ISOLATED INTRA-ORAL GRANULAR CELL TUMOR: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE

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ABSTRACT

Granular cell tumor (GCT) is a relatively uncommon lesion occurring in almost any part of the body, including the orofacial region. The tongue and the buccal mucosa are common intra oral sites. Although aggressive and malignant variants of this neoplasm have been described, most GCTs are benign. The histogenesis of the lesion still remains unknown. However, histochemical and ultra-structural studies propose the origin of the lesion from Schwann cells, striated muscle, mesenchymal cells, histiocytes and epithelial cells. The tumor generally occurs in middle-aged or older adults. The lesion is typically seen as an uninflamed asymptomatic mass measuring about two cm in diameter with reddish surface coloring. As most granular cell tumors are benign, surgical excision of the lesion is the treatment of choice. In this study, 2 oral GCT cases are presented, corresponding to 2 male patients, with a mean age of 27 years and a mean time of evolution of the lesions of 8 months. Both lesions were located on the tongue. Differential diagnoses include fibrous hyperplasia, minor salivary gland tumor, condyloma acuminatum and neurilemmoma. In all the cases a resection with safety margins of the lesions was carried out under local anesthesia. The samples were fixed and processed for histopathological study. The main clinical pathology and diagnostic features of this neoplasm are reviewed and discussed.

Key words: granular cell tumor, oral neoplasm.

TUMOR INTRAORAL ISOLADO DE CÉLULAS GRANULARES: RELATO DE DOIS CASOS E REVISÃO DA LITERATURA

RESUMO

O tumor de células granulares (TCG) é uma lesão relativamente incomum que pode acometer qualquer parte do corpo, incluindo a região buco-maxilo-facial. A língua e a mucosa bucal são localizações intraorais comuns. Embora casos de transformações malígnas e agressividade terem sido descritos, a maioria dos TCG são benignos. A histogênese desta lesão continua desconhecida. No entanto estudos de imunohistoquímica e ultraestruturais sugerem que a lesão se origina das células de schwann, musculatura estriada, células mesenquimais, histiócitos e células epiteliais. O tumor geralmente ocorre na meia idade ou em pacientes idosos. A lesão é tipicamente vista como uma massa assintomática não inflamatória que mede cerca de dois centímetros de diâmetro com uma superfície de coloração avermelhada. A maioria dos tumores de células granulares são benignos cuja excisão cirúrgica é o tratamento de escolha. Neste estudo, 2 casos orais de TCG são apresentados sendo ambos em pacientes do sexo masculino, com media de idade de 27 anos e tempo médio de evolução da lesão de 8 meses. A localização de ambas as lesões foi o dorso da lingual. O dignóstico diferencial incluiu a hiperplasia fibrosa, tumor de glândulas salivares menores, condiloma aculminado e neiurilenoma. Em todos os casos a ressecção com margens de segurança foi realizado sob anesthesia local. As amostras foram fixadas e processadas para o estudo histopatológicos. As principais características clinicopatológicas e de disgnóstico foram revisadas e discutidas.

Palavras chave: tumor de células granulares, neoplasia oral.

INTRODUCTION

Granular cell tumor (GCT) is an uncommon benign neoplasm, with low prevalence among soft tissue lesions that affect the oral cavity. GCTs have been reported mostly in female patients with mean ages ranging from the fourth to sixth decades of life. This tumour has received different names in addition to myoblastoma, such as myoblastic myoma, uniform granular cell myoma, embryonic rhabdomyoblastoma myoblastoma, granular cell Neuroma, granular cell Schwannoma and congenital epulis. However, the name granular cell tumor (GCT) is supported by the nomenclature regulations of the World Health Assembly (WHO)[1,2].

Correct analysis of the histological findings plays an important role in the correct diagnosis of this

tumor. Epithelium variations may lead to misdiagnosis of squamous cell carcinoma and consequent radical surgical excision[3].

This report describes and discusses two cases of granular cell tumor involving the tongue, and reviews the literature.

CASE 1

A 41-year-old black male came to the Oral and Maxillofacial Surgery Outpatient Clinic of the Pernambuco School of Dentistry, University of Pernambuco (FOP/UPE) with a main complaint of a nodule on the tongue. Physical examination revealed a slightly red, raised, firm, asymptomatic lesion, 3 cm in diameter, on the dorsal surface of his tongue (Fig. 1). Results of the remaining examination of the oral cavity, pharynx and larynx were normal. He reported no previous surgical intervention in the area, and no family history of similar cases was elicited during the history taking. The patient reported that the lesion on the tongue had been present for approximately one year. No cervical adenopathy was present and there was no history of previous illness or hospitalization.

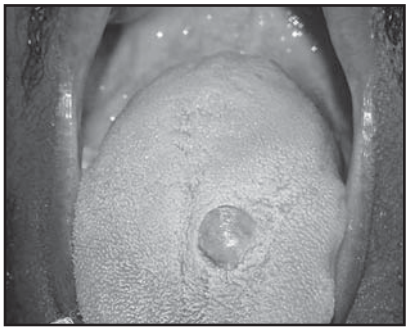

Fig. 1: Clinical aspect of Granular cell tumor with nodule on the midline dorsal surface of tongue.

An excisional biopsy was carried out and the material was sent to the oral pathologist at the Oral Pathology Laboratory of the Pernambuco School of Dentistry (LPBFOP/UPE). The histopathology showed histological sections stained with hematoxiline-eosine (HE) displaying underlying connective tissue with a large amount of granular cells in the sub-epithelial portion of the tissue far from the basal lamina (Fig. 2B-C). The photomicrographs showed pseudoepitheliomatous hyperplasia (Fig. 2A) and at higher magnification showed the typical granular and eosinophilic cytoplasm of tumoral cells (Fig. 2D). The histological diagnosis was granular cell tumor with pseudoepitheliomatous hyperplasia of the overlying squamous epithelium.

The case has been under observation for two years with no clinical signs of relapse or other lesions in the oral cavity to date.

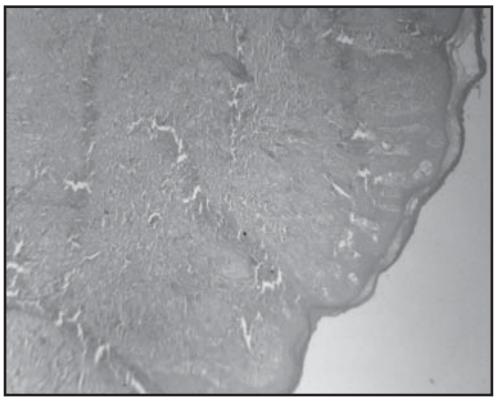

Fig. 2A: Pseudoepitheliomatous hyperplasia of the lining of surface (H.-E.- 40x.

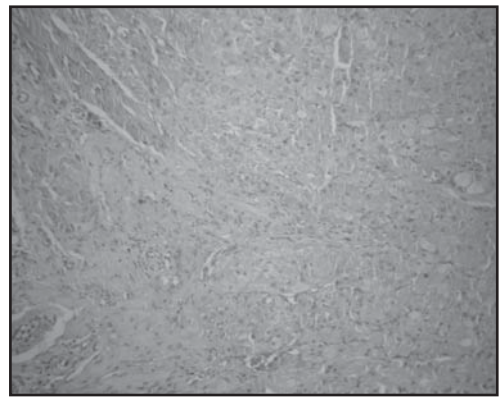

Fig. 2B: Amount of granular cells in depth of tumor specimen (H.-E.- 100x).

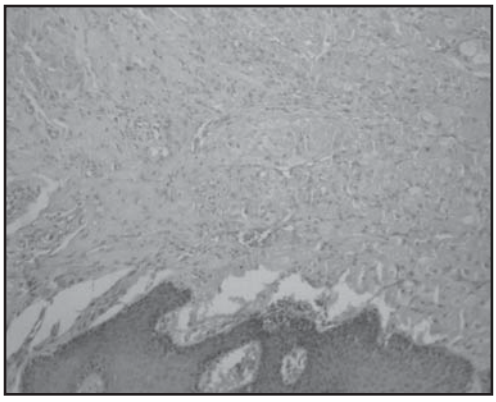

Fig. 2C: Granular cells in the sub-epithelial portion of specimen (H.-E.- 100x).

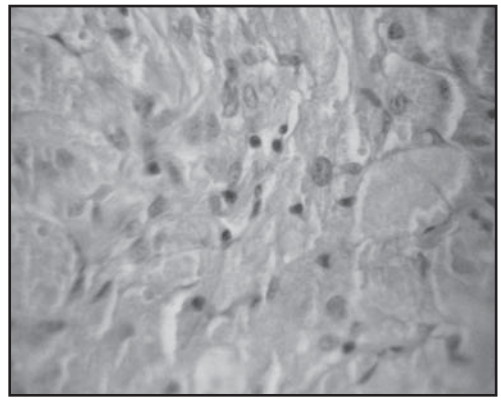

Fig. 2D: View of the typical granular and eosinophilic cytoplasm of the tumoral cells (H.-E.- 400x).

CASE 2

A 13-year-old white male was referred for evaluation of a painless swelling on the tongue with a two-year history. Clinical examination revealed a single, firm nodular mass about 4 cm. in size with a reddish white cast on the dorsum of the tongue. It was mildly tender on palpation (Fig. 3). A differential diagnosis of a pyogenic granuloma, lipoma, traumatic fibroma or neurilemmoma was given. No other associated lesions were found.

An excisional biopsy was performed, which revealed histopathological features consistent with a granular cell tumor, similar to the first case. The patient is currently being monitored at six-month intervals and no signs of recurrence or any malignant transformation have been found during a three-year follow-up.

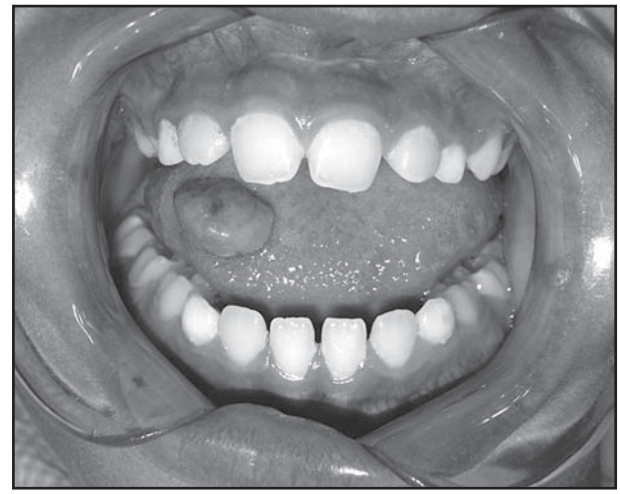

Fig. 3: Granular cell tumor of the tongue mimicking pyogenic granuloma showing a firm nodular mass of about 4 cm. laterally located on the dorsum of the tongue.

DISCUSSION

A GCT is a slow-growing tumor of undefined origin, first called "granular cell myoblastoma" based on Abrikossoff's first report of a GCT in 1926, suggesting an apparent association between granular cells and skeletal muscle[4,5].

Others investigators have also suggested an origin from macrophages, histiocytes, fibroblasts and undifferentiated mesenchymal cells. However, these theories have been incompletely supported[6,7]. More recently, the unique granular cells that make up the tumor are believed to be of neural origin (Schwann-cell) based predominantly on immunohistochemical stains (S-100 protein and neuron-specific enolase) and scanning electron microscope studies (myelin sheath-like structure)[8,9]. Non-neural granular cell tumors have been described in the literature and differ from traditional GCTs in that they show expansible growth, cellular growth, cellular atypia and negative staining for S-100[10]. Histological findings of our cases did not present mitoses or cytologic atypia.

GCTs appear in a range of patients, from children to the ederly, but usually involve individuals in their fifth to sixth decades of life (Table 1)[11,12]. This report shows one patient in his fifth decade of life and another aged 13 years, who confirm the broad age-range of this kind of tumor.

Most studies demonstrate a female predilection. However, apparent gender predilection may depend on tumor site. The difference varies from 2:1 female predilection for oral cavity lesions to 5:1 for larynx tumors[13,14]. The two cases presented in this study differ from the findings described in the literature because the patients are men and the lesions are located on the tongue.

Typically, these soft tissue lesions occur as small (less than 2 cm. diameter), well-circumscribed, solitary, painless, uninflamed, non-ulcerated nodules, as in our described cases. Tumors can occur on skin and subcutaneous tissue, and occasionally some may be identified in lung, gastrointestinal tract and heart tissue. In the head and neck, the tongue is by far the most common location for GCTs[15-17], in agreement with our cases. Congenital granular cell tumor (congenital epulis) usually arises from alveolar mucosa and may occur in the mandible or tongue[18].

Most GCTs are solitary; however, multiple lesions occur in 7% to 25% of the cases. Multiple tumors are most often located in the oral mucosa, skin, gastrointestinal tract, respiratory tract and biliary system[19,20].

GCTs are usually benign, while malignant tumors are extremely rare, making up approximately 1% to 2% of such tumors. Most malignant lesions are larger than the benign form, usually measuring more than 4 cm maximum diameter. Malignant GCTs can occur at the same sites as the benign forms and exhibit a high rate of recurrence and metastasis after surgical excision[21,22]. Our cases have been followed for up to three years without malignant recurrence.

Pseudoepitheliomatous hyperplasia of the overlying oral epithelium is seen in a variety of cases. This

Table 1: Isolated Intra-Oral Granular Cell Tumor – Review from 1981 to 2007.

Author	Year	Age (Yrs)	Gender	Race	Intra-Oral Site	Total No. of Tumors	Treatment
Apisarnthanarax	1981	39 (Mean)	62% -Females 38% -Males	69.5% - B 31.5% - W	Tongue	88 – 06 Oral tumors	Surgical Excision
Stewart et al.	1988	-	2:1 Female / Male	-	Tongue (67%) Oral Mucosa (13%) Lip (8%) Soft palate (6%) Other sites (6%)	35	Surgical Excision
Okada et al.	1990	29	Female	-	Tongue	01	Surgical Excision
Payne-James	1990	59	Female	-	Tongue	01	Surgical Excision
Seki	1993	74	Female	-	Oral mucosa	01	Surgical Excision
Sica	1995	58	Female	-	Palate	02	Surgical Excision
Zahid	1996	45	Male	-	Oral mucosa	01	Surgical Excision
Gürsoy	1997	32	Female	-	Tongue	01	Surgical Excision
Bernat Gili et al.	1999	19	Male	-	Soft Palate	01	Surgical Excision
Becelli et al	2001	53	-	-	Palate	01	Surgical Excision
Van der Meij	2001	56	Female	W	Tongue	01	Surgical Excision
Boulos et al.	2002	45	Female	-	Palate	01	Surgical Excision
Giuliani et al.	2004	32	Female	-	Tongue	01	Surgical Excision
Brannon	2004	3 - 19	3.3:1 Female / Male	-	50% - Tongue 25% - Lip 25% - Other sites	34	Surgical Excision
Pino Rivero et al.	2005	18	Female	-	Tongue	01	Surgical Excision
Xue et al.	2005	11-50	2.5:1 Female /Male	-	13 – Tongue 01 – Oral Mucosa	14	Surgical Excision
Tosios et al.	2006	48	Female	-	Floor of the mouth	01	Surgical Excision
Sposto et al.	2006	30-42	Female	-	1 – Oral mucosa 2 – Tongue	03	Surgical Excision
Nagaraj et al.	2006	6	Female	-	Tongue	01	Surgical Excision
Eguia et al.	2006	25-60	5 Females 3 Males	-	6 – Tongue 1 – Gingiva 1 – Oral mucosa	08	Surgical Excision
Angiero et al.	2006	28-66	6 Females 5 Males	-	10 – tongue 1 – Oral mucosa	11	Surgical Excision - Laser
Tapia et al.	2007	45	Female	W	Tongue	1	Surgical Excision

may be such a prominent feature that subjacent GCTs are overlooked and a superficial biopsy from a such a lesion may be misdiagnosed as a well-differentiated squamous cell carcinoma[1,23-25]. However, pseudoepitheliomatous hyperplasia was observed in both our cases, and excisional biopsy with safety margins was carried out deeply in the lesion, where granular cells could be visualized. Oral pathologists should be careful in the analysis of incisional biopsy of tumors located on the lateral border of the tongue, since this site is one of the most prevalent locations of oral cancer. Apart from the histopathological picture, the clinical size of the tumor, pain, speed of growth, invasion of underlying and adjacent struc-

tures and the presence of regional and distant metastasis will aid in differentiating a benign GCT from a malignant lesion. The interface between surgeon and pathologist should evaluate the need for other procedures, removing deeply-located tissue, where characteristic features of the tumor are located.

In terms of differential diagnosis, other benign connective and neural tumors, such as fibromas, lipomas, neuromas, neurofibromas or schwannomas with their malignant variants should be considered. Granular cell change is a nonspecific finding noted in many tumors of the oral cavity. GCTs, congenital epuli and odontogenic tumors such as ameloblastomas and granular cell odontogenic fibromas are among the most common tumors of the oral cavity to contain granular cells[26-31].

Spontaneous regression has been noted but is apparently a rare event[14]. Surgical excision is the treatment of choice for GCT regardless of whether the lesions occur as isolated tumors or demonstrate multifocal involvement[32]. In most cases this procedure is curative, even if the tumor is incompletely excised; however, a small percentage has recurred when tumor remained in the margins of excision[33]. Nevertheless, locally aggressive and manifestly malignant variants of this tumor have been described in the literature[34]. In our cases no recurrences after excision have been observed to date.

The prognosis following treatment is excellent. Malignant variants, however, present 60% mortality after diagnosis, principally caused by metastasis[1,12,15]. In this report, neither case presented malignant features.

In conclusion, GCT is a relevant pathologic entity among oral tumors, principally for great number of differential diagnosis between soft tissue lesions and for misdiagnosis of squamous cell carcinoma after an incorrect incisional or excisional biopsy and mistaken histological analysis resulting in an unnecessary radical treatment.

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