

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

Emanuel S. S. Andrade<sup>1</sup>, José R. Laureano Filho<sup>1</sup>, Nelson S. Rocha<sup>1</sup>,  
Ivo C. Pita Neto<sup>2</sup>, Igor B. Camargo<sup>1</sup>

<sup>1</sup> Oral and Maxillofacial Surgery, School of Dentistry of Pernambuco (FOP/UPE),  
Recife, Brazil.

<sup>2</sup> School of Dentistry of Federal University of Ceará (UFCE), Brazil.

### 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 uninfamed 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 malignas 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 aver-

melhada. 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 média 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 diagnóstico diferencial incluiu a hiperplasia fibrosa, tumor de glândulas salivares menores, condiloma acuminado e neurilemoma. Em todos os casos a ressecção com margens de segurança foi realizado sob anestesia local. As amostras foram fixadas e processadas para o estudo histopatológicos. As principais características clínico-patológicas e de diagnóstico 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)<sup>1,2</sup>.

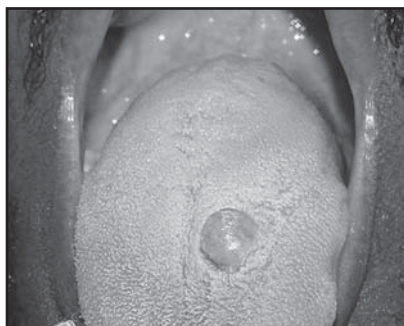
Correct analysis of the histological findings plays an important role in the correct diagnosis of this

tumor. Epithelium variations may lead to misdiagnosis of squamous cell carcinoma and consequent radical surgical excision<sup>3</sup>.

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

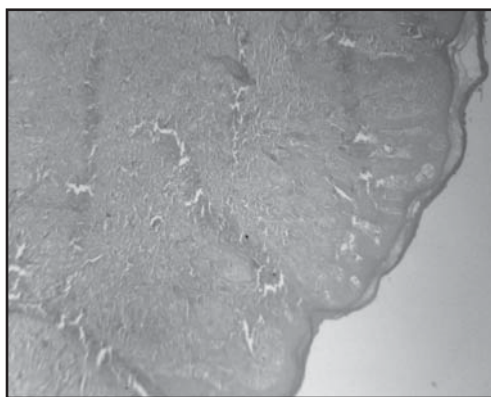


*Fig. 1: Clinical aspect of Granular cell tumor with nodule on the midline dorsal surface of tongue.*

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.

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 hematoxyline-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.

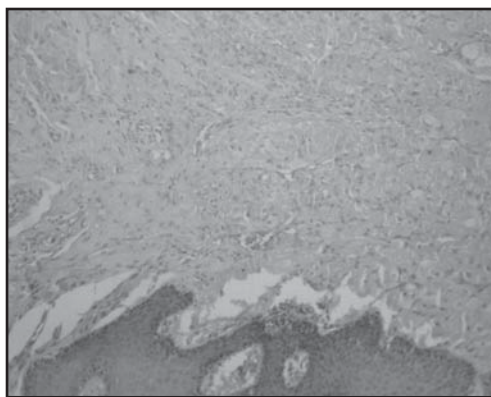
The case has been under observation for two years with no clinical signs of relapse or other lesions in the oral cavity to date.



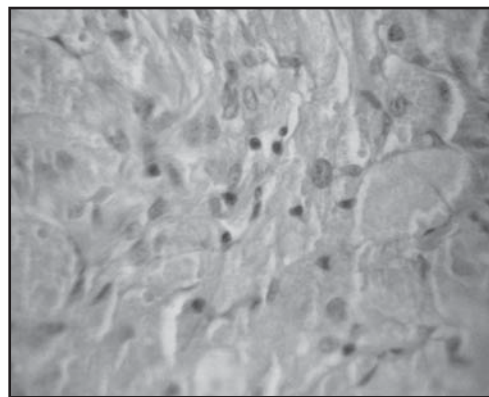
*Fig. 2A: Pseudoepitheliomatous hyperplasia of the lining of surface (H.-E.- 40x.*



*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.

## 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<sup>4,5</sup>.

Others investigators have also suggested an origin from macrophages, histiocytes, fibroblasts and undifferentiated mesenchymal cells. However, these theories have been incompletely supported<sup>6,7</sup>. 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)<sup>8,9</sup>. 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<sup>10</sup>. Histological findings of our cases did not present mitoses or cytologic atypia.

GCTs appear in a range of patients, from children to the elderly, but usually involve individuals in their fifth to sixth decades of life (Table 1)<sup>11,12</sup>. 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<sup>13,14</sup>. The two cases presented in this study



*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.*

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, uninfamed, 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<sup>15-17</sup>, in agreement with our cases. Congenital granular cell tumor (congenital epulis) usually arises from alveolar mucosa and may occur in the mandible or tongue<sup>18</sup>.

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<sup>19,20</sup>.

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<sup>21,22</sup>. 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<br>38% -Males | 69.5% - B<br>31.5% - W | Tongue  | 88 – 06 Oral tumors | Surgical Excision            |
| Stewart et al.     | 1988 | -         | 2:1 Female /<br>Male       | -                      | Tongue (67%)<br>Oral Mucosa (13%)<br>Lip (8%)<br>Soft palate (6%)<br>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<br>/ Male     | -                      | 50% - Tongue<br>25% - Lip<br>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<br>/Male      | -                      | 13 – Tongue<br>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<br>2 – Tongue   | 03                  | Surgical Excision            |
| Nagaraj et al.     | 2006 | 6         | Female                     | -                      | Tongue  | 01                  | Surgical Excision            |
| Eguia et al.       | 2006 | 25-60     | 5 Females<br>3 Males       | -                      | 6 – Tongue<br>1 – Gingiva<br>1 – Oral mucosa  | 08                  | Surgical Excision            |
| Angiero et al.     | 2006 | 28-66     | 6 Females<br>5 Males       | -                      | 10 – tongue<br>1 – Oral mucosa  | 11                  | Surgical Excision -<br>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<sup>1,23-25</sup>. 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<sup>26-31</sup>.

Spontaneous regression has been noted but is apparently a rare event<sup>14</sup>. Surgical excision is the treatment of choice for GCT regardless of whether the lesions occur as isolated tumors or demonstrate multifocal

involvement<sup>32</sup>. 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<sup>33</sup>. Nevertheless, locally aggressive and manifestly malignant variants of this tumor have been described in the literature<sup>34</sup>. 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<sup>1,12,15</sup>. 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.

#### CORRESPONDENCE

Dr. Igor Batista Camargo or  
Dr. Nelson Studart Rocha  
University of Pernambuco,  
Department of Oral Maxillofacial Surgery.  
General Newton Cavalcanti Av 1650 Camaragibe  
PE Brazil 54753-220  
E-mail: igorildo@hotmail.com or nelsonstudart@hotmail.com

#### REFERENCES

- Eguia A, Uribarri A, Gay-Escoda C, Crovetto MA, Martinez-Conde R, Aguirre JM. Granular cell tumor: report of 8 intraoral cases. *Med Oral Patol Oral Cir Bucal* 2006;11:425-428.
- Angiero F, Crippa R, Stefani M. Granular cells tumour in the oral cavity: report of eleven cases treated with laser surgery. *Minerva Stomatol* 2006;55:423-430.
- Tapia JL, Neiders ME, Aguirre A. Polypoid lingual lesion. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;103:727-730.
- Abrikosoff A. Über myome ausgehend von der quergestreiften willkürlichen muskulatur. *Virchows Arch [A]* 1926;260:215.
- Lack EE, Worsham GF, Callihan MD, et al. Granular cell tumor: a clinicopathologic study of 110 patients. *J Surg Oncol* 1980;13:301-316.
- Kyrmizakis DE. Lingual granular cell tumor. *Otolaryngol Head Neck Surg* 2001;124:422-423.
- Papageorgiou S, Litt JZ, Pomeranz JR. Multiple granular cell myoblastomas in children. *Arch Dermatol* 1967;96:168-171.
- Stewart CM, Watson RE, Eversole LR, Fischschweiger W, Leider AS. Oral granular cell tumors: a clinicopathologic and immunocytochemical study. *Oral Surg Oral Med Oral Pathol* 1988;65:427-435.
- Mirchandani R, Sciubba JJ, Mir R. Granular cell lesions of the jaws and oral cavity: A clinicopathologic, immunohistochemical, and ultrastructural study. *J Oral Maxillofac Surg* 1989;47:1248.
- Basile JR, Woo SB. Polypoid S-100 negative granular cell tumor of the oral cavity: a case report and review of literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;96:70-76.
- Apisarnthanarax P. Granular cell tumor. *J Am Acad Dermatol* 1981;5:171.
- Lack EE, Worsham GF, Callihan MD. Granular cell tumor: A clinicopathologic study of 110 patients. *J Surg Oncol* 1980;13:301.
- Regezi JA, Sciubba JJ. Connective tissue lesions. In: Regezi JA, Sciubba JJ, editors. *Oral pathology clinical-pathologic correlations*, 3rd ed. Philadelphia: WB Saunders 1999;176-216.
- Kershisnik M. Granular Cell Tumors. *Ann Otol Rhinol Laryngol* 1994;103:416.
- Brannon RB, Amand PM. Oral granular cell tumors: an analysis of 10 new pediatric and adolescent cases and a review of the literature. *J Clin Pediatr Dent* 2004;29:69-74.
- Okada H, Yamamoto H, Kawana T, Katoh T, Kozawa Y, Izumi H. Granular cell tumor of the tongue: na electron

- microscopical and immunohistochemical study. *J Nihon Univ Sch Dent* 1990;32:35-43.
17. Payne-James JJ, Watkins RM. Granular cell tumor (myoblastoma): two cases and a review of the literature. *Br j Clin Pract* 1990;44:334-336.
  18. Nagaraj PB, Ongole R, Bhujanga-Rao BR. Granular cell tumor of the tongue in a 6-year-old girl – a case report. *Med Oral Patol Oral Cir Bucal* 2006;11:162-164.
  19. Jones JK, Kuo T, Griffiths CM. Multiple granular cell tumor. *Laryngoscope* 1980;90:1646.
  20. Collins BM, Jones AC. Multiple Granular Cell Tumors of the Oral Cavity : Report of a Case and Review of the literature. *J Oral Maxillofac Surg* 1995;53:707-711.
  21. Nishida M et al. Malignant Granular Cell Tumor of the Masseter Muscle: Case Report *J Oral Maxillofac Surg* 2000;58:345-348.
  22. Pino Rivero V, Marcos Garcia M, Rejas Ugena E, Trinidad Ruiz G, Pardo Romero G. Granular cell tumor of the tongue (Abrikossoff's tumor). Report of a case and review of the literature. *An Otorrinolaringol Ibero Am* 2005; 32:65-70.
  23. Xue JL, Fan MW, Wang SZ, Chen XM, Li Y. A clinico-pathological study of 14 cases of oral granular cell tumor. *Zhonghua Kou Qiang Yi Xue Za Zhi* 2005;40:302-305.
  24. Seki N, Kameyama T, Kihara T, Yoshida M, Hashimura S, Fujimasa T, Okina T. A granular cell tumor of the buccal mucosa – a case report. *Kurume Med J* 1993;40:229-232.
  25. Sica GS, Russo A, Dell'Aquila A. Granular-cell tumor of the oral cavity (a case report and statistical notes). *Minerva Stomatol* 1995;44:257-261.
  26. Zahid L, Cariappa KM. Granular cell tumor of buccal mucosa – a case report. *Int J Oral Maxillofac Surg* 1996;25:134-135.
  27. Bernat Gili A, Ayerbe TV, Baena AA, Rivares EJ, Oncins TR. Abrikossoff's tumor of the soft palate. A case report. *An Otorrinolaringol Ibero Am* 1999;26:47-53.
  28. Gürsoy B, Energin K. Granular cell tumour ( a case report). *J Marmara Univ Dent Fac* 1997;2:631-633.
  29. Boulos R, Marsot-Dupuch K, De Saint-Maur P, Meyer B, Tran Ba Huy P. Granular cell tumor of the palate: a case report. *AJNR Am J Neuroradiol* 2002;23:850-854.
  30. Tosios K, Vallianatou D, Vlachodimitropoulos D. Yellow-white tumor on the floor of the mouth. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;101:701-704.
  31. Van der Meij EH, Van der Waal I. Granular cell in oral lichen planus. *Oral Dis* 2001;7:116-118.
  32. Giuliani M, Lajolo C, Pagnoni M, Boari A, Zannoni GF. Granular cell tumor of the tongue (Abrikossoff's tumor). A case report and review of the literature. *Minerva Stomatol* 2004;53:465-469.
  33. Becelli R, Perugini M, Gasparini G, Cassoni A, Fabiani F. Abrikossoff's tumor. *J Craniofac Surg* 2001;12:78-81.
  34. Sposto MR, Navarro CM, Andrade CR. Granular cell tumor (Abrikossoff's tumour): Case series. *Oral Oncology* 2006; 42:194-197.