

Squamous Cell Carcinoma Arising Within Gingival Lichen Planus

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This report describes the appearance and management of an oral squamous cell carcinoma (SCC), which arose within an area of gingival lichen planus in an 80-year old female patient. The patient was under regular recall to monitor an area of desquamative gingivitis, the underlying cause for which was gingival lichen planus. In this paper we describe the rapid appearance of a superficial spreading invasive SCC, the investigations performed and the clinical course and management of the tumour. This paper also discusses the possibility that utilisation of topical oral steroids in the symptomatic management of erosive or atrophic oral lesions, may play a role in the initiation or progression of the malignancy.

Key words: gingival lichen planus, gingival squamous cell carcinoma, topical steroid therapy.

INTRODUCTION

Oral squamous cell carcinoma (SCC) is a malignant tumour of the epithelial cells of the oral mucosa and accounts for more than 90% of all head and neck cancers (Silverman, 2001). SCC's may arise in different areas of the oral cavity, the most common sites being the posterior ventero-lateral border of the tongue and floor of mouth (McGaw and Pan, 1996). Gingival SCC's account for approximately 9% of all intra-oral malignancies and are more commonly observed in the mandibular gingival tissues (60%) than the maxillary gingivae (40%) (McGaw and Pan, 1996).

This report documents a case of gingival SCC arising in an area of gingival lichen planus in the anterior mandible. The case is discussed and highlights the importance of clinical signs in ultimately arriving at a definitive diagnosis, the need to closely monitor the use of oral steroids and the importance of regular review of desquamative gingival lesions, in view of their potential for malignant transformation.

CASE REPORT

An 80-year-old woman attended the Periodontal Clinic at Birmingham Dental Hospital in October 2000 complaining of redness of the gums in her lower jaw. She had first noticed this appearance 18 months previously and the appearance and symptoms had persisted since this time without resolution. In addition she had soreness of the ocular mucosa. Medically she was taking the Angiotensin-Converting Enzyme (ACE) inhibitor Tanatril® (Imidapril Hydrochloride) for mild hypertension, but her symptoms had pre-dated any anti-hypertensive therapy. She had also undergone a hip replacement 12 months previously. The patient was a non-smoker and there was no history of significant alcohol intake. She had no detectable sub-mandibular or cervical lymphadenopathy and her oral hygiene was fair anteriorly, poor posteriorly and there was mild clinical xerostomia. There was a generalised desquamative gingivitis with some atrophic areas, but no evidence of ulceration or proliferation of the gingival epithelium. Careful exami-



Fig 1a–b A firm exophytic lesion approximately 3.5x2.5cm involving the right lower labial and lingual anterior gingivae adjacent to the 41, 42, 43 and 44 teeth.



Fig 2a–b Case radiographs at initial presentation.

Examination of the non-gingival oral mucosa revealed white striae in the left buccal sulcus and lower labial sulcus, classical of lichen planus. In view of the ocular soreness and mild clinical xerostomia the differential diagnosis included:

- atrophic lichen planus
- cicatricial pemphigoid
- primary Sjögren’s syndrome
- chronic periodontitis.

The following serological investigations were undertaken at the initial appointment to exclude the possibility of dual pathology:

- immunological screening (immunoglobulins, complement C3 & C4)
- anti-epidermal antibody screen (anti-basement membrane & anti-intercellular cement) to eliminate vesiculobullous disease.

- anti-Ro, anti-La, anti-centromere antibodies for Sjögren’s syndrome.

Serological investigation revealed a mildly raised IgM (2.92g/l; normal range 0.50-2.00g/l), but otherwise normal immunoglobulin and complement levels, no evidence of epidermal antibodies or markers of Sjögren’s syndrome, and therefore no labial salivary gland biopsy was performed. A clinical diagnosis of atrophic gingival lichen planus was made, the temporal relationship with her anti-hypertensive medication ruling out a lichenoid drug reaction. The patient was placed on soluble prednisolone 5 mg to be dissolved in water and used as a mouthrinse three times daily to manage her gingival symptoms, and a review appointment was arranged for three months’ time. At the review appointment she reported an im-

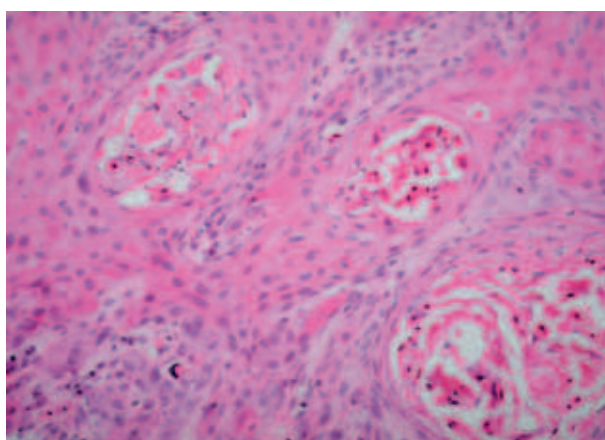
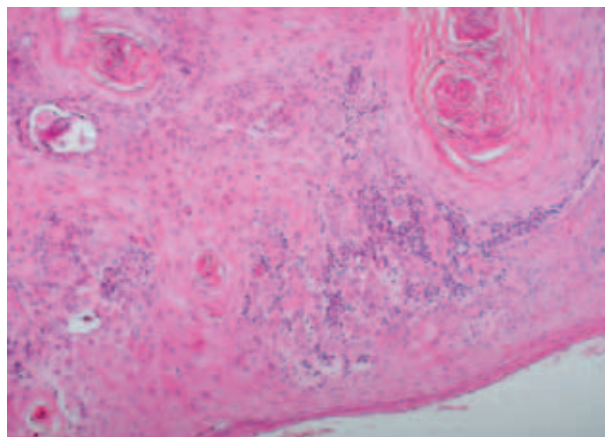
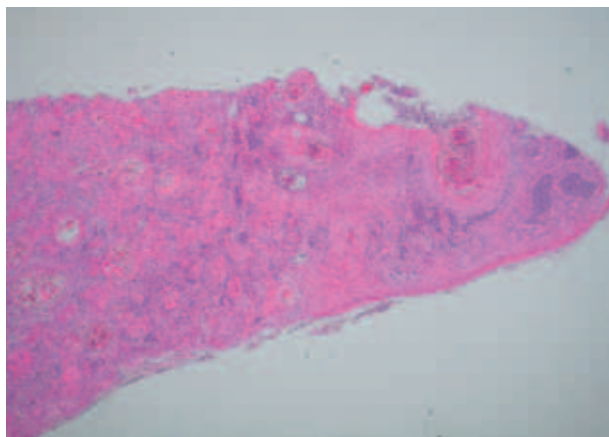


Fig 3a–c Histopathology of gingival carcinoma at various levels of magnification, demonstrating histological and cytological features of invasive epithelial cell tumour.

provement in her symptoms, having used the steroid mouth rinse for one month. She had also received oral hygiene instruction and scaling with the hygienist at her general dental practice. The overall appearance of the gingival and buccal mucosal tissues had improved, although a firm exophytic lesion approximately 3.5 x 2.5 cm had developed involving the right lower labial and lingual gingivae adjacent to the 41, 42, 43 and 44 teeth over the previous few weeks (Fig 1). This appeared as a superficial spreading lesion and had a granular surface and an indurated lower margin. The associated teeth had become slightly mobile. The rapid change in clinical appearance at this time led to the decision to perform an incisional biopsy of the area and a provisional diagnosis of gingival SCC arising within an area of gingival lichen planus was made. A difficulty arose in assessing the extent of the lesion with respect to the extent of involvement of underlying bone, because the bone loss demonstrated on radiographs may have been due to the pre-existing periodontal bone loss in the area (Fig 2).

An ellipse of tissue (10 x 3 x 2 mm) was removed under local anaesthesia and the histopathological report confirmed a gingival SCC. The histopathology is illustrated in Fig 3 and demonstrated '*mucosa covered by parakeratinised squamous epithelium arising in which is a SCC which infiltrates into the underlying corium. The carcinoma shows a variable degree of differentiation and is composed of sheets of neoplastic epithelial cells showing cellular pleomorphism and in some places*

vesicular nuclei. A moderate number of mitoses are also seen.'

At the review appointment, the implications of the diagnosis were discussed with the patient and immediate arrangements were made with a local consultant maxillo-facial surgeon for an assessment in the regional head and neck oncology clinic.

Pre-operatively, the patient had a gastric peg inserted in July 2001 to facilitate parenteral feeding, and she underwent a resection of the tumour on the right mandibular alveolus with a rim resection of the mandible. At the time of surgery, a right selective neck dissection (Level IV) was performed with reconstruction of the mandibular resection site using a left radial forearm free microvascular flap. A lower arch dental clearance and posterior repositioning of the left submandibular gland duct was also performed. The pathology revealed the tumour extended towards the deep surgical margin, but all of the other margins were reported as free of tumour. She had 16 lymph nodes in the neck dissection of which one positive intra-capsular node for SCC was recorded at level II.

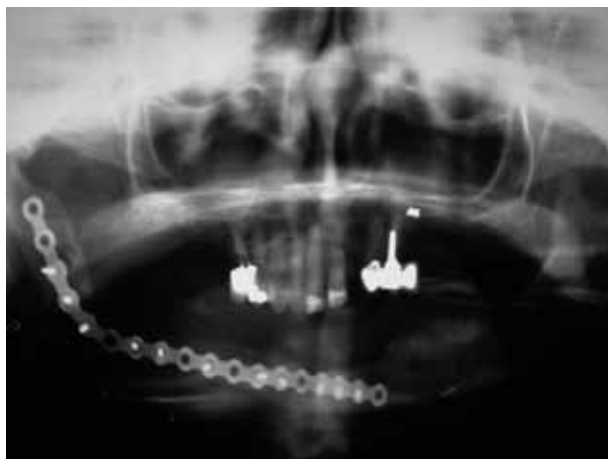


Fig 4a–b Case radiographs of mandibular reconstruction pre-prosthetic management.

In February 2002 she developed a lump in the left neck in the submandibular area, and cytology was inconclusive following a fine needle aspiration biopsy. In view of this, she underwent removal of a lymph node at level I in her left neck which showed an intra-capsular metastatic lesion. Consequently, a left selective neck dissection (Level IV) was performed, with no positive nodes reported for SCC. In November 2002 the patient developed a further lump in her right mandibular alveolus which proved positive on biopsy for SCC. In view of this, she underwent a tracheostomy and right hemimandibulectomy, with reconstruction using a composite scapular flap. The histopathology demonstrated tumour at depths of 7mm with no perineural or intravascular invasion, and complete excision was confirmed. However, as a precaution, and given that the tumour size was staged at T4, surgical management was supplemented with post-operative radiotherapy.

Subsequently, the patient has had her gastric peg removed and has made excellent progress (Fig 4).

DISCUSSION

The case presented raises a number of important issues:

The absence of risk factors other than gingival lichen planus

Squamous cell carcinoma, and indeed malignancies in general, have a complex and multifactorial



aetiology, whereby extrinsic factors such as tobacco, alcohol, nutrition and viruses may play a role along with non-modifiable risk factors such as age, immunity and genetics. All of these may be risk factors for the development of SCC within the 'co-carcinogen' model of carcinogenesis, whereby several factors interplay either simultaneously or consecutively to initiate the malignant transformation. In the current case, the likelihood of tobacco and alcohol playing a significant role is minimal, although other risk factors for tumour development cannot not be excluded. It is well reported in the literature that the incidence of malignant change arising within erosive and plaque-like lichen planus is increased, relative to normal tissue (range 0.4–3.2%), although the mechanisms underlying this are unclear (Silverman et al, 1985; Murti et al, 1986; Holmstrup et al, 1988; Silverman and Bahl, 1997; Rajenthiran et al, 1999; van der Meij et al, 2003). Of interest is that males and females are equally affected by gingival SCC, although this is in contrast to other oral SCC's where males have a twofold increased prevalence relative to females (Overholt et al, 1996). The majority of cases present in patients over the age of 40 years (Silverman, 2001) although extremely rare cases have been

described in paediatric and adolescent patient groups (Son and Kapp, 1985; Bill et al, 2001). The difficulty with the reported case was that the lichen planus presented as a desquamative gingivitis with no ulceration and no evidence of plaque formation. The clinical categorisation in this case was of an atrophic gingival and reticular mucosal lichen planus.

The possible role of topical oral steroids leading to suppression of local mucosal immunity.

At the initial appointment, a clinical diagnosis of desquamative gingivitis was made, and in the light of serology and other oral mucosal signs, atrophic lichen planus became the working diagnosis. The patient was prescribed soluble prednisolone tablets and instructed to use these as a mouthwash for two weeks to help alleviate her gingival soreness. Prednisolone used in this manner undergoes minimal transmucosal absorption relative to other topical steroids (Miller-Larsson et al, 2001). However, it remains a possibility that this topical steroid application suppressed mucosal immunity sufficiently to trigger malignant transformation in an area of incipient malignant disease, or acted as a co-factor in accelerating the rate of progression of a pre-existing sub-clinical lesion.

The importance of rigorous review of cases of gingival lichen planus.

This present case serves as a reminder of the importance of recognising the increased risk of malignant transformation within all forms of oral lichen planus. Whilst serology reduced the likelihood of dual pathology existing, the issue of whether a biopsy should have been performed to eliminate the existence of an in-situ lesion or cellular dysplasia is worthy of discussion. The clinical diagnosis of lichen planus can frequently be made with classical reticular disease (Fig 5) without subjecting patients to a biopsy. However, when desquamative gingivitis is the only oral sign of mucosal disease, the value of gingival biopsies is limited at best (for review see the focus article 'Desquamative Gingivitis: Investigation, Diagnosis and Therapeutic Management in Practice' by Andrea Richards in this volume). Histological inflammation is ubiquitous within the gingival connective tissues due to the presence of irritation from the subjacent plaque biofilm. Such inflammation masks more subtle characteristic inflammatory



Fig 5 Typical reticular lichen planus with associated pigmentary incompetence affecting the buccal mucosa.

changes associated with conditions such as lichen planus, rendering the biopsy of limited, if any, diagnostic value. In the current case, the existence of obvious mucosal lichen planus in conjunction with the negative serology was deemed sufficient to diagnose the desquamative gingivitis as lichen planus. Whilst there was no evidence of erosive or plaque-like lesions clinically at presentation and no suggestion of a localised area of malignancy within the desquamative gingivitis, histological confirmation was not possible for the above reasons and due to the impossible decision about which area of a uniform and generalised condition should be biopsied. The appearance of gingival SCC is variable ranging from the typical appearance of an aggressive lesion to that of a benign lesion, emphasizing the importance of establishing a correct diagnosis for all lesions (Kirkham et al, 1985). Indeed, gingival SCC has been reported within drug induced gingival overgrowth (McLoughlin et al, 1995). If any characteristics of the lesion change then an early biopsy is essential particularly given the variable nature of SCC presentation. The gingival SCC described in this report was a superficial spreading lesion whose clinical course was rapid and in view of this regular review of all forms of gingival lichen planus, irrespective of their clinical sub-categorisation is strongly recommended.

Assessment of extent of the lesion.

It is not unusual to observe periodontal bone loss on radiographs in 80-year-old patients. However, this case highlights the difficulties that may arise when SCC's of the gingival and periodontal tis-

sues arise. In the present case, it was not possible to determine whether the bone loss observed was due to periodontal disease, progression of the gingival SCC, or indeed a combination of both disease activities.

In summary, this paper has highlighted to the reader that oral squamous cell carcinoma and specifically gingival carcinoma may arise within all forms of gingival lichen planus and may result in a large area of field change, with rapid and superficial spread. Clinicians should interpret radiographs with caution, as there is a potential difficulty in differentiating bone loss due to tumour invasion and untreated periodontal inflammation. If changes in the appearance or consistency of lichen planus are noted, an immediate biopsy should be arranged. Finally, the use of topical steroids in the management of, in particular erosive oral disease should always be contemplated in the knowledge that there may be a role for local immunosuppression in the aetiology or pathogenesis of squamous cell carcinoma or indeed in the development of second primary tumours.

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REFERENCES

- Bill TJ, Reddy VR, Ries KL, Gampper TJ, Hoard MA. Adolescent gingival squamous cell carcinoma: Report of a case and review of the literature. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics* 2001;91: 682–685.
- Holmstrup P, Thorn JJ, Rindum J, Pindborg JJ. Malignant development of lichen planus-affected oral mucosa. *Journal of Oral Pathology* 1988;17:219–225.
- Kirkham DB, Hoge HW, Sadeghi EM. Gingival squamous cell carcinoma appearing as a benign lesion: report of case. *Journal of the American Dental Association* 1985;111:767–769.
- McGaw WT, Pan JT. Cancer of the gingiva, buccal mucosa, and palate. *Journal of the Canadian Dental Association* 1996;62:146–150.
- McLoughlin P, Newman L, Brown A. Oral squamous cell carcinoma arising in phenytoin-induced hyperplasia. *British Dental Journal* 1995;178:183–184.
- Miller-Larsson A, Gustafsson B, Persson C, Brattsand R. Gut mucosal uptake and retention characteristics contribute to the high intestinal selectivity of budesonide compared with prednisolone in the rat. *Aliment Pharmacol Ther* 2001;15:2019–2025.
- Murti PR, Daftary DK, Bhonsle RB, Gupta PC, Mehta FS, Pindborg JJ. Malignant potential of oral lichen planus: observations in 722 patients from India. *Journal of Oral Pathology* 1986;15:71–77.
- Overholt SM, Eicher SA, Wolf P, Weber RS. Prognostic factors affecting outcome in lower gingival carcinoma. *Laryngoscope* 1996;106:1335–1339.
- Rajenthiran R, Mclean NR, Kelly CG, Reed MF, Nolan A. Malignant transformation of oral lichen planus. *European Journal of Surgical Oncology* 1999;25:520–523.
- Silverman S, Jr., Bahl S. Oral lichen planus update: clinical characteristics, treatment responses, and malignant transformation. *American Journal of Dentistry* 1997;10: 259–263.
- Silverman S, Jr., Gorsky M, Lozada-Nur F. A prospective follow-up study of 570 patients with oral lichen planus: persistence, remission, and malignant association. *Oral Surgery, Oral Medicine, Oral Pathology* 1985;60: 30–34.
- Silverman SJ. Demographics and occurrence of oral and pharyngeal cancers. The outcomes, the trends, the challenge. *J Am Dent Assoc* 2001;132:7S–11S.
- Son YH, Kapp DS. Oral cavity and oropharyngeal cancer in a younger population. Review of literature and experience at Yale. *Cancer* 1985;55:441–444.
- Van Der Meij EH, Schepman KP, Van Der Waal I. The possible premalignant character of oral lichen planus and oral lichenoid lesions: a prospective study. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics* 2003;96:164–171.

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