Peripheral giant cell granuloma – case report

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SUMMARY
Peripheral giant cell granuloma (PGCG) or “Epulis gigantocelularis” is the most common oral lesion that originates from giant cells. It typically manifests in the form of soft tissue tumor purple-red or red-watery color consisting of multinuclear giant cells in the mononuclear stroma and extravascular erythrocytes. This lesion is not considered true neoplasm, rather reactive lesion stimulated by local irritation and trauma. However, the cause is not known with certainty. This paper presents a 13-year-old boy with a large lesion in the region of right maxillary canine that was retained in jaw despite favorable vertical position and available space to accommodate in the dental arch. The lesion was completely removed under local anesthesia and histopathological findings confirmed the diagnosis of PGCG. Postoperative period went without complications. After four months additional surgical procedure was needed due to the recurrence, which after tooth naturally erupted and positioned in the dental arch.

Keywords: Peripheral giant cell granuloma; Epulis gigantocelularis

INTRODUCTION
Epulis name originates from the Greek epi – on and Oulon - gums, and, in general, considers any growth on gingiva regardless of etiology [1]. Clinically, most epulis lesions look similar and it is difficult to differentiate these from other tumor-like masses. Since large number of gingival lesions macroscopically looks similar to epulis, the literature has not yet determined the official classification of such lesions.

The most common epulis located on gingiva is made up of connective tissue and covered with stratified squamous epithelium - epulus gigantocellularis. It can be found in the literature under different names such as: peripheral giant cell tumor or peripheral giant cell granuloma. It is most commonly found in the intercanine sector on interdental papilla [2], more often on buccal side in the lower jaw [3]. It is five times more common than central giant cell granuloma that develops in bone [4].

Peripheral giant cell granuloma (PGCG) is of unknown etiology and has slow growth [2]. According to most authors, the cause may be permanent irritation or trauma [5]. In some patients diagnosed with PGCG cytomegalovirus has been isolated [6]. However, it has not been confirmed whether it is the cause or just contributes to the development of the disease.

Initially, mucosa shows unchanged color and looks thickened but PGCG eventually grows to an impressive mass, red or dark red in color and soft consistency that can destroy bone [2]. Also, ulcerations may be present on the surface. PGCG usually does not exceed the size of 5 cm in diameter, but can be bigger. Due to its volume it can push away adjacent teeth [4]. Its base is narrower than its entire volume and impressions of adjacent structures of the oral cavity (teeth, cheeks, language) can be seen on its surface.

It the early stage of its development x-ray does not show any change however after some time changes become noticeable. At this point differential diagnosis should include the central giant cell granuloma.

Treatment is surgical and sometimes requires removing the tooth from the affected area. Recurrent lesions are quite common but they are usually interpreted as the result of inadequate surgery.

The aim of this case report was to present PGCG in 13-year-old boy that was removed by simple surgical procedure that enabled normal eruption of canine and its placement in the dental arch.

CASE REPORT
A 13-year-old boy presented at the Clinic for Oral Surgery, Faculty of Medicine Foca, with evident tumefaction on the alveolar ridge of maxilla in the region of the right canine. Lesion was 3.5×2.5 cm in size, kidney-shaped, red-purple in color and localized in the space of mesial surface of the first right premolar up to the mid part of upper right central incisor, both on vestibular and palatal sides, fulfilling almost the entire vestibule (Figures 1 and 2). X-ray revealed right canine present in the bone that could not erupt due to this lesion on gingiva (Figure 3). The patient underwent fine aspiration biopsy, which after histopathologic examination confirmed the presence of mul-
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Tinucleate giant cells with hemorrhage around. Spindle / inflammatory cells were not detected.

Surgical removal of the lesion was performed under local anesthesia when it was completely removed in one piece and sent for histopathological analysis (Figure 4).

Histopathology revealed the presence of numerous multinuclear cells of different shapes and sizes, containing 8-15 nuclei in fibroblast stroma. Expanded endothelial cells with extravasal erythrocytes were also detected. Moreover, the presence of several giant cells within the vascular space, as well as signs of ossification within the stroma was observed (Figure 5). Based on found histopathological changes it was evident that it is a peripheral giant cell lesion. After surgical procedure was done packaged bandage was placed in the defect, which was removed seven days after the procedure.

After four months, the patient came back with the recurrence of the lesion in the form of blue-purple nodule 5 mm in size (Figure 6), which was again completely re-
moved under local anesthesia (Figure 7). Canine finally erupted into its space. One year after the intervention, there was no sign of possible recurrence while soft-tissue structures around the teeth fully healed.

DISCUSSION

Etiology and nature of PGCG remains undefined. In the past there have been several proposed hypotheses that tried to explain the nature of multinuclear giant cells. These include the hypothesis that they are remnants of osteoclasts that perform natural resorption of primary dentition or that have arisen in response to violations of the periosteum.

PGCG can occur any time in life, but the most common incidence is in the mixed dentition [4]. The lesions are more common in the lower jaw [3, 7] while its size can reach over 2 cm in diameter. Clinically it is similar to pyogenic granuloma, but PGCG typically have blue-purple color compared to red pyogenic granuloma. Recently, there was published case of PGCG associated with dental implants [8]. Although PGCG develops in the soft tissue, local bone resorption of the alveolar ridge can be observed as well. Sometimes it is difficult to assess whether the tumor mass is peripheral lesion or central giant cell granuloma (CGCG) that originate in bone tissue of the alveolar ridge and spreads into gingiva [9, 10, 11].

Histologically, PGCG consists of islands of multinuclear giant cells in the stroma filled with oval and spindle mesenchymal cells and extravasal erythrocytes. Giant cells can contain several to several tens of nuclei. Some of them are large vesicular nuclei, while others are small, pyknotic nuclei. The origin of giant cells is unknown. Ultrastructural and immunological studies [12-16] have shown that they, in fact, originate from osteoclasts [17]. Some researchers believe that they represent reactive component of the lesion, in fact, mononuclear cells from bone marrow that mature through the bloodstream and their sequential extravasation in response to an unknown stimulus from the stroma. This concept is based on the results of recent studies using cell culture and transplantation [18, 19], where giant cells with short life were found and disappeared in culture, in comparison with active proliferation of stromal cells.

According to the findings of Willing et al. [20] it was revealed that stromal cells secrete cytokines and other factors of cell differentiation, including monocyte chemoattractant protein-1 (MCP1), osteoclasts differentiating factor (ODF), and macrophage-stimulating factor (M-CSF). MCP1 is essential for osteoclast differentiation, indicating that stromal cells stimulate migration of monocytes into the tumor tissue fusing in multinucleated giant cells that resemble osteoclasts.

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**Periferni gigantocelularni granulom – prikaz bolesnika**

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**KRATAK SADRŽAJ**

Periferni gigantocelularni granulom (PGCG) ili tzv. epulis gigantocellularis je najčešća oralna lezija porekla džinovskih ćelija. Obično se manifestuje u formi mekotkivnog tumora purpurno crvene ili crveno-ljubičaste boje, koji se sastoji od više do nạnih džinovskih ćelija u monojedarnoj stromi i ekstravazovanim eritrocitima. Ova lezija uglavnom ne predstavlja pravu neoplazmu, a po svojoj prirodi može biti reaktivna jer je stimuliru trauma i lokalna irritacija, dok je uzrok najčešće neznatno.

Ovaj prikaz predstavlja 13-godišnjeg dečaka sa velikom lezijom u frontalnoj regiji gornje vilice, u području očnjaka sa desne strane, koji je zaostao u vili i pored povoljne vertikalne pozicije i dovoljno raspolaživog prostora za smeštaj u zubni niz. Lezija je u potpunosti uklonjena u lokalnoj anesteziji, a histopatološki nalaz je bio karakterističan za PGCG. Postoperativni tok je bio bez komplikacija, a početni recidiv nakon četiri meseca je onaj u ponovnom zahvatu kompletno uklonjen.

**Čelije:** periferni gigantocelularni granulom; epulis gigantocellularis

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**UVOD**

Naziv epulis nastao je od grčkog ἐπι– na i ουλον – desni, a podrazumeva, generalno, svaku izrazlun na desnima bez obziра na njenu etiologiju [1]. Klinički, većina epulisa izgleda slično, te problem predstavlja razlikovanje tih tumoru sličnih masa. Budući da veliki broj promena na gingivi, bar makroskopski, izgleda identično epulisu, u dostupnoj literaturi još uvek nije utvrđena zvanična podela ovakvih lezija.

Najčešće uočena formacija epulisa na desnima, građena od vezivnog tkiva i prekrivena pločastoslojevitim epitelom, jeste utvrđena zvanična podela ovakvih lezija. Budući da veliki broj promena na gingivi, bar makroskopski, izgleda identično epulisu, u dostupnoj literaturi još uvek nije utvrđena zvanična podela ovakvih lezija.

**PRIKAZ BOLESNIKA**

Na Kliniku za oralnu hirurgiju Medicinskog fakulteta u Foči roditelji su doveli 13-godišnjeg dečaka sa evidentnim tumefakcijom na alveolarnom grebenu gornje vilice u regiji očnjaka sa desnog gornjeg gornjeg sekundaca i desne strane. Lezija veličine 3,5×2,5 cm, bubrežastog oblika, crveno-ljubičaste boje bila je lokalizovana između strane premolara do polovine prvog gornjeg sekundaca i sa vestibularne i palatalne strane) i ispunjavala je skoro cesto vestibularum (Slike 1 i 2). Nakon urađenog retroalveolarnog rendgen snimka (Slika 3) uočeno je i prisustvo neizniklog očnjaka i njegovo smeštanje u zubni niz.

Lezija je u lokalnoj anesteziji u potpunosti uklonjena od okoline u jednom komadu (Slika 4) i poslata na histopatološku analizu. Histopatološki je uočeno prisustvo više doも多く džinovskih ćelija sa hemorrhagijom u okolini. Pretime/upsalne celi je nisu detektovane.

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**Cilj ovog rada je bio da se predstavi neobičajena lokalizacija perifernog gigantocelularnog granuloma i ukaže na jednostavno – na i i očuvanje no hirurško rešenje kojim je istovremeno omogućeno nicanje neizniklog očnjaka i njegovo smeštanje u zubni niz.**
DISKUSIJA

Etiologija i priroda PGCG i dalje je nedefinisana. U prošlosti su postojale hipoteze koje su pokušale da objasne prirodu višejedarnih džinovskih celija, uključujući i hipoteze da su one ostaci osteoklasta, koji vrše prirodnu resorpciju mlečne denticije ili da su nastale kao reakcija na povrede peristota.

PGCG se može javiti tokom celog života, ali sa najčešćom incidencom u mešovitoj denticiji [4]. Lezije su češće u donjoj vilici [3, 7], a u svojoj veličini mogu doznati i preko dva centimetra u promjeru. Klinički je sličan piogenom granulum, ali se razlikuje uglavnom po plavo-ljubičastoj boji u poređenju sa crvenom bojom tipičnog piogenog granuloma. Nedavno je i objavljen slučaj PGCG povezanog sa dentalnim implantima [8]. Iako se PGCG razvija u mekom tkivu, često se zapaža i lokalna resorpcija kosti alveolarnog grebena. S vremena na vreme teško je oceniti da li je tumorska masa periferna lezija ili je centralni gigantocelularni granulom (GGCG) nastao u koštanom tkivu alveolarnog grebena, koji se širi u mera tkiva gingive [9, 10, 11].

Histološki, PGCG se sastoji od ostrva višejedarnih džinovskih celija u stromi ispunjenoj ovalnim i vetrenastim mezenhimalnim celijama i ekstravazovanim eritrocitima. Džinovske celije mogu sadržavati nekoliko jedara pa do nekoliko desetina. Neka od njih su velika vezikularna jedara, dok su kod drugih prisutna mala, piknotična jedara. Poreklo džinovskih celija je nepoznato. Ultrastrukturne i imunološke studije [12–16] pokazale su da su one, zapravo, nastale od osteoklasta [17]. Većina smatra da one predstavljaju reakciju komponentu lezije, i da su to mononuklearne celije iz koštane srži koje su tu dospele putem krvotoka i njihovom sledstvenom ekstravazacijom, a predstavljaju odgovor na podsticaj iz same strome. Ovaj koncept se zasniva na rezultatima nedavnih studija, korišćenjem kulture celija i transplantacijom [18, 19], gde su pronadene džinovske celije, kratkog životnog veka, koje nestaju u kulturi, u poređenju sa aktivnom proliferacijom stromalnih celija.

Prema nalazima Willing et al. [20] otkriveno je da stromalne celije luče citokine i druge faktore diferencijacije celija, uključujući monocitni hematotraktantni protein-1 (MCP1), osteoklastični diferencionci faktor (ODF) i makrofag stimulišući faktor (M-CSF). MCP1 je od suštinskog značaja za diferencijaciju osteoklasta i izazuje da stromalne celije stimulišu migraciju monocita u tkivo tumor fuzionišući se u multijedarne džinovske celije, nalik osteoklastima.