Central giant cell granuloma (CGCG) is a benign jaw lesion predominantly found in the mandible of young female patients with a variable clinical behavior. Although surgical management is regarded as the main treatment modality for this lesion, the use of intralesional injections of steroids has been recently advocated for its treatment. In addition to this conservative management, the use of fine needle aspiration cytology (FNAC) for diagnosing CGCGs has been proven a safe and efficient approach, especially useful in cases with lesions located in esthetic regions. Herein, it is described a case of CGCG extending to the overlying gingiva of a 15-year-old male patient diagnosed by FNAC and subsequently treated with intralesional injections of a solution of triamcinolone acetonide and ethanolamine oleate that led to an important clinical remission, allowing a more conservative surgical procedure for preservation of gingival esthetics. Therefore, both procedures can be considered as management options for CGCG of the jaws.

Introduction
Gingival reddish lesions account for an important number of disorders frequently diagnosed in the regular dental practice and central giant cell granuloma (CGCG) represents one of the main entities of this group. CGCG is defined by the World Health Organization as a non-neoplastic condition that consists of cellular fibrous tissue containing multiple foci of hemorrhage, aggregations of multinucleated giant cells and occasional trabeculae of bone (1-3). The lesion is predominantly found in young adults before the age of 30 years with a female preponderance. The anterior portion of the mandible is the most frequently affected region, commonly extending across the midline (4).

Although the regular histopathological evaluation of this lesion does not pose difficulties for its correct diagnosis, the use of fine-needle aspiration cytology (FNAC) for the primary diagnosis of CGCG has been advocated, since this method has been proven safe and efficient, causing less injury to the patient, what is especially important for pediatric patients and cases of lesions located in esthetic regions (5-7). In addition, the conventional surgical management of CGCG usually causes major esthetic defects (2). Therefore, the intralesional injection of corticosteroids represents an important alternative non-surgical approach for treating this condition and successful results have been reported (8-10).

This paper presents the case of a young patient who had a CGCG diagnosed by FNAC and subsequently underwent intralesional injections of triamcinolone acetonide for treatment, emphasizing the usefulness and importance of both techniques for the management of CGCG of the jaws.

Case Report
A 15-year-old male patient was referred to our department by his dentist for evaluation of a reddish lesion in the gingiva. Extraoral examination revealed no facial asymmetry, swelling or regional lymphadenopathy. Intra-orally, a reddish-purple lesion involving both the attached and marginal gingiva was noted between the mandibular right lateral incisor and canine (Fig. 1A and 1B). Panoramic and periapical x-rays were carried out and showed a well-circumscribed radiolucent lesion in the affected region (Fig. 2).

Conventional biopsy was avoided due to the involvement of the marginal gingiva, and FNAC was performed. The material obtained was spread on glass slides. Three of them were immediately air fixed for Diff-Quik staining and other two slides were fixed in 95% ethanol for Papanicolaou staining. Cytological smears revealed the presence of multinucleated giant cells immersed in a hemorrhagic background with scattered neutrophils, establishing the diagnosis of CGCG (Fig. 3A and 3B). Laboratory values of serum calcium, alkaline phosphates, phosphorous and parathyroid hormone were within normal limits, ruling out
Because of the location of the lesion and the possible periodontal defects that could arise as a result of the surgery, the corticosteroid intralesional injection treatment was proposed to the patient and his parents with the understanding that surgery was left as an option if the steroid treatment could not achieve the expected outcome.

Treatment comprised 6 administrations of intralesional corticosteroid injections. The first application consisted of a mixture of triamcinolone acetonide (Theracort 40 mg/mL; Theraskin Farmacêutica Ltda., São Bernardo do Campo, SP, Brazil) and 2% lidocaine with 1:200,000 epinephrine (mixed in a 1:1 ratio) with total volume of 0.3 mL. As a significant bleeding was observed during the injection, it was decided to add ethanolamine oleate (mixed in a 1:1 ratio with triamcinolone acetonide) using the same 0.3 mL of total volume in the next injection. The second application was performed after 21 days and the following two injections also had the same interval between each other. The fifth injection was performed after 1 month and the last one 2 months later (Fig. 4A). A decrease in size and color was noticed after every each injection. Although following the fifth injection clinical changes were less evident, the lesion did not involve the marginal gingiva. At this time, it was decided to keep the patient under systematic follow-up (Fig. 4B).

Interestingly, despite important clinical improvement, no radiographic changes were observed. Therefore, after approximately 2 years of follow-up with stable clinical and radiographic aspects, a surgical removal was planned. Computed tomography was obtained and showed in more details an intraosseous and well-circumscribed hypodense lesion. Surgical curettage was performed preserving the marginal gingiva. The histological evaluation revealed the presence of a thick band of collagenous tissue and deposition of hemossiderin beneath the overlying normal epithelium. Deeper in the connective tissue there were aggregations of multinucleated giant cells distributed in a cellular fibrous tissue containing multiple foci of hemorrhage and occasional trabeculae of bone confirming the diagnosis of CGCG (Fig. 5).

The patient is in post-operative follow-up for 30 months without evidence of recurrence or periodontal defects (Fig. 6).
Figure 3. Cytological features showing the presence of numerous multinucleated giant cells immersed in a hemorrhagic background with scattered neutrophils. A: Diff-Quik staining (100x). B: Papanicolaou staining (100x).

Figure 4. Composite figure of clinical images. A: Intralesional corticosteroid injection. B: Clinical appearance of the region after the sixth injection, revealing the marginal gingiva free of lesion.

Figure 5. Histopathological exam revealing aggregations of multinucleated giant cells distributed in a cellular fibrous tissue containing multiple foci of hemorrhage (Hematoxylin and eosin; 100x).

Figure 6. Clinical aspect of the affected region 30 months after the surgery, showing complete recovery with no evidence of recurrence or periodontal defects.
<table>
<thead>
<tr>
<th>Authors</th>
<th>No. patients</th>
<th>Sex/Age</th>
<th>Administration and dose</th>
<th>Treatment length</th>
<th>Results</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present case (2013)</td>
<td>1</td>
<td>1M</td>
<td>Intralesional injections of 0.3 mL of a solution consisting of a mixture of 40 mg/mL of triamcinolone and 2% lidocaine that was later substituted by ethanolamine oleate.</td>
<td>Six injections given in different intervals for 4 months</td>
<td>Partial remission</td>
<td>6 months</td>
</tr>
<tr>
<td>Ferretti C, et al. (2011)</td>
<td>1</td>
<td>1F</td>
<td>Intralesional injection of 6 mL of local anesthetic and steroid solution (0.5% bupivacaine plus triamcinolone acetone 40 mg/5 mL diluted to 5 mg/mL).</td>
<td>Injections given every two weeks for 4 weeks</td>
<td></td>
<td>4 yrs</td>
</tr>
<tr>
<td>Nogueira RLM, et al. (2010)</td>
<td>21</td>
<td>11M:10F</td>
<td>Intralesional injection of 20 mg/mL triamcinolone hexacetonide diluted in an anesthetic solution of lidocaine 2%; 1.0 mL of the solution was infiltrated for every 1 cm² of radiolucent area of the lesion.</td>
<td>Injections given every two weeks for 12 weeks</td>
<td>2 patients with no response, 4 patients with partial response, 15 patients with good response</td>
<td>3 to 8 yrs</td>
</tr>
<tr>
<td>Shirani G, et al. (2010)</td>
<td>1</td>
<td>1F</td>
<td>Intralesional injection of 40 mg/mL triamcinolone acetone mixed with 5 cc Lidocaine 1%.</td>
<td>Injections given weekly for 6 weeks</td>
<td></td>
<td>10 months</td>
</tr>
<tr>
<td>Mohanty S, et al. (2009)</td>
<td>2</td>
<td>1F/1M</td>
<td>Intralesional injections of 4 mL (Case 1) or 6 mL (Case 2) mixture of triamcinolone acetone plus lidocaine 2% (epinephrine 1:200,000).</td>
<td>Case 1: Injections given weekly for 5 weeks, Case 2: Injections given weekly for 9 weeks</td>
<td>Case 1: Complete remission, Case 2: Good response, with relapse after 10 months and then complete remission</td>
<td>18 months</td>
</tr>
<tr>
<td>Wendt FP, et al. (2008)</td>
<td>1</td>
<td>1F</td>
<td>Intralesional injection of 2 mL solution consisting of equal parts of triamcinolone acetone (10 mg/mL) and 0.5% bupivacaine.</td>
<td>Injections given weekly for 11 weeks</td>
<td>Complete remission</td>
<td>6 yrs</td>
</tr>
<tr>
<td>Graham RM, et al. (2008)</td>
<td>1</td>
<td>1M</td>
<td>Intralesional injections of an equal mixture of local anesthetic solution (levobupivacaine) and steroid solution (25 mg of triamcinolone acetone).</td>
<td>Injections given every two weeks for 12 weeks</td>
<td>Partial remission</td>
<td>4 months</td>
</tr>
<tr>
<td>Vargas PA, et al. (2006)</td>
<td>1</td>
<td>1M</td>
<td>Intralesional injections of a mixture of 1 mL of triamcinolone acetone and 1 mL of lidocaine 2%.</td>
<td>Injections given for 6 weeks</td>
<td>Complete remission</td>
<td>5 yrs</td>
</tr>
<tr>
<td>Comert E, et al. (2006)</td>
<td>1</td>
<td>1F</td>
<td>Intralesional injections of 60 mg prednisolone, 40 mg lidocaine and 0.025 mg adrenaline plus 30 mg oral fluocortone.</td>
<td>Injections given weekly for 2 months</td>
<td>Platelet increase, Partial remission</td>
<td>3 yrs</td>
</tr>
<tr>
<td>Sezer B, et al. (2005)</td>
<td>1</td>
<td>1M</td>
<td>Intralesional injection of 5 mL solution consisting of equal parts of triamcinolone acetone (10 mg/mL) and 2% lidocaine (epinephrine 1:200,000).</td>
<td>Injections given monthly for 6 months</td>
<td>Complete remission</td>
<td>3 yrs</td>
</tr>
<tr>
<td>Abdo EN, et al. (2005)</td>
<td>1</td>
<td>1F</td>
<td>Intralesional injections of corticosteroid.</td>
<td>Injections given weekly for 3 weeks</td>
<td>Complete remission</td>
<td>18 months</td>
</tr>
<tr>
<td>Carlos R, et al. (2002)</td>
<td>4</td>
<td>1F/3M</td>
<td>Intralesional injections of 10 mg/mL triamcinolone and either Lidocaine 2% (epinephrine 1:200,000) or Bupivacaine 0.5%. The average dosage was 6 mL for adults and 5 mL for children.</td>
<td>Case 1: Injections given every 3 weeks for 60 weeks, Case 2: Injections given every 2 weeks for 34 weeks, Case 3: Injections given every 2 weeks for 8 weeks, Case 4: Injections given every 2 weeks for 8 weeks</td>
<td>Case 1: Complete remission, Case 2: Complete remission, Case 3: Partial remission, Case 4: Complete remission</td>
<td>7 yrs, 6 yrs, 6 yrs, 2 yrs</td>
</tr>
</tbody>
</table>
Intralesional injections of a mixture of 7 cm³ of triamcinolone acetonide and Bupivacaine 0.5% (epinephrine 1:200,000) on the first and second appointments. On the other appointments, it was used 6 cm³ of the mixture.

Injections given weekly for 6 weeks
Partial remission 7 months

Intralesional injections of 15 cm³ of 10 mg/cm³ of triamcinolone acetonide. Injections given weekly for 12 weeks
Complete remission 1 yr

Intralesional injections of 40 mg triamcinolone acetonide and Bupivacaine 0.5%. Injections given weekly for 6 weeks
Complete remission 2 yrs

Intralesional injections of 2 mL of a mixture of triamcinolone acetonide 10 mg and Lidocaine 0.5% into every 2 cm of the lesion. Injections given weekly for 6 weeks
Complete remission 10 months

Intralesional injections of 4 mL of a mixture of 10 mg triamcinolone acetonide and Lidocaine 0.5%. Injections given weekly for 6 weeks
Complete remission 3 yrs

Intralesional injections of 2 mL of a mixture of 10 mg triamcinolone acetonide and Lidocaine 0.5%. Injections given weekly until bone regeneration be noted radiographically
Complete response 2 yrs

Intralesional injections of 20 mL of a solution of 10 mg/mL triamcinolone and Bupivacaine 0.5% (epinephrine 1:200,000) per 2 cm of radio lucrency. Injections given weekly for 2 weeks
No response NS

Intralesional injections of 20 mL of a solution of 10 mg/mL triamcinolone and Bupivacaine 0.5% (epinephrine 1:200,000) per 2 cm of radio lucrency. Injections given weekly until bone regeneration be noted radiographically
Complete response 2 yrs

Systemic administration of dexamethasone, 20 mg/day during 21 days; 15 mg during 10 days; 15 mg/every other day during 10 days; 5 mg/every other day during 15 days and 10 mg/every other day during 21 days. Partial remission followed by relapse and side-effects due to steroid use 6 weeks

NS: Not specified.

Discussion

Reddish nodular lesions affecting the gingival tissue of young patients may be easily found in the clinical practice. The lack of an adequate oral hygiene routine and due to its broadly variable clinical behavior ranging from an asymptomatic to a more indolent clinical behavior. Good oral hygiene status of the patient, gingival and radiographic features, and the possibility of inflammatory lesions associated to pulp necrosis or root resorption or root displacement could be identified. Considering the radiographic aspects, it is important to evaluate the relationship among alveolar crest between two vital teeth and the lamina dura preserved excluding the possibility of inflammatory lesions associated to pulp necrosis. Similarly, normal signs of root resorption or root displacement in the lamina dura were preserved excluding the possibility of inflammatory lesions associated to pulp necrosis. Thus, the radiographic examination is mandatory to highlight the importance of radiographic evaluation of cases involving lesions involving the alveolar crest and the lamina dura. Radiographic examination is mandatory to highlight the importance of radiographic evaluation of cases involving lesions involving the alveolar crest and the lamina dura.

CGCG was first described in 1953 (11) and due to its broadly variable clinical behavior ranging from an asymptomatic and to a more aggressive entity, the radiographic examination is mandatory to highlight the importance of radiographic evaluation of cases involving lesions involving the alveolar crest and the lamina dura. Radiographic examination is mandatory to highlight the importance of radiographic evaluation of cases involving lesions involving the alveolar crest and the lamina dura.

Radiographic examination is mandatory to highlight the importance of radiographic evaluation of cases involving lesions involving the alveolar crest and the lamina dura. Radiographic examination is mandatory to highlight the importance of radiographic evaluation of cases involving lesions involving the alveolar crest and the lamina dura.
Table 2. Diagnosis of giant cell granuloma (GCG) of the oral and maxillofacial region by FNAC previously reported in the English literature

<table>
<thead>
<tr>
<th>Authors</th>
<th>Lesions evaluated</th>
<th>No. of cytological diagnosis of GCG</th>
<th>No. of cases histologically confirmed</th>
<th>Sex/Age (yrs)</th>
<th>Site</th>
<th>Cytological description</th>
<th>Staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present case (2013)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1M/15 yrs</td>
<td>Mandible</td>
<td>Numerous multinucleated giant cells in a hemorrhagic background</td>
<td>Diff-Quik and Papanicolaou</td>
</tr>
<tr>
<td>Ghandi S, et al. (2011)</td>
<td>44</td>
<td>3</td>
<td>3</td>
<td>NS/NS</td>
<td>NS</td>
<td>NS</td>
<td>May-Grünwald-Giemsa and Papanicolaou</td>
</tr>
<tr>
<td>Baykul T, et al. (2010)</td>
<td>100</td>
<td>9</td>
<td>9</td>
<td>NS/NS</td>
<td>NS</td>
<td>NS</td>
<td>Hematoxilin-eosin and Papanicolaou</td>
</tr>
<tr>
<td>Vargas PA, et al. (2006)</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1M:2F/17 yrs</td>
<td>3 Maxilla</td>
<td>Numerous multinucleated giant cells and macrophages in a hemorrhagic background</td>
<td>May-Grünwald-Giemsa and Papanicolaou</td>
</tr>
<tr>
<td>Gupta K, et al. (2004)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5F/34.6 yrs</td>
<td>2 Mandible</td>
<td>Clusters of round mononuclear cells and scattered multinucleated giant cells</td>
<td>May-Grünwald-Giemsa and Hematoxilin-eosin</td>
</tr>
<tr>
<td>August M, et al. (1999)</td>
<td>30</td>
<td>2</td>
<td>2</td>
<td>NS/NS</td>
<td>NS</td>
<td>Mononuclear cells and multinucleated giant cells</td>
<td>Diff-Quik, Wright-Giemsa and Papanicolaou</td>
</tr>
<tr>
<td>Alatli C, et al. (1999)*</td>
<td>90</td>
<td>29</td>
<td>29</td>
<td>NS</td>
<td>NS</td>
<td>Mesenchymal cells and giant cells of the osteoclastic type</td>
<td>May-Grünwald-Giemsa and Papanicolaou</td>
</tr>
<tr>
<td>Platt JC, et al. (1993)</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1F/14 yrs</td>
<td>Mandible</td>
<td>Sheets of fibroblasts and numerous multinucleated histiocytes</td>
<td>Diff-Quik and Papanicolaou</td>
</tr>
<tr>
<td>Dakalopol D, et al. (1997)*</td>
<td>1022</td>
<td>2</td>
<td>2</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>Giemsa-quick stain, May-Grünwald-Giemsa and Papanicolaou</td>
</tr>
<tr>
<td>Kaw YT. (1994)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1M:1F/14 yrs</td>
<td>2 mandible</td>
<td>Moderately cellular smears with multinucleated giant cells and mononuclear cells</td>
<td>Diff-Quik and Papanicolaou</td>
</tr>
<tr>
<td>Günhan Ö, et al. (1993)</td>
<td>102</td>
<td>6</td>
<td>5</td>
<td>NS</td>
<td>NS</td>
<td>Proliferative lesion with benign giant cells</td>
<td>Hematoxilin-eosin and Papanicolaou</td>
</tr>
<tr>
<td>Ramzy I, et al. (1985)</td>
<td>23</td>
<td>1</td>
<td>1</td>
<td>NS</td>
<td>NS</td>
<td>Abundant spindle cells and multinucleated giant cells, lymphocytes and neutrophils</td>
<td>Papanicolaou</td>
</tr>
</tbody>
</table>

*Peripheral lesions; NS: Not specified.
slow-growing swelling to an aggressive lesion, the surgical approach has been regarded as the treatment of choice for this lesion, which may vary from curettage to en bloc resection. Therefore, both the destructive properties of the lesion and its aggressive management can result in significant functional and esthetic defects, what is particularly a concern in pediatric and young adult patients (12,13).

In the last years, different nonsurgical treatments have been proposed. Systemic calcitonin, interferon 2-alpha and intraleison corticosteroids have shown varying degrees of success and reduced the necessity of major surgical procedures (9,14,15). The use of steroids for treating CGCGs was first suggested in 1981; however, their systemic administration had to be stopped because of important side effects (16). So, the use of intraleisonal injections of steroids was proposed, what led to higher tissue concentration and smaller side effects (17). The satisfactory results obtained using intraleisonal injection of steroids in the treatment of CGCGs may be due to both the inhibition of the extracellular production of lysosomal proteases by multinucleated giant cells and to the steroid apoptotic action on osteoclast-like cells (2).

In 1994 a protocol for treatment of CGCGs of the jaws using a weekly intraleisonal injection of a mixture of triamcinolone acetonide and a local anesthetic (marcaine 0.5% with epinephrine 1:200,000), mixed in equal parts and given for at least 6 weeks was published (15) and thereafter it has been used by different authors that implemented several alterations not only in the dosage and type of drugs, but also in the duration, interval between injections and the number of applications used (Table 1). Although few authors have observed no or minimal decrease of the lesion following the use of intraleisonal steroid injections (18,19), the majority of the studies has reported complete resolutions, which it is well illustrated in the only clinical series published that revealed excellent results with the use of intraleisonal steroids in the treatment of CGCGs (9).

In the present case, the lesion extended to the overlying soft tissue and involved both the attached and marginal gingiva. Although surgery would completely remove the lesion, this procedure would cause periodontal defect. Therefore, in order to avoid or minimize periodontal sequelae, we opted for using the above-mentioned protocol of intraleisonal injection of corticosteroid, with the exception of changing 0.5% bupivacaine by 2% lidocaine. However, after the second injection, we decided to remove the anesthetic solution and add the sclerosing agent ethanolamine oleate in a 1:1 ratio because it was assumed that its sclerosing action would improve the results due to the extensive vascular component present in CGCGs. To the best of our knowledge, this is the first paper reporting the use of ethanolamine oleate in conjunction to triamcinolone for treating CGCG. It is important to emphasize that, although a complete remission was not observed, the main objective was reached, which was reducing the lesion size to permit a more conservative surgical procedure that could preserve the marginal gingiva. Although a satisfactory result was obtained in this case, further studies are necessary to evaluate the usefulness of ethanolamine oleate in combination with corticosteroid for the treatment of CGCGs.

In addition to the conservative treatment modality used in this case, we also opted for a non-invasive diagnostic approach. Thus, FNAC was performed for the diagnosis of CGCG. The role of this simple technique in the diagnosis of oral and maxillofacial lesions has increased dramatically in the last years especially because of its proven safety, accuracy and cost-effectiveness (20-23). Reviewing the English-language literature it is possible to find out several articles describing the value of FNAC in the diagnosis of oral and maxillofacial lesions and evaluating its efficacy in the diagnosis of giant cell lesions of the jaws (5-7). Taken together, the results obtained by these previous studies revealed a very high specificity and sensitivity of the cytological exam for diagnosing CGCG (Table 2). The aspirates obtained in the current case clearly revealed the typical presence of numerous multinucleated giant cells immersed in a bloody background, what is in accordance to the cases previously reported. Hence, the cytological features obtained in cases suspected of CGCG taken together with clinical, laboratory and imaging findings, easily allows the correct diagnosis of CGCG, reinforcing the usefulness of this approach in the identification of lesions affecting the oral and maxillofacial region.

Based on the current report and the satisfactory results consistently reported by different authors regarding the usefulness of intraleisonal injection of corticosteroid as a non-invasive treatment modality for CGCG and considering the accuracy and reliability of FNAC for its diagnosis, it is expected that both procedures will play an important role in the management of this lesion in the future, becoming an option for management of CGCG affecting the jaws.

Resumo

O granuloma central de células gigantes (GCCG) é uma lesão benigna dos maxilares predominantemente encontrada na mandíbula de pacientes jovens do sexo feminino com um variado comportamento clínico. Apesar de o manejo cirúrgico representar a principal modalidade terapêutica para esta lesão, o uso de injeções intralesionais de esteróides tem sido recentemente proposto para seu tratamento. Além do manejo conservador, o uso da punção aspirativa por agulha fina (PAAF) para o diagnóstico do GCCG tem sido comprovado ser uma abordagem segura e eficiente, especialmente útil em casos de lesões localizadas em regiões estéticas. Descrevemos aqui um caso de GCCG estendendo-se para a gengiva adjacente em um paciente do sexo masculino, 15 anos de idade,
diagnosticado por meio da PAAF e subsequentemente tratado com injeções intralesionais de uma solução de acetato de triancinolona e oleato de etanolamina que levou a uma importante remissão clínica, permitindo a realização de uma abordagem cirúrgica conservadora preservando a estética periodontal. Por este motivo, ambos os procedimentos podem ser considerados opções de manejo para o GCCG dos maxilares.

References

Received April 9, 2013
Accepted July 6, 2013