ABSTRACT
Introduction: Pyogenic granulomas represent tumor-like lesions affecting skin and the oral cavity. This classic definition can be somewhat misleading because such lesion is not associated with infection and lacks any clinical evidence of pus or histological evidence of actual granulation tissue. Scientific literature sources estimate its prevalence to 1:25000 per capita, affecting females twice as often. Pyogenic granuloma in the oral cavity affects the interdental papilla in 70% of the cases.

Purpose: The authors present a case series of pyogenic granulomas in the oral cavity with varying localization and therapeutic approach.

Materials and methods: This article presents six clinical cases of PG. Diagnosis is challenging due to similarities with number of tumorous and non-tumorous neo-plasms (formations) in the oral cavity. Two histological types of pyogenic granuloma can be identified: lobular and non-lobular capillary hemangioma. Surgical excision is treatment method of choice, followed by deep curettage of the lesion toward the underlying bone. Such precautions are necessary because 15.8% of the lesions tend to recur over time.

Results: Alternative therapeutic approaches for removal of PG are explored, which are aimed at reducing the recurrences after surgical treatment. Such opportunity is provided by utilization of Er:Yag laser, because its effect can reach the underlying bone.

Conclusion: Pyogenic granuloma represents a diagnostic challenge, specifically in cases of atypical localization. Effective surgical approach requires complete removal of the pathological process from the surrounding healthy structures in order to prevent recurrences.

Keywords: Oral, pyogenic granuloma, benign vascular tumors, Er-YAG laser.

INTRODUCTION:
Pyogenic granuloma is common, usually solitary, lobular formation of benign proliferation in the skin and mucous membrane of the oral cavity. It can be pedunculated or sessile, predominantly developing in children and young women [1, 2]. Hullihen was the first to report such case in 1844, and Hartzel introduced the term “pyogenic granuloma” in 1904 [3, 4]. According to other authors, the condition is first described in 1879 by Ponect and Dor under the term “botryomycosis hominis” and later in 1903 Crocker proposed the name “pyogenic granuloma” or “Crocker and Hârtzel disease” [2]. PG is a type of inflammatory hyperplasia. This definition summarizes a number of nodular overgrowths of the oral mucosa, histologically presented by inflammatory fibrous or granulation tissue [4]. Such overgrowths include inflammatory fibrous hyperplasia (clinical fibroma, epulis fissuratum and pulp polyp), giant cell epulis, epulis gravidarum, papillary palatal hyperplasia and PGhyperplasia”.

Etiology of PG is yet unknown, however most associated factors are trauma, inflammation, infectious agents, tartar, foreign bodies, immunosuppression, hormonal changes, medication [2, 3, 5]. Other causes can be gingival inflammation due to poor oral hygiene and trauma due to deciduous teeth, failure of eruption, orthodontic pathologies, dental implants [2, 6]. Pyogenic granuloma is usually presented as red, painless formation that is often localized in the gingiva and grows quickly, it is easily traumatized causing bleeding [3]. Other typical localizations include the tongue, lips, palate and buccal mucosa [7, 8, 9]. The treatment of PG is usually surgical excision, however a tendency for recurrence is observed, especially in female patients [3].

CASE PRESENTATION
Case 1:
A 52 years old female patient in good general health is referred to the Department of Oral surgery of FDM – Plovdiv because of formation on the back of the tongue (Fig. 1). The patient complaints of discomfort during talking and eating are dated back 2-3 months. Clinical evaluation reveals the presence of 5-7mm large formation on the back of the tongue that is soft and painless with palpation. Periodontal status reveals tartar and plaque deposits. Treatment – the formation was surgically excised and there was no recurrence during the 6 months follow-up period. Biopsy showed lobular capillary hemangioma.
Case 2:
A young male aged 17 without any comorbidities is referred to the Department of Oral surgery of FDM – Plovdiv because of suspicious formation, localized on the lingual frenulum (Fig. 2). The patient’s complaints of bleeding during eating date back 4 months ago, the formation meanwhile increased its size. Clinical evaluation revealed 10-6 mm large, soft and painless formation localized on the lingual frenulum. Periodontal evaluation revealed plentiful deposits of plaque.

A recurrence was discovered 1 month after surgical excision of the formation (Fig. 3). Healing process during the three month period after the second surgery was uneventful. Histopathological diagnostics confirmed lobular capillary hemangioma (Fig. 4).

Case 3:
A 36-years old male without comorbidities is referred to the Department of Oral surgery because of esthetically disconcerting formation localized on the lower lip that sometimes bleeds when traumatized (Fig. 5). The formation dates two months ago and the patient also reports having a domestic accident. Clinical evaluation reveals 7-5mm large formation that is soft, painless and with a tendency for provoked bleeding. Histopathological analysis after surgical excision revealed lobular capillary hemangioma.
Case 4:
A 34-years old female in good general health with no comorbidities, who gave birth two months ago, is referred to the Department of Oral surgery in FDM-Plovdiv with complaints of bleeding gums during brushing of teeth. Clinical evaluation revealed multiple formations on the gingiva of maxilla from tooth 13 to tooth 23 and on the mandibular gingiva around tooth 43 (Fig. 6). Periodontal assessment established deposits of plaque and tartar. The gingiva had pasty and edematous look and was painful with palpation. Treatment included surgical excision and curettage deep in the underlying tissues. There is no evidence of recurrence two months later. Biopsy results showed non-lobular capillary hemangioma (Fig. 7).

Case 5:
A 33-years old male patient in good general health is referred to the Department of Oral surgery because of 6-9mm sized formation in the region of teeth 33 and 34 (Fig. 8). Patient’s complaints include bleeding in the mandibular region when brushing the teeth, which started two months ago. During clinical examination a soft-elastic formation that bleeds upon mechanical provocation was discovered. Periodontal status established plaque deposits and multiple pathological pockets. Segment radiograph showed no evidence of pathology in the underlying bone structures (Fig. 9). Excision with Er:Yag laser of the formation and laser treatment of the adjacent soft tissues and the buccal cortical plate of tooth 34 was implemented (Fig. 10, Fig. 11 and Fig. 12). Histopathological evaluation documented non-lobular hemangioma. The patient received further instructions for personal oral hygiene. No recurrence was established in the 6th month follow-up.
Case 6:

A 39-years old female with no comorbidities complained of bleeding and discomfort during eating and brushing her teeth in the anterior palatal region. She gave birth four months prior to her visit in the Department of Oral surgery and she is currently lactating. Her complaints began two months ago. The patient also informed us about prior surgery in the region associated with removal of cyst at the anterior teeth 10 years ago. Clinical evaluation found gingival lesion between teeth 12 and 13 (Fig. 13). The pea-sized formation is soft and bleeds upon mechanic provocation. Periodontal status revealed plaque and multiple periodontal pockets. Treatment included excision followed by deep curettage of the underlying tissues. Diagnosis upon biopsy was non-lobular capillary hemangioma. The follow-up after six months does not reveal any recurring lesions.

Fig. 13. PG on the palatal mucosa. Between teeth 22 and 23
DISCUSSION:
Bhaskar et al. report that PG makes up for 1.85% of all oral pathologies [2,10]. The term “PG” is somewhat inaccurate because such formations are not associated with infection, does not produce pus and there is no clinical or histological evidence of true granulation tissue [3]. Instead, mild trauma or inflammation leading to quick connective tissue overgrowth are associated with the majority of the reported cases [6]. The infection may be caused by streptococci and staphylococci bacteria [11].

The presence of background infection and angiomatous skin lesions is relatively uncommon. Most infectious diseases are associated with exanthema-like reaction. A combination of angiomatous lesion and infection can be observed in cases with Caposi sarcoma or Bartonella infection. [11] Lately angiopoietin and efrin B2 in other tumors of the blood vessels along with Bartonella hanseniae, B. Quintana and HPV8 are found in recurring cases [12]. PG is additionally influenced by viral oncogenes, hormones, microscopic arterial malformations, as well as gene depression in the fibroblasts. [13,14]

It was evident that pregnancy has a role in the development of PG in our patients. More than 5% of intraoral PG is observed in pregnancy, thus supporting the terms “pregnancy tumor” and granuloma gravidarum. [3] Such lesions are frequent occurrences in pregnancy in the light of increased progesterone and estrogen levels. Hosseini et al. establish that gingival hypertrophies are seen during pregnancy and disappear in menopause. [15] Frequency of PG peaks in teenagers and young patients, notably females. [3,16] Our findings confirm its prevalence in females and teenagers.

It was evident that pregnancy has a role in the development of PG in our patients. PG affects predominantly the gingiva (in 75% of cases) [6] but can also occur on the lips, tongue, oral mucosa and palate [2,7,8,14,17] which corresponds to our clinical experience.

Intraoral gingival forms are usually located in maxilla. [2,18] Extraoral presentations most often include the skin and seldom the GI tract. [2,4] Multiple PG develop spontaneously or secondary to trauma, skin inflammation or immunosuppression, however such occasions are relatively rare. [1] The case of multiple PG we presented developed on the background of poor oral hygiene and no preceding trauma. A vicious cycle is at play because of pain during brushing of teeth, which impairs the oral hygiene even further. Our findings are in agreement with the conclusions of other authors [19] and we support the notion that one possible reason for this uncommon pathology can be the impaired oral hygiene.

Usually such lesions are clinically presented as single nodule or pedunculated papula with smooth or lobular surface, sometimes ulcerated, black color, various size from few mm to few cm. Matured lesions are characterized by poorer vascularization, increased amount of collagen and pink color. The formations are usually painless, but bleed easily when provoked or spontaneously due to increased vascularization. [2] Angelopoulos described them histologically as hemangiomatous granuloma, emphasizing the abundance of blood vessels and inflammatory nature of the process [6]. There are two histological types of PG: lobular capillary hemangioma and non-lobular capillary hemangioma [20]. The first type clinically presents as sessile lesion in 66.4% of the cases and the second type – as pedunculated lesion in 77% of the cases. [6,16] Our experience with the sessile, lobular PG on the lingual frenulum supports this differentiation. The lobular region of the lobular PG has more blood vessels of small diameter compared to the central region of non-lobular PG. The central region of non-lobular type has increased amount of blood vessels that are surrounded by mesenchymal cells non-reactive for a-smooth muscle actin and muscle-specific actin compared to the lobular region of lobular PG. [16]

The diagnosis of PG can often be challenging because of the similarities in the clinical presentation of many other intraoral angiomatous lesions. Differential diagnosis includes capillary hemangioma [21], periphery giant cell granuloma, periphery ossifying fibroma, hyperplastic gingival inflammation, pregnancy tumor, Kaposi sarcoma, metastatic carcinoma, angiosarcoma, non-Hodgkin lymphoma.

Surgical excision is treatment method of choice, followed by deep curettage of the lesion, combined with removal of the periosteum and granulation tissue around the adjacent teeth. [2,9] Recurrence is observed in 15.8% of the cases. [10] A lot of authors explore alternative treatment approaches in order to prevent such recurrences, including cryotherapy, laser excision, ethanol etc. [2] No recurrence 3 months following Er:Yag laser excision was found in our Case 5.

CONCLUSION:
PG is relatively uncommon finding in the oral cavity. Its diagnostics are hindered by the similarity to other tumorous and non-tumorous formations. The clinical experience we documented demonstrates different clinical presentations and therapeutic approaches in order to avoid recurrences after surgical excision of the pyogenic granuloma.
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