the salivary gland have different risk factors and are relatively rare. The major types of carcinomas encountered in the mouth are shown in the box.

Epidemiology and risk factors

Oral cancer is relatively rare in the United Kingdom—2000 new cases are diagnosed each year—but this is rising, especially among men.[5] Worldwide it is estimated to be the sixth most common cancer, prevalence being highest in India.[6] An increase in incidence

has also been reported in central and eastern Europe, especially among younger men.[7] Mortality remains high and although the prognosis for cancer of the lip is good, the prognosis for intra-oral squamous cell carcinoma remains poor.[5] There is good evidence that tobacco in all forms, including the tobacco in snuff and betel quid (a mixture of ingredients including betel leaf, areca nut, slaked lime, and tobacco, which is wrapped in a betel leaf and chewed), is carcinogenic in the upper aerodigestive tract, which includes the mouth.[8] There is fairly convincing evidence that alcohol is also a carcinogen and acts synergistically with tobacco.[9] There is little convincing evidence that mouthwash use, poor oral hygiene, or oral infections of viral origin play an important role in the aetiology.[10 11] Consuming fruit and vegetables may have a protective effect. It has been suggested that lichen planus and oral submucosal fibrosis are associated with an increased risk of intra-oral malignancy. Wide variations in the malignant potential of these lesions have been reported. There is a slight familial risk for oral cancer which may be related to the similar exposures to tobacco and alcohol which occur among family members.[12] Patients who have had renal transplants have a higher incidence of cancer of the lip which may be due to immunosuppression.[13]

Although a premalignant lesion (epithelial dysplasia) is recognised, many oral cancers do not go through a premalignant stage. Not all premalignant lesions become malignant, and some regress.[14] There is insufficient evidence to determine which features reliably predict malignant potential, but the degree of dysplasia may be a factor.

Prevention

Primary prevention involves stopping the use of tobacco. Regression of premalignant lesions has been reported in former smokers.[15 16] In the Indian subcontinent and in areas with large populations of Asian migrants, reducing the use of betel quid may also be beneficial. The prevalence of betel quid use remains high in immigrant populations in the United Kingdom.[17]

Early identification of premalignant lesions and small oral cancers will allow patients to be treated earlier. Screening for oral cancer is simple. It does not require any laboratory support; at the most it requires a good light source. Mass screening in the United Kingdom is not recommended because it does not fulfil the principles for screening suggested by Wilson and Jungner.[18 19] However, dentists should be encouraged to screen patients opportunistically especially if patients are males, smokers, and over 40 years old.

Public campaigns are necessary, however, to make patients aware of oral cancer; patients often delay seeking professional advice for over three months.[20 21] The 1992 US National Health Interview Survey showed that the 15% of adults who had had an oral examination were likely to be better educated about and more aware of the risks of oral cancer than those who had not had such an examination.[22]

Clinical features

Oral squamous cell carcinoma presents in a variety of ways but most early lesions are asymptomatic. Premalignant and early malignant lesions may present as painless white or red patches. Lesions that look speckled—that is, non-homogeneous—or those that exhibit erythroplasia are more likely to have evidence of severe dysplasia on histological examination than homogeneous white patches. Some malignant lesions present as small, indolent ulcers. Many premalignant lesions regress if tobacco use is stopped. Lesions of intermediate malignancy may present as persistent ulceration with fixation to underlying tissues and regional lymph node enlargement. Late stage oral malignancy may result not only in large, indurated, crater-like ulcers with rolled margins but also in bony destruction, leading to mobile teeth, loss of teeth, or even pathological fractures. These may be associated with pain, numbness, or paraesthesia.

Figure 1 shows a white homogeneous patch in the floor of the mouth of a smoker. A biopsy of this showed mild epithelial dysplasia. Figure 2 shows a speckled white patch in the buccal mucosa of a male smoker. Figure 3 shows an erythematous lesion on the lower alveolus near the wisdom tooth area. Biopsies of the lesions in figures 2 and 3 confirmed the presence of squamous cell carcinoma. Figure 4 shows a typical late stage squamous cell carcinoma.

Details of how rarer types of cancers present are shown in the table.

Fig 1 Homogeneous white patch in mouth of a smoker. Biopsy of the lesion showed mild epithelial dysplasia

Fig 2 Speckled white patch in buccal mucosa of male smoker. Identified by biopsy as squamous cell carcinoma

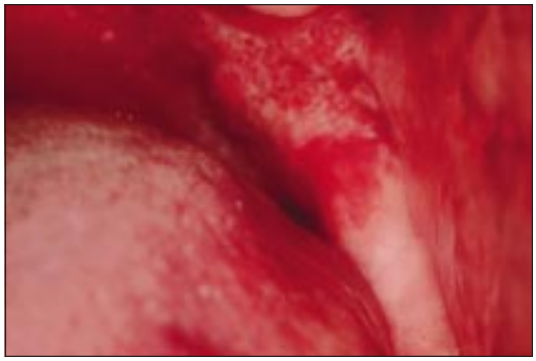

Fig 3 Erythematous lesion on lower alveolus near wisdom tooth area. Identified on biopsy as squamous cell carcinoma

Fig 4 Typical late stage squamous cell carcinoma

Investigations

The most useful investigations for suspected oral malignancy are representative biopsies, which may be taken from more than one area. These are usually done under local anaesthesia but occasionally an examination under general anaesthesia is useful. Intra-oral radiographs, orthopantomograms (radiographs of both jaws), and computed tomography scans may help define the extent of the lesion and any bony or nodal involvement.

Management

In the United Kingdom, upper aerodigestive tract neoplasms are treated by ear, nose, and throat specialists; oral and maxillofacial surgeons; plastic surgeons; and oncologists.[23] There is no systematic collection of basic data, there are few combined clinics, and the use of other support services is variable.[23]

Treatment for oral cancer is principally surgical. Few patients are treated solely with radiotherapy and even fewer with chemotherapy. Radiotherapy and chemotherapy are often used for adjuvant and adjunctive therapy. The factors that affect the choice of treatments for individual patients are beyond the scope of this article.

The aim of surgical management is to excise the entire lesion to eliminate possible channels of spread, such as the lymphatic system, nerves, and blood vessels. This ablative surgery is followed by reconstructive surgery which is used to improve healing and restore function and improve the patient's quality of life. Debulking surgery is used as a palliative measure for incurable tumours. Some surgical procedures only involve soft tissues. Others involve both hard and soft tissues. The patient in figure 3, for example, had an excision of the maxillary alveolus. Neck dissection is frequently required, with a consequent increase in postoperative morbidity. Reconstruction may involve not only skin grafts and flaps, but also bony grafts and implants.

Rarer types of oral cancer

Type of tumour	Principal site	Principal presentation
Salivary gland	Palate, floor of mouth	Soft lumps
Melanoma	Palate, gingiva	Brown or black patches
Lymphoma	Tongue, palate, gingiva	Rapidly growing ulcer
Leukaemia	Gingiva, whole mouth	Enlargement, redness, candidiasis

Radiotherapy is rarely used as a primary treatment; it is used either to debulk the tumour before surgery or to prevent recurrences and eliminate residual tissue after an incomplete resection. The complications of radiotherapy include oral mucositis and osteoradionecrosis, which present difficult management problems. Radiotherapy is also used if extracapsular spread is thought to have occurred; in this case, it is done within six weeks of surgery.

Chemotherapy is used nearly exclusively as a palliative treatment when there has been a local recurrence or metastases. However a meta-analysis of 42 randomised controlled trials involving 5079 patients has shown that adjuvant chemotherapy for squamous cell carcinomas of the head and neck results in a significant improvement in survival (relative hazard ratio of dying 0.89) but at the cost of a significant increase in morbidity (toxicity was increased with a relative proportion of 2.17).[24]

The principles of the treatment of oral cancer and its sequelae are well described in the specialist literature.[25] Few studies have assessed the quality of life and coping strategies of patients who have undergone surgery.[25-28]

A systematic review of the management of oral neoplasms is needed to provide the information required for patients and their medical advisers to make more informed choices about treatment.

Conclusion

The prognosis for large oral neoplasms remains poor. Healthcare professionals can make a large impact on the morbidity and mortality caused by oral cancer by referring patients with possible early or premalignant oral lesions for a specialist opinion as soon as possible. Raising public awareness of oral cancer may also assist in early diagnosis. A successful public health campaign to reduce the use of tobacco would also reduce the incidence of this condition, as has been shown in India.[16]

I thank Dr Martin Underwood for his constructive comments.
Competing interests: None declared.

1 Swango PA. Cancers of the oral cavity and pharynx in the United States: an epidemiologic overview. *J Public Health Dent* 1996;56:309-18.
2 Bhatti N, Downer MC, Bulman JS. Public knowledge and attitudes on oral cancer: a pilot investigation. *J Inst Health Educ* 1995;32:112-117.
3 Cochrane Collaboration. *Cochrane Library*. Issue 3. Oxford: Update Software, 1998.
4 *Best evidence 2: linking medical research to practice* [database on CD Rom]. Philadelphia: American College of Physicians, 1998.
5 Hindle I, Downer MC, Speight PM. The epidemiology of oral cancer. *Br J Oral Maxillofac Surg* 1996;34:471-6.

6 Boyle P, Macfarlane GJ, Zheng T, Maisonneuve P, Evstifeeva T, Scully C. Recent advances in epidemiology of head and neck cancer. *Curr Opin Oncol* 1992;4:471-7.
7 Macfarlane GJ, Boyle P, Evstifeeva TV, Robertson C, Scully C. Rising trends of oral cancer mortality among males worldwide: the return of an old public health problem. *Cancer Causes Control* 1994;5:259-65.
8 International Agency for Research on Cancer. *Tobacco smoking*. Lyons: IARC, 1986. (Monograph 38.)
9 International Agency for Research on Cancer. *Alcoholic beverages*. Lyons: IARC, 1989. (Monograph 42.)
10 Johnson NW, ed. *Oral cancer: detection of patients and lesions at risk*. Cambridge: Cambridge University Press, 1991.
11 McKaig RG, Baric RS, Olshan AF. Human papilloma virus and head and neck cancer: epidemiology and molecular biology. *Head Neck* 1998;20:250-65.
12 Goldstein AM, Blot WJ, Greenberg RS, Schoenberg JB, Austin DF, Preston-Martin S, et al. Familial risk in oral and pharyngeal cancer. *Eur J Cancer B Oral Oncol* 1994;30B:319-22.
13 King GN, Healy CM, Glover MT, Kwan JT, Williams DM, Leigh IM, et al. Increased prevalence of dysplastic and malignant lip lesions in renal-transplant recipients. *N Engl J Med* 1995;332:1052-7.
14 Gupta PC, Bhonsle RB, Murty PR, Mehta FS, Pindborg JJ. Epidemiologic characteristics of treated oral cancer patients detected in a house-to-house survey in Kerala, India. *Indian J Cancer* 1986;23:206-211.
15 Gupta PC, Mehta FS, Pindborg JJ, Bhonsle RB, Murti PR, Daftary DK, et al. Primary prevention trial of oral cancer in India: a 10-year follow-up study. *J Oral Pathol Med* 1992;21:433-9.
16 Gupta PC, Murti PR, Bhonsle RB, Mehta FS, Pindborg JJ. Effect of cessation of tobacco use on the incidence of oral mucosal lesions in a 10-yr follow-up study of 12,212 users. *Oral Dis* 1995;1:54-8.
17 Ahmed S, Rahman A, Hull S. Use of betel quid and cigarettes among Bangladeshi patients in an inner-city practice: prevalence and knowledge of health effects. *Br J Gen Pract* 1997;47:431-4.
18 National Screening Committee. *First report of the NSC*. London: Department of Health, 1998.
19 Wilson JMG, Jungner G. Principles and practice of screening for disease. Geneva: Public Health Papers, World Health Organisation, 1968;34.
20 Dimitroulis G, Reade P, Wiesenfeld D. Referral patterns of patients with oral squamous cell carcinoma, Australia. *Eur J Cancer B Oral Oncol* 1992;28B:23-7.
21 Jovanovic A, Kostense PJ, Schulten EA, Snow GB, van der Waal I. Delay in diagnosis of oral squamous cell carcinoma: a report from the Netherlands. *Eur J Cancer B Oral Oncol* 1992;28B:37-8.
22 Horowitz AM, Goodman HS, Yellowitz JA, Nourjah PA. The need for health promotion in oral cancer prevention and early detection. *J Public Health Dent* 1996;56:319-30.
23 Edwards D, Johnson NW, Cooper D, Warnakulasuriya KA. Management of cancers of the head and neck in the United Kingdom: a questionnaire survey of consultants. *BMJ* 1997;315:1589.
24 El-Sayed S, Nelson N. Adjuvant and adjunctive chemotherapy in the management of squamous cell carcinoma of the head and neck region: a meta-analysis of prospective and randomised trials. *J Clin Oncol* 1996;14:838-47.
25 Dimitroulis G, Avery BS. *Oral cancer: a synopsis of pathology and management*. Oxford: Wright, 1998.
26 Velanovich V. Choice of treatment for stage I floor-of-mouth cancer: a decision analysis. *Arch Otolaryngol Head Neck Surg* 1990;116:951-6.
27 Harrison LB, Zelefsky MJ, Pfister DG, Carper E, Raben A, Kraus DH, et al. Detailed quality of life assessment in patients treated with primary radiotherapy for squamous cell cancer of the base of the tongue. *Head Neck* 1997;19:169-75.
28 Chaturvedi SK, Shenoy A, Prasad KM, Senthilnathan SM, Premlatha BS. Concerns, coping and quality of life in head and neck cancer patients. *Supportive Care in Cancer* 1996;4:186-90.

Lesson of the week

Orbital trauma: do not blow your nose

G N Shuttleworth, D B David, M J Potts, C N Bell, P G Guest

Patients with proved or suspected orbital or sinus fractures should be told not to blow their nose and should be prescribed prophylactic antibiotics

Bristol Eye Hospital, Bristol BS1 2LX
G N Shuttleworth, *registrar in ophthalmology*
D B David, *fellow in orbital/oculoplastics*
M J Potts, *consultant in ophthalmology*
Department of Oral and Maxillofacial Surgery, Bristol Dental Hospital, Bristol BS1 2LX
C N Bell, *senior dental officer*
P G Guest, *consultant in maxillofacial surgery*
Correspondence to: Dr Shuttleworth

BMJ 1999;318:1054–5

Orbital infections may be divided into preseptal cellulitis, in which infection is located anterior to the orbital septum (a thin sheet of fibrous tissue arising from the periosteum of the orbital margin and inserting into the tarsal plates), and orbital cellulitis, in which there is infection of orbital tissues posterior to the orbital septum. Preseptal cellulitis generally responds to oral antibiotics and rarely has important sequelae. However, orbital cellulitis is a serious infection which may be complicated by abscess formation (subperiosteal, orbital, or brain), meningitis, septicaemia, cavernous sinus thrombosis, and death. Although orbital cellulitis is related to ethmoid sinusitis in 70-80% of cases,[1] it may also develop after orbital or sinus trauma.[2 3] Prompt and appropriate management of patients with orbital cellulitis or at risk of developing this minimises the risk of complications.

Case history

A 16 year old girl attended her local casualty department after sustaining a blow to the right side of her face. Facial radiography showed a minimally displaced fracture of her right zygoma. She was sent home and told to report three days later to the Bristol Eye Hospital. She was not given antibiotics or told not to blow her nose, nor was she warned about symptoms that would require prompt review.

When she was seen at the eye hospital, the girl was feverish and feeling unwell, and the right side of her face had become swollen, red, and tender (fig 1). She said that her facial swelling had increased suddenly on the previous day, after she had blown her nose. Ocular examination showed an immobile, proptotic eye with a fixed dilated pupil. She had an afferent pupillary defect and her vision was limited to perception of light. The patient's fundus was pale (infarcted) and looked funnel-like. Urgent computed tomography showed gross proptosis with the globe compressed into a conical shape (fig 2); fractures of the lateral wall of the maxillary sinus, the orbital floor, and the zygomatic arch; and diastasis of the zygomaticofrontal suture. There was opacification of the ethmoid, frontal, and maxillary sinuses, and gas was noted in the periorbital tissues.

The patient was immediately started on intravenous cefuroxime and flucloxacillin, and intravenous metronidazole was added 12 hours later. Despite this treatment her condition deteriorated and a purulent discharge began draining from her palpebral aperture. She had emergency surgery and a large amount of pus and necrotic tissue was removed from the posterior orbit and the maxillary and ethmoid sinuses. Postoperative antibiotic treatment consisted of intravenous cefotaxime (2 g three times daily), flucloxacillin (1 g four times daily), and metronidazole (500 mg four times daily).

After surgery the girl spent 18 hours in intensive care. *Streptococcus milleri*, a common cause of deep seated abscesses and an occasional inhabitant of the upper respiratory tract, was cultured. Over the course of a week her facial swelling reduced and she was discharged home and given oral antibiotics. At discharge her facial swelling and proptosis had reduced appreciably, but her eye remained virtually immobile, her pupil was still fixed and dilated, and her vision was limited to perception of light. Four months later there was still little ocular movement or lid function and visual acuity was limited to hand movements.