

A Look at Oral Cancer - Specifically Tongue Cancer

Una nic Ionmhain, 5th Year Medicine

Clinical Points

- Oral cancers arise between the lips and the anterior pillar of the fauces. They are the 6th most common malignancy worldwide. 90% being SCCs
- Risk factors include, smoking, alcohol, family history and premalignant lesions
- A thorough history and physical are necessary. A 3 week history of a mouth ulcer and cervical lymphadenopathy should be treated as urgent.
- Management is multidisciplinary. Depending on staging, treatment is surgical or with radiotherapy. A dissection of the neck may also be necessary.
- The 5 year survival rate for lesions less than 2cm, without lymph node involvement, is 80%. This is reduced by 50% with cervical node involvement. Therefore, focus should be on early diagnosis and preventative measures

ABSTRACT

Oral cancers are defined as neoplasms arising between, and including, the lips and the anterior pillar of the fauces. Ninety percent of carcinomas arising in this region are squamous cell carcinomas¹. These cancers are managed differently depending on their staging and location. Many are silent lesions, presenting at a late stage, making treatment difficult and resulting in a low survival rate with this form of cancer. It is very rare in the West, with over 4500 cases diagnosed a year in the UK², in contrast with Asia where it accounts for up to 40% of cancers³. Treatment is either surgical or radiotherapeutic, depending on the staging of the tumours. Prognosis is significantly worse in later stages, with a 45% to 65% survival rate when metastatic nodes in the neck are present⁴.

Case History

Patient A, a gentleman in his sixties, presented to the outpatient department with a five month history of a tongue lesion that was initially noticed on a routine dental examination.

He reported constant throbbing pain confined to the right side of the tongue. The pain worsened while eating. The lump had enlarged over the past 5 months and he reported some dryness of the mouth, halitosis and an intermittent tingling sensation in the lower jaw, neck and shoulders.

There was no dysarthria, dysphagia or odynophagia. He had no history of mouth ulcers, leucoplakia, erythroplakia or lichen planus. He reported no alteration in sensation or taste, no bleeding, no hoarseness or dysphonia. He denied weight loss, fatigue, loss of appetite and was not aware of any palpable lumps specifically in the head and neck region.

Patient A had a significant smoking history of 22.5 pack years. He ceased smoking 30 years ago. He consumes 28 - 36 units of alcohol a week. He had no family history of malignancy.

Investigations

He was referred for biopsy which diagnosed squamous cell carcinoma (SCC) of the tongue. Subsequent investigations, including CT and MRI, did not reveal any metastatic spread. He was admitted for laser excision of the lesion and selective neck dissection.

ENT Examination

Mouth: The right lateral border of A's tongue showed a palpable raised, irregular, poorly demarcated swelling, approximately 1 - 2 cm in size. The lesion was non ulcerated and non necrotic. It was not bleeding and had no rolled edges. There was no evidence of leukoplakia, lichen planus, erythroplakia or other premalignant lesions. All mucosal surfaces were intact. There were no other palpable masses on the base of the tongue or the floor of the mouth.

Ear and Nose: No abnormality

Neck: There were no palpable or visible lumps or cervical lymphadenopathy.

All cranial nerves were intact.

All other systems were normal on examination.

Summary

In summary, Patient A is a gentleman in his sixties admitted for partial glossectomy and selective neck dissection to resect a lateral tongue SCC and a clinically node negative neck.

DISCUSSION

Definition

Oral cancers are defined as neoplasms arising between, and including, the lips to the anterior pillar of the fauces.¹ More than 90% of carcinomas arising in the head and neck are SCCs.¹ Others include salivary gland tumours, lymphoreticular, haemopoetic, primary bone tumours, malignant melanomas, sarcomas and metastatic disease.^{5, 6} Clinically, the most common sites include the buccal mucosa, the floor of the mouth, the lateral and ventral tongue and the retromolar trigone.³

Epidemiology

Oral cancers are rare in the UK and Ireland. Over 4500 new cases (2003) are reported each year in the UK.² The incidence is rising primarily amongst men.⁷ In combination, oral and oropharyngeal are the 6th most common malignancy globally.⁵ Although the incidence is low in the West (2-4%), in Asia, it ranks amongst the three most common malignancies,⁸ with an incidence of up to 40% in some parts of India.³ It is most commonly seen in the male population over 60 years of age.⁷ There have, however, been recent reports of increasing incidence amongst females and young males in Europe and North America without a history of alcohol or tobacco use.³ The disease carries significant morbidity and mortality. In Britain, over 1400 people die of oral SCC every year.² Survival is very dependent on staging. Late presentation results in late treatment and poor prognosis.⁸

Risk Factors

The best documented risk factor for oral neoplasia is smoking tobacco. Approximately 75% of patients have a smoking history.⁶ In Asia and the Far East, there is a large association with smoking PAN (a combination of betel vine, areca nut, lime and tobacco) or the practice of reverse smoking - with the burning end in the mouth.^{3,5} Alcohol, especially brown spirits, acts synergistically with tobacco to increase the risk of cancer.⁹

Other risk factors include genetic susceptibility, poor oral hygiene and oral mouthwashes⁹, and a poor diet low in vegetables and anti oxidants. Some newer studies have linked HPV 16, 18 and 33 with increased risk of developing the disease.¹⁰

There seems to be no doubt that significant associations exist between premalignant lesions and oral cancers, although the precise nature of these associations continues to be debated. Leucoplakia is defined as "a white patch or plaque that cannot be characterised clinically or pathologically as any other disease"³. Its appearance varies. Previously thought to carry a high risk of malignant change, it is now thought to be between 3-6%¹⁰. The risk increases with the age of the patient.

Erythroplakia, a very rare velvet red lesion seen in the mouth, on the tongue or soft palate of patients in their sixties to seventies, is more significantly associated. On biopsy, 70 - 90% are invasive carcinoma, carcinoma in situ, or dysplastic.¹¹ The incidence of malignant change is 17 times higher in erythroplakia than leucoplakia, and the lesion must be excised.³ Other associated conditions include chronic hyperplastic candidiasis, oral submucosal fibrosis, syphilitic glossitis, and sideropenic dysphagia.³ The role of lichen planus is still debated. It is worth noting that many of these premalignant lesions do regress and are not necessary for the cancer to occur.^{3, 11}

Clinical Features of Tongue Cancer

Most patients with tongue cancer are asymptomatic or may be misdiagnosed by their health care provider and given anti fungal treatment, steroids or mouthwash. This often results in late diagnosis.

Of the tongue cancers:

- 51% occur on the lateral margin of the middle third of the tongue
- 25% occur in the posterior third
- 20% in the anterior third
- 4% occur on the dorsum.³

They manifest in different ways:

- An exophytic and ulcerated lesion
- An ulcer within a fissure,
- An area of superficial ulceration in which muscle infiltration has occurred
- A leucoplakia associated lesion
- An asymptomatic atrophic depapillated area.³

Intermediate lesions present as a persistent fixated ulcer and there may be lymphadenopathy. Late lesions manifest as large indurated crater ulcers with granular floors and rolled margins. There may be pain, numbness or parasthesia. Pain may be severe and radiate to the neck and ears.⁵ Lesions may be bleeding and necrotic.

Lymph node metastases are common in later stages. Fifty percent of patients have palpable nodes at presentation. There is early nodal spread in this form of cancer, so that 12% of patients who present with a lump in the neck show no evidence of a primary cancer.³ Any patient with an ulcer present for more than three weeks and cervical lymphadenopathy should be considered at risk.⁶

Investigations

An extensive history and examination must be carried out with emphasis on dates and onset. The physical examination must include examination of the inner and outer oral ring and mucosa, the area behind the fauces pillar, the parotid duct and the tongue. The floor of the mouth and base of tongue must be palpated. Bite

should be assessed, and relevant cranial nerves examined.⁹ A thorough examination is needed as there is a high association with synchronous and metachronous primaries occurring in the aerodigestive tract in up to 15% of patients¹². The neck must be palpated thoroughly for cervical lymphadenopathy. A full clinical work up should include liver function tests, as head and neck cancers may metastasise to the liver. A full blood count, urea and electrolytes, coagulation screen, along with a group and hold should be obtained if considering surgical management.

The lesion must be biopsied under local or general anaesthetic depending on its size. The most suspicious part of the lesion must be taken and some normal adjacent mucosa, taking care not to biopsy bleeding or necrotic areas as this will interfere with the findings. Some lesions are examined under anaesthetic so the patient can be in a relaxed state permitting thorough visualisation. If there is a neck lump, a fine needle aspirate must be performed.

Due to the high incidence of synchronous and metachronous tumours in the oropharyngeal area, endoscopic investigations are commonly performed. These investigations include laryngoscopy, oesophagoscopy and bronchoscopy and any suspicious lesion will be biopsied. A dental examination must be performed with focus on dental hygiene, dentition status and the integrity of the mandible. This is paramount if considering radiotherapy.

Radiographic investigations should include plain film x-rays of the oral cavity to assess involvement of the mandible. A chest x-ray should also be obtained in view of metastatic spread and also as part of the preoperative assessment. A CT (which will show metastatic spread) and MRI (which will illustrate the soft tissue infiltration) should be obtained. Radionuclear scanning is of little value in primary oral cancer - obvious clinical disease usually precedes any findings. An ultrasound can be obtained of the abdomen when investigating liver metastases^{3,5,6}. After radiographic scanning, the patients stage increases in 30% of cases. Staging follows the TNM or TANIS guidelines¹ (Table 1).

Table 1 - TNM Staging in Oral Cancer

Stage I	T1 N0 M0
Stage II	T2 N0 M0
Stage III	T3 N0, T1-3 N1, and M0
Stage IV	T4 any N, T1-3 N2-3, any T any N M1

Management

Management is multi disciplinary, involving an oncologist, otolaryngologist or maxillofacial surgeon, plastic surgeon, radiotherapist, pathologist and speech and language therapy. Treatment of choice is dependent on several factors. Can the lesion be easily excised or should radiotherapy be considered? There is debate with regards to which is the better of these, especially as cure rates are similar in the intermediate stages T1, T2, T3.

Surgery is indicated in lesions which are easily accessible and also if there are multiple primaries. Larger masses with bony involvement are treated with extensive surgery. Any involvement of cervical lymph nodes requires surgical resection with either a radical neck dissection or selective neck dissection. Surgery is also indicated in a patient with a history of recurrent tumours and previous irradiation. As radiotherapy may induce malignant change at a later stage in a younger patient, surgery is preferable. Histologically, adenocarcinomas and melanomas are radioresistant, therefore surgery should be considered. The grade of SCC does not influence management as much, except with verrucous carcinoma, in which radiotherapy may make it more anaplastic.

Radiotherapy is indicated in primary treatment. It can also be used to debulk the cancer or to prevent recurrences. It should also be considered in older patients who are poor surgical candidates.³ Post operative combination radiotherapy and chemotherapy are offered in advanced disease.¹³ If radiotherapy is being provided, a dental evaluation must be sought to decide if teeth in the field of irradiation need to be extracted. This generally involves

- 1) removal of teeth with advanced caries
- 2) teeth with advanced periodontal involvement
- 3) teeth with periapical pathology.¹⁴

Chemotherapy is mainly used in palliation.⁵

Surgical Management

Treatment of choice is intraoral excision. The size of the lesion dictates the surgical management. If less than a third of the tongue is involved, it is excised without any grafting and allowed to heal by secondary intention³. Excision is performed with a 2cm margin. For partial glossectomies a CO₂ laser is frequently used as it decreases post operative pain, oedema and scarring. If the lesion is greater than 2cm, a hemiglossectomy is done. If there is more extensive involvement a major resection is necessary, involving radial or pectoral flap reconstructions.

Neck Management

There is significant evidence of early micrometastatic spread to the cervical lymph nodes with oral cancers. They are thought to be present in up to 20% of

node negative patients. Survival of patients is far lower once cervical lymph nodes become involved. Therefore, there is a debate about whether a selective neck dissection should be done on a patient with a clinically node negative neck.

Retrospective studies have shown an improvement in survival with an elective neck dissection versus later surgical salvaging. Some centres employ a watch and wait policy, but problems occur with patients failing to attend follow up. Block dissection does carry negligible mortality and acceptable morbidity. Failure to control neck metastases results in death.

However it is worth noting that it is no guarantee against recurrence and lymph node removal might make recurrence of the primary or a second primary more difficult. Prospective studies have shown little statistical difference in survival between those treated with neck dissection and those that were monitored.³ To guarantee the removal of all positive nodes, one would have to remove 96% of them.

The neck is divided into five levels. The neck dissection can be radical or more recently modified or selective where the internal jugular vein, sternocleidomastoid and the accessory nerve are preserved. Depending on the extent of the spread in the neck these levels are dissected. Squamous cell carcinoma of the tongue drains to levels I and II initially with involvement of the inferior groups in the chain as the disease spreads.⁴ In clinically node negative necks, only the supraomohyoid levels (levels I - III) are dissected.¹⁵ Prospective studies show control rates in selective neck dissection that are similar to modified radical neck dissection with N0. If there is involvement of level IV, then post operative radiotherapy is offered which improves regional control.¹⁶ Oral cancers rarely present with bilateral nodal involvement. If there is an unusually large primary, it is treated with external radiation. A bilateral neck dissection is performed with a radical dissection done on the ipsilateral side and selective neck dissection on the contralateral side.

Expected Course / Prognosis

Prognosis is largely dependent on stage of presentation. In spite of surgical advances, the overall five year mortality has changed little over the past few decades. Without nodal involvement the 5 year survival rate is 80%. Survival rate is reduced to between 45% and 65% in patients with metastases, depending on the extent of nodal involvement⁴. Many of these patients have co-morbidities related to their drinking or smoking habits which lead to a worse prognosis.

Prognosis is worse with lesions which arise posteriorly in the oral cavity as they tend to be diagnosed later and have rich lymphatic drainage which favours early metastatic spread. Females tend to have a better

prognosis as they tend to be diagnosed and treated earlier than their male counterparts. This is a reflection of the fact that females attend the dentist more regularly than males. Age also influences prognosis as patients become less able to withstand surgery and radiotherapy with advancing age. As previously explained, these patients are at risk of additional primary neoplasms in the aerodigestive tract. This occurs in up to 25% of patients who have oral cancer for greater than 3 years and in up to 40% of those that continue to smoke.⁵ Additional complications of treatment must also be noted, such as infection, bleeding, a reaction to the general anaesthetic and an overall reduction in the patient's quality of life secondary to the resection. Radiotherapy is associated with an increased risk of oral mucositis, xerostomia and osteoradionecrosis.

Prevention

Primary prevention can be achieved by advising cessation of smoking and moderation of alcohol intake. Smoking cessation has also been shown to be associated with regression of pre-malignant lesions such as leucoplakia. Other suggestions include the improvement of diet and the use of antioxidants to prevent recurrence or prevent malignant transformation. However, this has not been proven. Among the reasons cited for poor prognosis in oral cancer are poor knowledge and education about the presentation of oral cancer. Screening and educational campaigns have also been suggested, however, in the west oral cancers are rare so that screening may not be cost effective.

Dental care has a major role in the prevention and detection of oral squamous cell carcinoma. However, lower socio-economic groups and other groups such as the elderly rarely attend for dental care. Therefore, in the interest of preventive care, regular dental check ups should be encouraged by offering financial assistance to patients within such groupings.⁸

Poor referral rates from doctors are believed to arise from a failure to recognise signs and symptoms. This is thought to be partly due to the lack of emphasis on oral examination in medical school. Therefore medical student education is an important target in prevention.

CONCLUSIONS

Oral Cancers are extremely rare in Ireland, but they carry significant rates of mortality. As early diagnosis vastly improves the 5 year survival rate, more time should be spent educating patients and health care professionals about the condition. Doctors should be aware that it is a clinical necessity to examine the oral cavity and be aware of the possibility of oral malignancy.

REFERENCES

1 Zakrzewska Joanna M. Fortnightly review: Oral cancer British Medical Journal 1999;318;1051-1054 BMJ

- 2 Scully C, Porter S: ABC of oral health Oral Cancer. BMJ 2000;321:97-100
- 3 Bailey H, Love McN. Short Practice of Surgery 24th edition London, Hodder Arnold 2004 702 -717
- 4 Hindle I, Downer MC, Speight PM. The epidemiology of oral cancer. Br J Oral Maxillofac Surg 1996; 34: 471-476.
- 5 Hindle I, Nally F. Oral cancer: a comparative study between 1962-67 and 1980-84 in England and Wales. Br Dent J 1991;170:15-20.
- 6 Hutchison IL Editorials Improving the poor prognosis of oral squamous cell carcinoma BMJ 1994;308:669-670 (12 March)
- 7 Cushieri A, Grace PA, Darzi A, Borely N, Rowley DI. Clinical Surgery 2nd edition Oxford, Blackwell Science 2003 719 - 721
- 8 Kumar, Cotran, Robbins Basic Pathology 7th Edition Philadelphia Elsevier 2003
- 9 Scully C, Porter S. Clinical review ABC of oral health. Swellings and red, white, and pigmented lesions. BMJ 2000;321:225-228 (22 July)
- 10 Carr RJ, Langdon JD. Multiple primaries in mouth cancer - the price of success. Br J Oral Maxillofac Surg 1989;27:394-9.
- 11 Sanderson R J , Ironside J A D. Squamous cell carcinomas of the head and neck. BMJ 2002;325:822-827
- 12 Bradley A. Schiff, MD; Dianna B. Roberts, PhD; Adel El-Naggar, MD, PhD; Adam S. Garden, MD; Jeffrey N. Myers, MD, PhD. Selective vs Modified Radical Neck Dissection and Postoperative Radiotherapy vs Observation in the Treatment of Squamous Cell Carcinoma of the Oral Tongue Arch Otolaryngol Head Neck Surg. 2005;131:874-878.
- 13 N. W. Yip, S. G. Patel, P. H. Rhys-Evans, N. M. Breach (1999) Management of the N0 neck in early cancer of the oral tongue Clinical Otolaryngology 24 (1), 75-79.
doi:10.1046/j.1365-2273.1999.00224.x
- 14 Poul Erik Petersen. Strengthening the prevention of oral cancer: the WHO perspective. Community Dent Oral Epidemiol 2005; 33: 397-9
- 15 UK Oral Cancer incidence statistics 2003
<http://info.cancerresearchuk.org/cancerstats/types/oral/incidence/>
- 16 Soames J.V. , Southam J.C. , Oral Pathology 4th Edition, Oxford, Oxford University Press. 2005 133-149
- 17 Ord Robert A., Blanchaert Remy H. Current management of oral cancer - A multidisciplinary approach; JADA, Vol. 132, November 2001
- 18 Meraw Stephen J., Reeve Charles M.; Dental Considerations and Treatment of the Oncology Patient receiving Radiation Therapy ; JADA, Vol. 129, February 1998