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原文作者姓名：	F Haikal, JP Maceira, EP Dias, M Ramos-e-Silva
通訊作者學校：	Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
報告者姓名(組別)：	蔡欣慈 A 組
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內文：

Introduction

1. Abrikossoff tumour (granular cell tumour,簡稱 GCT) is an **uncommon** neoplasia.
2. **Benign** in most of the cases.
3. Its histogenesis is uncertern.
   Four possible origin：
   (1). myogenic origin (Aleksei Ivanovich Abvrikosov, 1926)
   (2). mesenchymal origin (Oliveira&Taube)
   (3). neuroendocrine origin (Willians&Willians)
   (4).**Schwann cell origin** (Reichler et al.)
4. Schwann cells is the presence of **vimentin** (also found in **schwannoma**, and immunoreactivity for the lineage marker of the neural crest,S-100.)
5. Antigen-melanoma associated and the **neuron-specific enolase (NSE)** are tumour markers with the origin in the **neural crest**, not in Schwann cells.
6. Other researchers believe that GCT **isn't a specific** entity, but a modification that can occur not only in the Schwann cells, but also in other cells.

Literature review

1. Occur between the **second and sixth decade**, greater proportion among woman and blacks.
2. 45-65% in head and neck, 70%in oral cavity, especially on the **tongue**.
3. Papule or nodule shape, diameter<3cm in oral cavity, asymptomatic.
4. Benign form： granular cells-large size, polygonal or fusiform, with small nucleus, separated by collagen.
5. Malignant form：
   (1) criteria-necrosis, distribution of the cells in fusiform strings, large nucleus with vesicular core, increased mitotic activity, N/C ratio↑,nuclear pleomorphism.(3 or more of the criteria)
   (2) occasionally **local invasive**, 2% distant metastases
6. First case of GCT：Abrikosov in 1926.He proposed a **myogenic origin**, and the tumour result in cell degeneration of the striated muscles.
7. Other authors agree with the **neurogenic origin** through immunoenzymatic

studies：(1) S-100(+) in **neurons and Schwann cells**.
(2) benign GCT：S-100(+), neuron enolase (+)

8. Four antibodies used in evaluation of the histogenesis of GCT：
   (1) PGP9.5(human gene protein)：a monoclonal antibody(單株抗體),a neuron-specific protein, a marker for nervous and **neuroendocrine cells**. Function: unknown.
   (2) S-100：a polyconal antibody(多株抗體).It's used in a description of an acid protein fraction of the bovine brain, so designated for its solubility in saturated ammonium sulphate. Present in glial cells(神經膠細胞), **Schwann cells**, condrocytes, melanocytes, Langerhans cells.
   (3) Neuro-specific enolase(NSE)：a monoclonal antibody. Used as marker to define **neuroendocrine** tumour histogenesis, present in **neural cells, neuroendocrine cells**, but absent in Schwann cells.
   (4) Vimentin：monoclonal antibody. One of the proteins of the **intermediate filament** (a protein which present in all nucleated cells as integrating structures),reacts with **mesenchymal cells** , located mainly in the **immature glia**, widely found in **schwannomas**.

Table 1. **Immunohistochemical differences between Schwann cell and neuroendocrine cell**

Antibody	Schwann cell	Neuroendocrine cell
PGP 9.5	+/−	+
S-100 protein	+	+/−
ENE	−	+
Vimentin	+	+/−

Immunohistochemical reaction (+) reacts; (−) does not react; (+/−) reacts weakly.

Objectives

1. To study and analyse the **histogenesis** of the GCT of the oral cavity, using four antibodies commonly employed in evaluation of neoplasia of the neural and neuroendocrine lineage.
2. Analyse the differences found in GCT in staining by the HE method.

Material and methods

1. 11 Samples of oral cavity tissues of the buccal mucosa, tongue or lips.
2. **Immunoperoxidase technique** in incubation with four antibodies：anti-PGP9.5,anti-S-100,anti-NSE, and anti-vimentin.
3. Histological sections stained by **HE** method.

4. Results were referred as with positivity when
   (1) Located focally-some limited areas.
   (2) Located diffusely-dispersed areas.
   (3) Light intensity-little stained (light brown).
   (4) Moderate intensity-little more evident colouration (brown/brownish).
   (5) Marked intensity-stronger colouration (brown).
5. Controls：
   (1) Normal nervous tissue observed on the sides of the tumour-for S-100,PGP9.5,and NSE
   (2) Endocrinal cells of the normal pulmonary tissue.
   (3) Sample of schwannoma-for vimentin

Results

1. Histopathological findings：
   nests and more diffuse areas of large, polygonal cells, with small nucleus and abundant granular eosinophilic cytoplasm in all cases. **Pseudoepitheliomatous hyperplasia** in almost all cases.
2. Disposition(特性)：
   The tumour cell were **compacted**, some cases have **imprecise limits**, and some cases present **delimit areas**.
3. Immunohistochemical findings：(Table2)
   (1) Most of the cases show marked positivity (3+) for S-100 and vimentin diffusely in the nucleus and cytoplasm of the tumour cells.
   (2) 1 case was negative (0) for NSE, and the other cases were positive.
   (3) Four cases were negative (0) for PGP9.5, and the other cases were positive.

Table 2. **Immunohistochemical findings in 11 cases of GCT of the oral cavity**

Case	Gender	Location	S-100	Vimentin	ENE	PGP9.5
1	W	Tongue dorsum	3+/D	3+/D	2+/D	0
2	W	Lip	3+/D	3+/D	0	1+/F
3	W	Tongue side	3+/D	3+/D	2+/D	0
4	M	Tongue	3+/D	3+/D	1+/F	1+/D
5	W	Tongue tip	3+/D	3+/D	2+/F	1+/F
6	W	Tongue	3+/D	2+/D	1+/F	0
7	W	Tongue dorsum	3+/D	3+/D	1+/F	1+/D
8	M	Buccal mucosa	3+/D	3+/D	2+/D	1+/D
9	M	Tongue tip	2+/D	3+/D	1+/F	2+/F
10	W	Tongue	3+/D	3+/D	1+/D	2+/F
11	W	Lip	3+/D	3+/D	1+/F	0

Positivity intensity graduated in a scale of negative 0, mild; 1+, moderate; 2+, marked; 3+, D-diffuse; F, focal; M, man; W, woman; GCT, granular cell tumour.

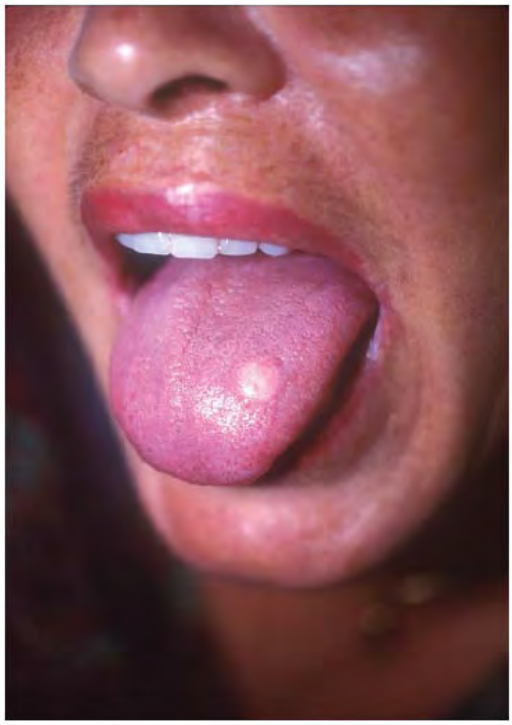

Fig. 1. Case 3 Abrikossoff tumour of the dorsum of the tongue.

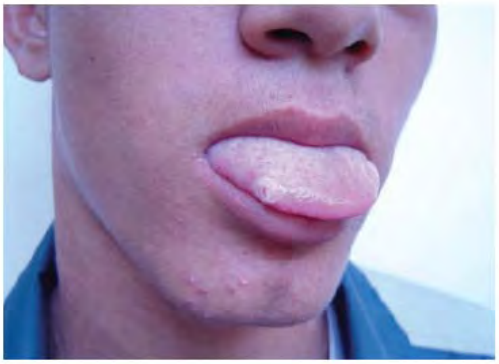

Fig. 2. Case 9 Abrikossoff tumour of the right side of tongue.

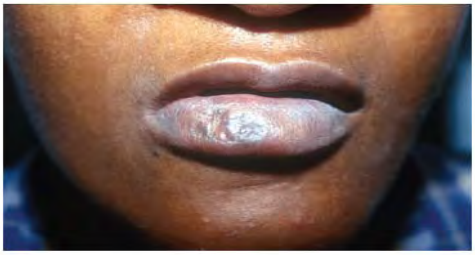

Fig. 3. Case 11 Abrikossoff tumour of the lower lip.

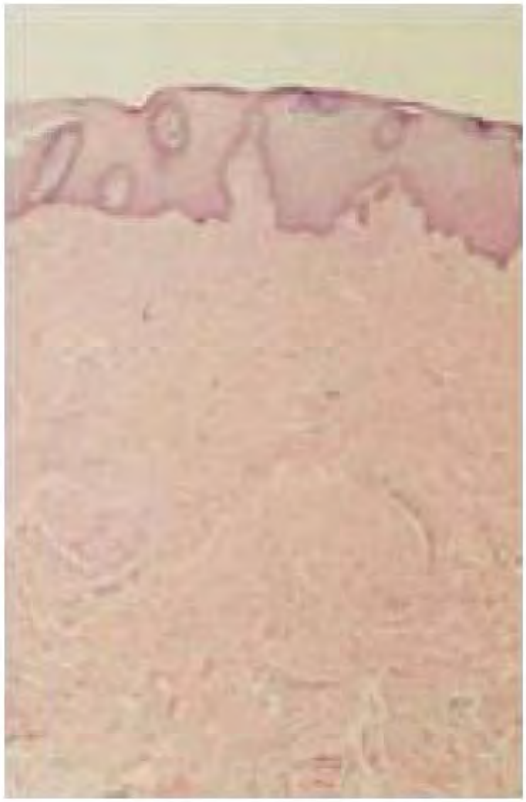

Fig. 4. Case 2 epidermal pseudoepitheliomatous hyperplasia – granular cells scattered in all dermis.

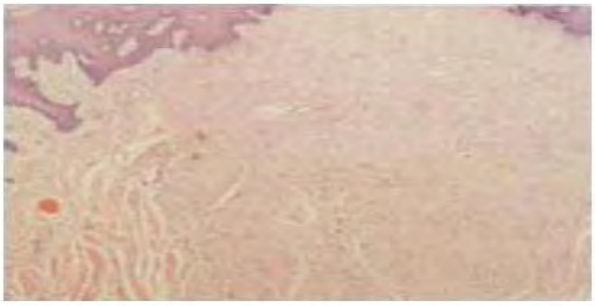

Fig. 5. Case 3 exuberant pseudoepitheliomatous hyperplasia compacted tumoural cells limited to muscular tissue.

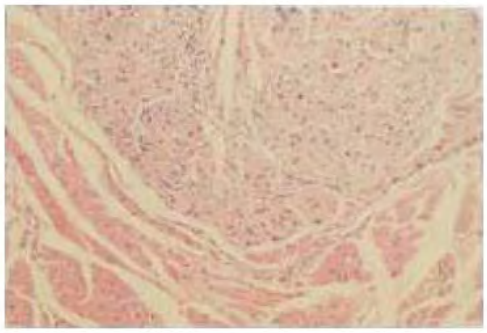

Fig. 6. Case 3 detail of the intimal relationship between granular cells and muscular tissue.

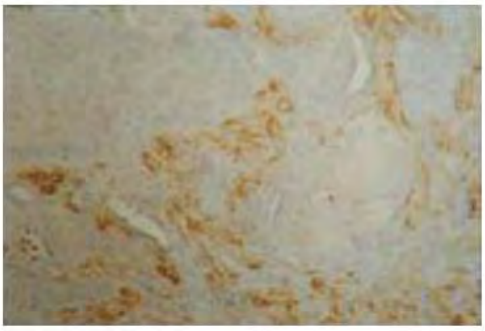

Fig. 9. Case 9 S100 positivity in cells granular detail of the pseudoepitheliomatous hyperplasia.

Fig. 7. Case 7 PGP9.5 mild positivity of granular cells.

Fig. 10. Case 1 ENE moderate positivity in granular cells.

Fig. 8. Case 4 S100 marked positivity of granular cells.

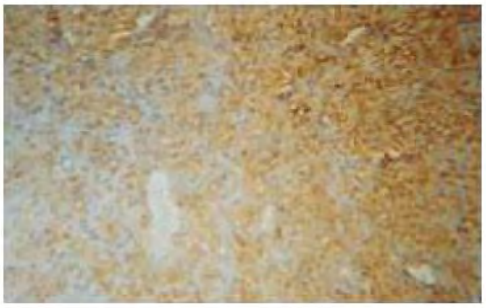

Fig. 11. Case 4 vimentin marked positivity in granular cells.

Discussion

1. It is revalent in **females**, with the patients' age varying from 14 to 52 years (average 40 years) in this study.

2. Most of the cases were located in the **tongue**.
3. Histopathological analysis showed that GCT may be well present as well delimited affecting the dermis focally, or poorly delimited, being distributed and more diffused.
4. 10 cases presented pseudoepitheliomatous hyperplasia .Highly irregular or milder **pseudoepitheliomatous hyperplasia** is a characteristic, but not invariable aspect of the GCT, and can be mistaken as SCC.
5. The **neuroendocrine** and/or from **Schwann cells origin** in GCT was questioned.
6. The reactivity for **S-100** is also used to confirm the GCT diagnosis (due to marked pseudoepitheliomatous hyperplasia).
7. The expression of S-100 sustains the hypothesis that the GCT has origin in **Schwann cells**.
8. Vimentin suggests mesenchymal origin, however it is also expressed in other cells, being **unspecific**. It is additional support in the confirmation of the origin on the Schwann cells.
9. The NSE is more specific marker, and is used as marker of **neuroendocrine cells**.
10. PGP9.5 is a new marker for **neuroendocrine** tumors.
11. In our study, the moderate or weak possibility for NSE and PGP9.5 **does not favour the neuroendocrine origin**, but does not discard it.
12. Although almost all the GCT studies think its origin is Schwann cells, it is possible that GCT appears from **more than one cell type**.
13. Many authors consider GCT as a true neoplasia, while others think it represents a **degenerative alteration** or an **abnormal metabolic process**.
14. Some authors believe that this tumour presents so many controversies because the epithelial, mesenchymal and neurogenic cells originate from a **common cellular precursor**.
15. Schwann and neuroendocrine cells have origin in the **neural crest**, what may justify the positivity of all the markers and different intensities and patterns
16. The result may be associated to the **low sensibility** of the immunoperoxidase technique .

Conclusions

1. The GCT is immunoreactive with the four tested markers：anti-PGP9.5, anti-S-100, anti-NSE, and anti-vimentin.
2. The origin of the GCT in lesions of the oral cavity is in the **Schwann cells**, although a neuroendocrine origin can’t be ruled out.
3. There is **no specific** immunohistochemical marker to define the histogenesis of GCT.

題號	題目
1	Abrikossoff tumour (granular cell tumour) 的來源有許多不同的說法,其中較多學者採信的是哪一種 origin? (A) Mesenchymal origin (B) Neuroendocrine origin (C) Schwann cell origin (D) Myogenic origin
答案 (C)	出處：**Oral &Maxillofacial Pathology- second edition** **Page 465**
題號	題目
2	以下何者為 granular cell tumour malignant form 的 criteria? (A) Increased mitotic activity, N/C ratio↑,nuclear pleomorphism. (B) Pseudoepitheliomatous hyperplasia ,N/C ratio↑,nuclear pleomorphism (C) Local invasive, large size, polygonal or fusiform granular cells (D) Pseudoepitheliomatous hyperplasia , N/C ratio↑,small nucleus
答案 (A)	出處：International Journal of Dental Hygiene, 2008 Histogenesis of Abrikossoff tumour of the oral cavity