Peer reviewed paper; submitted February 2020; accepted August 2020

Granular Cell Tumour of the tongue – a case report and literature review

Antunovic DM, Hunt J

Abstract

Granular cell tumour (GCT) is a relatively uncommon tumour. Although it is generally benign, malignancy can be a feature in up to 3% of cases. Most tumours are located in the head and neck, and 70% are intraoral. Whilst the tongue and the buccal mucosa are common intraoral sites, its presentation on the lateral aspect of the tongue can be alarming to both patient and clinician, as it may mimic a squamous cell carcinoma. The cellular origin of the lesion has historically been unclear. It has been thought to have arisen from striated muscle, histiocytic, mesenchymal and epithelial cellular origin. Current histochemical and ultrastructural studies favour neuroectodermal origin of the lesion from peripheral nerve/Schwann cells. The tumour generally occurs in middle or older aged adults but has also been seen in children. It is typically seen as a non-inflamed, asymptomatic mass measuring up to 2 cm in diameter of pink colouration with a yellowish surface. Complete surgical excision of the lesion is the treatment of choice.

Introduction

Granular cell tumour (GCT) is a mostly benign neoplasm that occurs in almost any part of the body. There is a very rare chance of these lesions becoming malignant (< 3%) (Barnes et al., 2005; Ramraje and Choudhury, 2010). Common sites include skin, upper respiratory-digestive tract (particularly the tongue and larynx), breast and vulva. There is a female preponderance of 2:1 (Thompson et al. 2013). It is a tumour composed of round and/or spindle cells with pink, granular cytoplasm due to abundant intracytoplasmic lysosomes. It was first described by Weber in 1854 and in 1926 Abrikossoff postulated a myogenic origin, terming the lesion a granular cell myoblastoma (Noonan et al., 1979).
The basic histologic features he described were a cellular framework of lenticular myeloblastic cells, some with longitudinal and crossed striations and others containing dark staining granules. It was this microscopic similarity to muscle fibres that led Abrikossoff to attribute the origin of this tumour to a myoblastic stem cell and to classify the lesion as a myoblastic myoma (myoblastenmyome) (Noonan et al., 1979). It has also been known as a granular cell myoblastoma, granular cell nerve sheath tumour and granular cell schwannoma (Barnes et al., 2005). Tumours are usually solitary but can be multiple in 10-15% of cases. They usually present as a slow growing, non-tender, rubbery, sessile submucosal mass. If the tumour is near the surface, a yellowish to creamy white colour is apparent (El Nagger et al., 2017).

Case report

A 32-year-old female was referred by her general medical practitioner with “a lump on her tongue”. It had been present for four weeks, with no pain or bleeding but she was extremely anxious that it could be “cancerous”. Her family history includes both her father and grand-father having had tongue cancer and her father had recently passed away. She had a history of infrequent cigarette smoking, taking no medications and had no known drug allergies and confessed to light-moderate alcohol use. She was also extremely anxious as she had attended “in tears worrying about this lesion”. There was no history of paraesthesia, dysphagia or referred earache.

On examination there was a firm, raised lesion on the left lateral aspect of the tongue which was well circumscribed (Figure 1). The lesion was 8 mm in diameter. There was no associated ulceration in the region of the tongue and on examination she exhibited no lymphadenopathy or any further signs or symptoms .

In May 2018, under local analgesia, the lesion was excised in toto and the material sent for microscopy.

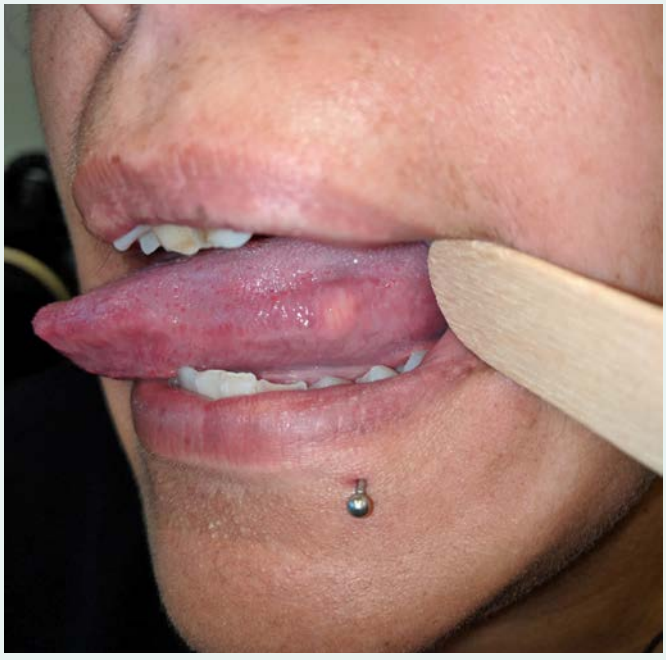


Figure 1. The lesion on the lateral aspect of the tongue at initial presentation.

Under the microscope, the squamous mucosal epithelium was intact along with bundles of striated muscle and connective tissue. The tumour was formed from polygonal cells with a well-defined outline, a large amount of granular pink cytoplasm and no cytological atypia or pleomorphism. The diagnosis was granular cell tumour. In early July, the patient was reviewed and she presented with a healthy tongue and no signs of recurrence or infection. Healing had been uneventful.

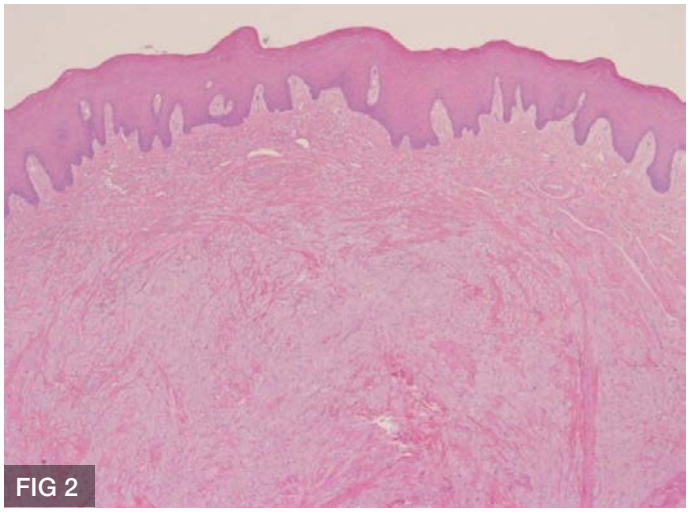
Pathology

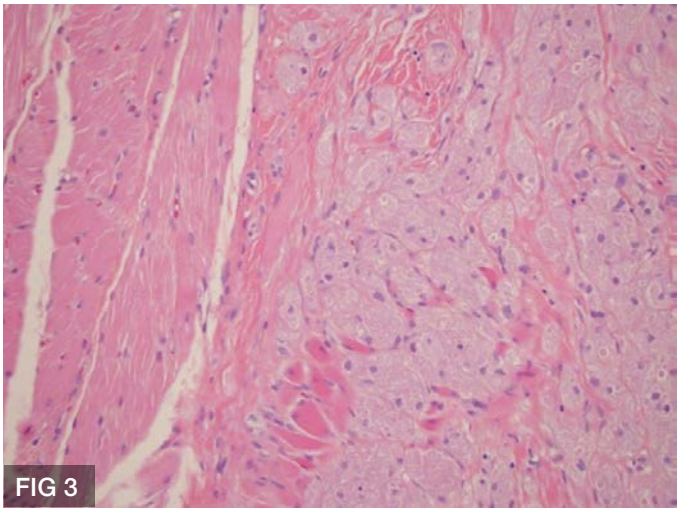
The excised specimen was composed of oral squamous mucosa down to superficial bundles of striated muscle. Occupying most of the tissue was a tumour demonstrating the features of GCT. The lesion involved the connective tissues and showed no connection to the overlying squamous epithelium which demonstrated reactive hyperplastic thickening (Figure 2). Tumour cells were large and polygonal. They had a characteristic large amount of granular pink cytoplasm, with a generally small regular nucleus (Figure 3). Cells were arranged as cords, nests and dispersed single cells, generally monomorphic and these levels showed no mitotic activity. The tumour cells demonstrated positive staining with S100 immunostain (Figure 4) and weak but focal granular PAS positive, diastase resistant staining (Figure 5). Desmin immunostain was negative.

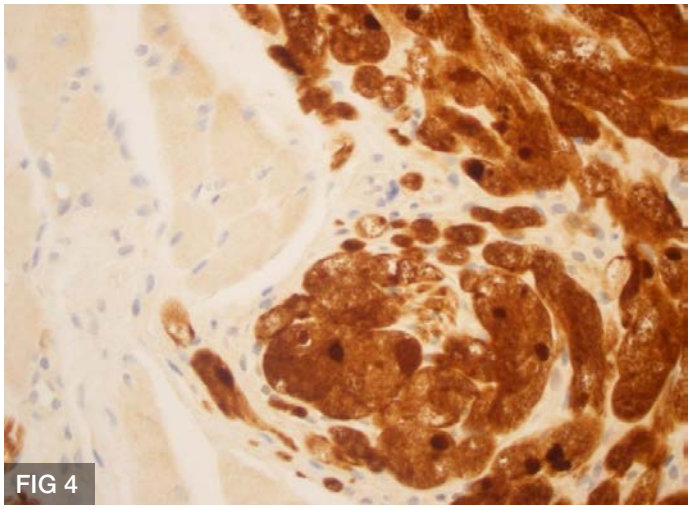
In the sections the tumour measured 5 mm maximum diameter. Although showing focal extension to the biopsy edge it showed no histological features to suggest aggressive behaviour and it was determined that the likelihood of recurrence was low. This was confirmed clinically at follow up.

Histogenesis

The histogenesis of GCT has been a source of controversy since its recognition as an entity by Abrikossoff in 1926 (Koutsias et al 2018). GCT is defined as “A neural tumour composed of round and/or spindle cells with pink, granular cytoplasm due to abundant intracytoplasmic lysosomes” (Barnes et al., 2017). The main morphologic feature is the granularity of the cytoplasm which is caused by a massive accumulation of lysosomes. The combined input from immunohistochemistry and electron microscopy has greatly clarified the understanding of the morphology of this lesion. Immunohistochemistry greatly aids correct identification when the differential diagnosis is a problem.







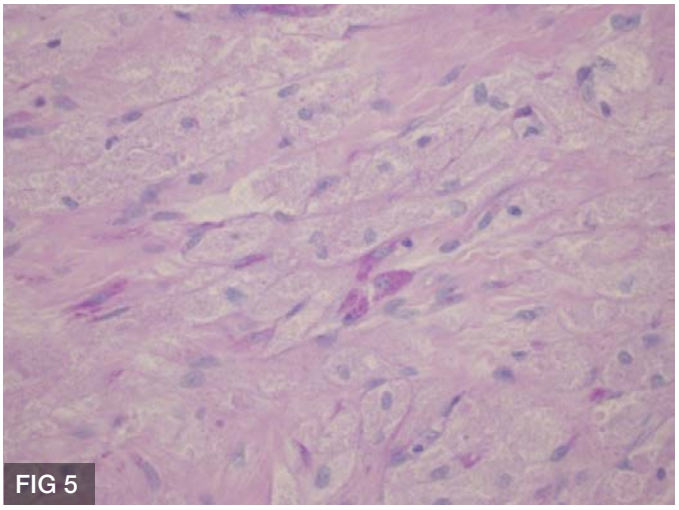


Figure 2. Squamous mucosa with underlying tumour in sub-chorion (H+E; 4 x Low power).
Figure 3. Polygonal cells infiltrating muscle (H+E; 10 x Medium power).
Figure 4. Tumour cells showing strong positivity with S100 immunostain (S100; 40 x High power).
Figure 5. Tumour cells showing patchy granular staining with PAS+ Diastase stain (PASD; 40 x High power).

These lesions can occur in virtually any location, with the tongue being the most common oral site. Benign GCTs are not uncommon, but malignant GCT is rare and at times difficult to diagnose. Early suggestions that GCT may have a myoblastic origin have been discounted and use of the term granular cell myoblastoma as a designation for this tumor has been discouraged. Most investigators currently favour a neuroectodermal/ Schwann cell derivation based on immunohistochemical and electron microscopic findings, and the designation, granular cell schwannoma has found favour with some authors. Other investigators believe that GCT is not a specific entity but rather a degenerative change that can occur not only in Schwann cells but also in a variety of other normal and neoplastic cells. Until more research information becomes available, especially those derived from cytogenetic studies, this lesion should be considered a separate entity and the descriptive designation of granular cell tumor continues to be used (Ordóñez and MacKay, 1999).

Discussion

GCT is found in almost any skin or mucosal surface, although the head and neck region accounts for 45-65% of cases. The tumour has been found to be both benign and malignant, although malignancy is rare and comprises only 2% of all granular cell tumours (Dive et al., 2013). Of the head and neck lesions, 70% of these are found intraorally and of these, the tongue shows a prevalence of about 40% (Noonan et al., 1979). The next most common location within the head and neck region is the larynx, and in adults, most commonly the posterior half of the true vocal cord. Hoarseness is the usual presenting symptom of laryngeal tumours, while stridor or airway obstruction, which can be mistaken for asthma, is characteristic of those in the trachea.

GCT is a slow growing lesion, yet they tend to be locally invasive. Sometimes there is difficulty in histopathological identification due to insufficient clarity of the specimen. Not infrequently, benign pseudoepitheliomatous hyperplasia in the overlying epithelium in these lesions may mimic squamous cell carcinoma (SSC). Although malignancy amongst this group of tumours is very low, Caltabiano et al. (2008) reported a case of a 47-year-old with a GCT of the tongue colonised with a squamous cell carcinoma (SCC). A few cases have been reported of a simultaneous SCC of the tongue and a GCT exhibiting this characteristic pseudoepitheliomatous hyperplasia. The pathological diagnosis therefore generally requires confirmatory immunohistochemistry for the correct identification and careful interpretation of the overlying squamous epithelium as demonstrated with this case. Recognition of co-existent pseudoepitheliomatous hyperplasia and GCT avoids overcalling the latter for SSC.

GCTs have been reported in all age groups however it most frequently occurs between ages 50 to 70 years of age. Females are more commonly affected than males (Nagaraj et al., 2006). Although the tumours have a predisposition for middle age, they have also been found in young children (Nagaraj et al., 2006). Given that GCT of the oral cavity is relatively rare, it is feasible that the general dental practitioner may be unfamiliar with this lesion. It is usually a well-demarcated, uninflamed, asymptomatic mass less than 2 cm in diameter, normally with yellow surface colouration.

As the vast majority of GCTs are benign, surgical excision of the lesion is the treatment of choice with a desired attempt to preserve the normal adjacent anatomical structures and minimise morbidity, especially in structures such as the tongue.

GCT can present a dilemma for the surgeon who is tasked with its removal. Although the surgeon is mindful of the need to have clear margins with an excisional biopsy, they do not want to increase morbidity with a large surgical site, if deemed unnecessary. This is in contrast to the importance of a wider surgical margin surrounding an oral SSC. GCT should be followed up for possible recurrence or metastasis. In benign tumours the recurrence rates are 2-8% with negative margins and greater than 20% if positive margins are present.

Summary

Oral GCTs may demonstrate a wide variety of morphological features with an accumulation of polygonal cells with abundant granular cytoplasm, but they still exhibit benign behaviour in the vast majority of cases. Furthermore, GCT is a slow growing benign lesion and usually only locally invasive. Although rare, it is a pathology dentists should be aware of, as most cases are located in the head and neck region. Approximately 70% present inside the mouth with the tongue being the most common site. At the time of surgical removal, conservative yet complete surgical excision is the treatment of choice for these tumours, preserving normal structures with planned follow up care for possible recurrence.

Acknowledgement

Special thanks to Mr Peter Liston, Oral and Maxillofacial Surgeon, Taranaki Base Hospital, New Plymouth, New Zealand

References

Abrikossoff AI. (1926). Uuber myome ausgehend von der quergestreifeten willkurlichen muskulatur. Virchows Arch. Pathol Anat. 260:215-233.

Barnes L, Eveson JW, Reichart P, Sidransky D. (2005). WHO Organisation Classification of Tumours. Pathology and Genetics of Head and Neck Tumours. Tumours of the hypopharynx, larynx and trachea (pp. 154 – 155). Lyon, IARC Press. ISBN 92 832 2417 5.

Caltabiano R, Cappellani A, Di Vita M, Lanzafame S. (2008). The unique simultaneous occurrence of a squamous cell carcinoma and a granular cell tumor of the tongue at the same site: a histological and immuno-histochemical study. J Craniofac Surg. 19(6):1691-1694.

Dive A, Dhobley A, Fande PZ, Dixit S. (2013). Granular cell tumour of the tongue: Report of a case. J Oral Maxillofac Pathol. 17:148.

El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ. (2017). WHO Classification of Head and Neck Tumours (4th Edition) (pp. 121 – 122). Lyon, IRAC Press.

Koutsias G, Chatzifotiou E, Tsompanidou C, Pavlidis P, Zagelidou E, Anestakis D. (2018). Granular Cell Tumour of the Tongue: A case report. Clin. Oncol. Res. 1(1):1005.

Nagaraj PB, Ongole R, Rao BRB. (2006). Granular cell tumour of the tongue in a 6 year old girl- a case report. Med Oral Patol Oral Cir Bucal. 11: E162-4.

Noonan JD, Horton CE, Old WE, Lane T. (1979). Granular cell myoblastoma of the head and neck. Review of the literature and 10-year experience. Am J Surg. 138: 611.

Ordóñez NG, MacKay B. (1999). Granular cell tumor: a review of the pathology and histogenesis. Ultrastruct Pathol. 23(4):207-222.

Ramraje SN, Choudhury B. (2010). Granular Cell Tumour. Bombay Hospital
Journal. 52(4):541-544.

Thompson, L Head and Neck Pathology (2013) 2nd Ed pp 132- 137, Saunders ISBN 978-1-4377-2607-7

Weber CO. (1854). Anatomische Untersuchung einer hypertrophischen Zunge nebst Bemerkungen uber die Neubildung quergestreifter Muskelfasem. Virchows Arch A Pathol Anat. 7:115-125.

Author details

David M. Antunovic
Clinical Leader-Dental, Taranaki District Health Board (TDHB), David Street, Westown, New Plymouth, New Zealand 4310
Corresponding author: *david.antunovic@tdhb.org.nz*

Dr. James Hunt
Anatomical Pathologist, Taranaki Pathology Services, New Plymouth, New Zealand