A Rare Case Of A Salivary Gland Clear Cell Malignancy In The Nasal Cavity.
C Carmody, R Grigg

INTRODUCTION
The following is a rare case of clear cell carcinoma within the nasal cavity. The patient had a previous excision of a tumor that was said to be a pleomorphic adenoma. The original tumor had been sampled in Sri Lanka and the slides were not available for review. The definitive surgical specimen demonstrated that the tumour was definitively a clear cell carcinoma supported by immunostains (Professor John Chan Queen Elizabeth Hospital, Kowloon Hong Kong). This has never previously been reported in this location before.

Pleomorphic adenomas are the most common tumor of the major salivary glands. In addition, they may also occur in the minor salivary glands of the upper aerodigestive tract. Intranasal pleomorphic adenomas are unusual and may be misdiagnosed because they have greater myoepithelial cellularity and fewer myxoid stromata compared to those elsewhere.

CASE PRESENTATION
A 29-year-old Sri Lankan man initially presented to the department of Otolaryngology Head and Neck Surgery in Toowoomba Queensland Australia in December 2007, following referral from a local General Practitioner with a six-month history of nasal obstruction; additionally, there was no history of nasal discharge or epistaxis. It was non-responsive to decongestive sprays and a diagnosis of nasal polyps was made by the General Practitioner.

The patient also reported a blocked feeling in his ears (left > right), that had worsened recently. He experienced mild otalgia at times on the left side. There was no history of discharge from his ears.

His past medical history was significant in that he had a tumor excised from his hard palate in 1997 in Sri Lanka (pleomorphic adenoma). This initial diagnosis was unable to be verified here as no tissue or slides were available for re-examination. The report was given to the patient prior to the civil war in Sri Lanka but was apparently verified at a tertiary hospital.

His risk factors for head and neck cancer included the above mentioned lesion, combined with him being an ex-smoker ceased in March 2008 (3-4 cigarettes per day). There was no recent record of weight loss and the patient had a normal BMI.

Initial examination revealed a nasal lesion which was obvious endoscopically, totally blocking the right nasal airway at the posterior septum. Examination of the oral cavity revealed a scar to his hard palate but no obvious tumor. There were no palpable cervical nodes at the initial presentation. A biopsy of the tumor was performed.

Other investigations included CT and MRI scans of the Head and Neck. This reported a well-circumscribed lesion centered on the posterior hard palate and soft palate with bony destruction, illustrated below.
Figure 1
Figure 1: T1-weighted MRI with contrast demonstrating the centrally positioned lesion.

The pathology from the biopsy of the tumor demonstrated poorly differentiated malignant cells in varying sized fragments in a background of macrophages and abundant blood.

The case was discussed at a multidisciplinary Head and Neck Meeting, following this the young man was booked and consented and underwent a combined-approach resection of the tumor at the junction of the hard palate and soft palate along with a selective neck dissection. A radial forearm flap was used to reconstruct the through and through defect of the palate.

Initial histology from the resection demonstrated a mass of tumor tissue; 3x3x3cm (locally invasive tumor). The tumour appeared to show an infiltrative pattern with extensive stromal invasion. There was no evidence of vascular spread or perineural invasion; postoperative radiotherapy was undertaken. There were no lymph node metastases at the initial operation. This was consistent with a salivary gland carcinoma. Some clear cells were noted and the specimen sent for further opinion at a tertiary centre.

This opinion stated that the tumor may be a mucoepidermoid carcinoma; it was referred off-shore for further analysis. Repeat testing in Hong Kong by Professor John Chan Queen Elizabeth Hospital, Kowloon, demonstrated that the tumour was definitively a clear cell carcinoma supported by immunostains. This has never previously been reported in this location before.

Figure 2
Figure 2: MRI T1-weighted axial image outlining the above-mentioned lesion.

Figure 3
Figure 3: Post-excisional-biopsy image, histology shows a mass of tumor tissue; the tumor appears to show an infiltrative pattern with apparent stromal invasion and consists of uniform sheets of cells with a fairly low mitotic rate (morphology consistent with clear cell tumor).
Figure 4
Figure 4: The tumor of the soft palate is infiltrative, with islands and cords of polygonal tumor lying in a fibrous to desmoplastic stroma. Clear cells are seen in many areas. Thus the main considerations are mucoepidermoid, clear cell, and myoepithelial tumors.

Figure 5
Figure 5: Mucin PASD stain shows that there is no definitive intracytoplasmic mucin; this does not fit with mucoepidermoid carcinoma. The distinction between clear cell carcinoma and myoepithelial tumors is difficult on morphological grounds and immunostains are critical in the determination. The above slide demonstrates necrosis on the far right and tumor mass bordered by inflammatory stroma on the left.

The patient underwent subsequent postoperative radiotherapy, 50Gy in 25 fractions of 3d, conformal radiotherapy to hard palate/nasopharynx/postnasal cavity and both necks, and an additional 10Gy in 5 fractions to the tumor/surgical bed.

In September 2009 the patient developed a right-sided neck lump, and had a salvage right-sided modified radical neck dissection for regional recurrence. This showed only one node positive.

Figure 6
Figure 6: CT scan demonstrating a right-sided neck node prior to salvage surgery

A revision pharyngoplasty was performed for secondary velophalatine insufficiency and retropharyngeal incompetence. The patient was readmitted for a left buccinator flap and debulking of the palate after the original repair contracted and broke down. Since then the patient has made an uncomplicated recovery.

The patient has returned to work and is undergoing regular follow-up. He is now over 2 years out from the salvage neck dissection with no sign of recurrence.

DISCUSSION
Primary clear cell tumors of salivary origin fall into 2 distinct lineage restrictions – those that require evidence of myoepithelial differentiation and those that do not. Clear cell carcinoma is a classic and distinct entity that represents the latter differentiation pathway [26]. By definition, clear cell carcinoma contains a significant proportion of clear cells, but it does not fit into any other recognised neoplastic entities [26]. Although non-lipid and non-mucin, but glycogen-rich clear cell tumors in salivary glands have long been recognised [16-29], they were only recently included in the third WHO classification as a distinct low-grade carcinoma [30]. Most of these tumors have been reported as sporadic cases with the exception of a few well-documented series [18,26]. The natural course is an indolent, painless, submucosal mass that occurs predominantly in the minor
salivary glands of elderly women [16-20,22-30]. Little is known about the behaviour of malignant clear cell carcinomas of the nasal cavity. This case illustrates the risk of lymph node metastases.

Midline primary cancers are difficult to treat prophylactically and despite selective neck dissection and radiotherapy this patient had a recurrence in the neck. This was presumably a node that was missed at the original neck dissection and was resistant to radiotherapy. Thankfully, this has not led to disseminated metastatic disease at this point.

The most common benign tumors of the major salivary glands are pleomorphic adenomas, but in rare instances, they can occur in the respiratory tract (via minor salivary glands). Cases have been reported in the nasal cavity, paranasal sinuses, nasopharynx, oropharynx, hypopharynx, and larynx. In the upper respiratory tract, the most favored site of origin is the nasal cavity, followed by the maxillary sinus and the nasopharynx [2]. The first reported case in the literature of a pleomorphic adenoma of the nasal cavity was in 1929 [3]. Although the vast majority of minor mucous and serous glands are located in the lateral nasal wall, pleomorphic adenomas in the nasal cavity mostly originate from the nasal septum. Larger studies of intranasal pleomorphic adenoma include 40 cases reported by Compagno and Wong and 59 cases reported by Wakami et al. [4,5].

Pleomorphic adenomas of the nasal cavity and have been shown to be misdiagnosed in over half of cases leading to inadequate treatment initially. In view of the potential for tumor recurrence, long-term follow-up and careful examination of the nose with an endoscope are necessary [6,10]. They have a higher epithelial and lower stromal component compared to their major salivary gland counterparts and may be misdiagnosed at an early stage leading to more aggressive treatment. Malignant change arising in pleomorphic adenoma of the salivary glands is uncommon, with a reported incidence of 2-10 per cent [1,7]. Most of these tumors are carcinoma ex pleomorphic adenoma.

Carcinoma ex pleomorphic adenoma is a highly malignant tumor that should be considered in a differential screen, accounting for 11.7% of salivary malignancies [8,10]. It usually develops from malignant transformation of a long-standing pleomorphic adenoma. Five-year survival for all stages of carcinoma ex pleomorphic adenoma ranges from 30-76%, decreasing markedly for stage IV metastatic disease [8,9]. Only 27% of patients are alive one year after diagnosis of recurrence or metastasis.

Myoepitheliomas are other tumors to be considered, generally benign tumors with the parotid gland and palate accounting for three-fourths of all cases [11]. The age range is wide, and there is no significant gender predisposition of this tumor [11,13]. The plasmacytoid variant appears to have a predilection for the palate in slightly younger individuals, while the spindle cell type tends to occur in the parotid gland of older individuals [13,14]. On the other hand, clear cell tumors of the salivary glands are almost invariably malignant in nature, with rare exceptions in the form of myoepitheliomas and oncocytomas [14]. When benign, the tumor most often presents as an asymptomatic mass that slowly enlarges over a course of several months to years. Parotid lesions never produce facial dysfunction and those of the palate rarely ulcerate [11]. The lack of myoepithelial differentiation in clear cell carcinoma is consistent with the concept that this tumor is histomorphogenically distinct from epithelial-myoeipithelial carcinomas and that it is not merely a monomorphic variant [15].

CONCLUSION

The importance of this case report is the recognition of a rare tumor and the discussion of its behavior. Clear cell tumors of the salivary glands are almost invariably malignant in nature, with rare exceptions in the form of myoepitheliomas and oncocytomas. This is one of the first cases of a clear cell carcinoma of the nasal cavity. In this case radical treatment was required to control the disease. Unfortunately the original diagnosis can not be confirmed; however, the review is still valid, because of the rarity of this tumor and its recognition at a new location for this subtype of minor salivary gland tumor.

References
7. Laurie SA, Licitra L: Systemic therapy in the palliative
A Rare Case Of A Salivary Gland Clear Cell Malignancy In The Nasal Cavity.

Author Information

Cameron Carmody
Department of Otolaryngology Head and Neck Surgery, The Toowoomba Hospital

Roger Grigg
Department of Otolaryngology Head and Neck Surgery, The Toowoomba Hospital