Journal of Dentistry Indonesia

Volume 27
Number 1 *April*

Article 1

4-27-2020

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## Recommended Citation

Morilla, L. M., Subarnbhesaj, A., & Klanrit, P. Differential Diagnosis and Histopathological Analysis of Localized Gingival Overgrowths: Study of 218 Cases from Northeast Thailand. J Dent Indones. 2020;27(1): 1-5

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## Cover Page Footnote

Special thanks to Ms. Pawinee Wisetsak and the rest of the staff of the Oral Pathology Laboratory, Division of Oral Diagnosis, Department of Biomedical Sciences, Faculty of Dentistry, Khon Kaen University, Thailand for all of their assistance. Thank you very much for all your support.

*Journal of Dentistry Indonesia 2020, Vol. 27, No. 1, 1-5*
*doi: 10.14693/jdi.v27i1.1004*

***ORIGINAL ARTICLE***

# Differential Diagnosis and Histopathological Analysis of Localized Gingival Overgrowths: Study of 218 Cases from Northeast Thailand

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## ABSTRACT

Localized gingival overgrowths (LGOs) are relatively common clinical findings. These lesions can be associated with chronic irritation, infections, or they can represent benign or malignant tumors that can either be primary or metastatic. The etiology of these lesions is multifactorial, but the most prevalent cause is reactive hyperplasia and inflammation induced by dental plaque. **Objective:** This study presents the prevalence of LGOs in Northeast Thailand and identifies the most common LGOs in the region. **Methods:** A series of 218 LGO cases was studied. **Results:** Pyogenic granuloma (PG), gingival squamous cell carcinoma (GSCC), and peripheral ossifying fibroma (POF) were the three most common LGOs in this study. There were also interesting cases of soft tissue counterparts of benign odontogenic tumors and metastatic carcinomas to the gingiva with no evidence of bone invasion observed. **Conclusion:** The three most common LGOs in Northeast Thailand were PG, GSCC, and POF. This study provides baseline data on the prevalence of LGOs in Northeast Thailand.

**Key words:** gingival overgrowth, metastatic carcinoma, peripheral ossifying fibroma, pyogenic granuloma, squamous cell carcinoma

How to cite this article: Morilla LM, Subarnbhesaj A, Klanrit P. Differential diagnosis and histopathological analysis of localized gingival overgrowths: study of 218 cases from Northeast Thailand. J Dent Indones. 2020;27(1):1-5

## INTRODUCTION

Localized gingival overgrowths (LGO) are relatively common clinical findings that comprise a substantial number of oral pathology cases. Most are reactive lesions as responses to various stimuli, such as chronic irritation and infection. They can also represent neoplasms, which are benign or malignant and either primary or metastatic lesions. This variation in appearance is confusing for diagnosing these lesions clinically and histologically. The etiology of these lesions is multifactorial. The most prevalent reason for the reactive hyperplasia and inflammation of the adjacent gingival tissues is dental plaque[1], which can be resolved by eliminating dental plaque through encouraging patients to improve their oral hygiene. It can also be induced by hormonal imbalances, such as during puberty and pregnancy.[1-3] These overgrowths can greatly affect oral functions, such as speech, mastication, esthetics, and oral hygiene.[2,4,5] LGOs are papillary, marginal, or diffuse relative to their location. These overgrowths are further categorized into isolated, discrete, or regional. Isolated gingival overgrowths are limited to the gingiva along a single tooth or two teeth. Discrete gingival overgrowths are those isolated sessile or pedunculated, tumor-like enlargements. Lastly, regional gingival overgrowths involve the gingiva adjacent to three or more teeth.[6]

Based on a study by Rossman[3] among the reactive lesions, the most common is peripheral fibroma followed by pyogenic granuloma (PG), peripheral ossifying fibroma (POF), and peripheral giant cell granuloma. All of these are reactive lesions except for peripheral giant cell granuloma, which shows no consistent gender bias, are commonly found in females.[3] However, the most common localized gingival overgrowth reported on the other studies is

PG.[7,8] Neoplasms, such as squamous cell carcinoma (SCC), also appear as a gingival enlargements.[9] These look like other reactive overgrowths of the gingiva.[10] Therefore, a thorough clinical examination combined with a radiographic evaluation and a histopathological examination should be performed on any gingival overgrowth to diagnose these lesions as early as possible to achieve a good prognosis. Suitable management, which includes patient awareness and motivation, will depend mainly on how precise the diagnosis of the lesion is made.

Northeast Thailand, which is the largest region of the country in terms of area, has 32.21% (22.04 million) of the Thai population. It is the most populated region in Thailand according to the 2018 census. Almost all inhabitants of Northeast Thailand are Thai nationals. However, a majority of them are ethnically from Lao descendants. The Oral Pathology Laboratory of the Faculty of Dentistry, Khon Kaen University is the only oral pathology center in the region; hence, almost all of the oral pathology specimens in the area are submitted to this laboratory.

This study presents the prevalence of LGOs in Northeast Thailand and identifies the most common LGOs in the region. Data from this study will add to the current literature, as no data are available for the prevalence of LGOs in any region of Thailand. However, the large degree of variation in clinical and histological features is a limitation to describe all possible features. Thus, only the most outstanding features will be covered in this study.

## METHODS

An analysis of LGOs submitted to the Oral Pathology Laboratory, Division of Oral Diagnosis, Department of Biomedical Sciences, Faculty of Dentistry, Khon Kaen University, Thailand from the year 2000–2019 was conducted. The authors retrieved glass slides of LGO cases stained with hematoxylin and eosin from the archives with a histopathological interpretation agreed upon by three oral pathology residents (AS, PK, and ST). The authors gathered the clinical data regarding age, gender, and location for each case. As not all cases contained dental radiographs, radiographic interpretations were excluded from this review. Data analyses were performed using IBM® SPSS® Statistics version 22 software (IBM Corp., Armonk, NY, USA) and are presented in descriptive and tabular forms.

## RESULTS

A total of 218 LGO cases were diagnosed histopathologically from the biopsy records with a prevalence rate of 71.48 among all gingival specimens submitted to the Oral Pathology Laboratory. The most common LGO in this study was PG, which constituted 48.62% (106 cases) of all gingival biopsy cases, followed by SCC (29.82%, 65 cases) and POF (8.72%, 19 cases) (Table 1). Among the cases in this study, 146 were females and 72 were males with a female-to-male ratio of 2:1 (Table 1). In general, LGOs in this study occurred 34% more frequently in females than in males. The mean age of the patients was 51.17 ± 22.42 years old (range, 1–100 years old).

The LGOs in this study were commonly observed in the ≥ 60 year old group and least as often as in the 20–30 year old age group (Table 1). The most frequently affected age group between females (43.84%, 64 out of 146 cases) and males (31.94%, 23 out of 72 cases) was ≥ 60 years. Apart from the mandibular bias (59.63%, n = 130) (Table 1) of the LGOs in this study, the most common site was the incisor-canine region (63.30%, n = 138) on either the maxilla or mandible (Table 1).

## DISCUSSION

The first report on the prevalence of LGOs in Northeast Thailand is presented in this study. The results show that PG was the most common LGO in Northeast Thailand. This agrees with previous reports by Al-Rawi and Effiom et al.[7,8] However, Rossmann[3] reported contrasting results. PG, an exophytic non-neoplastic vascular growth associated with a history of chronic irritation[2] , most commonly occurs in younger age groups in areas prone to dental plaque/calculus accumulation. Some reports point to poor oral hygiene as the precipitating factor in the development of PG.[8,11] This lesion may also be induced by hormonal changes and may cause some bleeding. However, the lesion decreases in size after the local irritants are removed or spontaneously disappears.[5] PG is very vascular and bleeds easily. This vascularity renders its bright red color (Figure 1A). PGs present as an ulcerated epithelial surface overlying connective tissue containing numerous small channels lined by endothelial cells with red blood cells within the channels. The connective tissue stroma is infiltrated with lymphocytes (Figure 1B).[3,8]

Oral squamous cell carcinoma (OSCC) can also arise solely from the gingiva (Figure 2A), and can be mistaken for other LGOs.[9,10] At the early stage, it can cause local bone destruction mimicking chronic localized periodontitis and is symptomless.[9] However, the pattern of bone invasion of gingival squamous cell carcinoma (GSCC) is usually ill-defined or moth-eaten that lacks peripheral sclerosis, unlike periodontitis that shows loss of a sharp border with the lamina dura of the adjacent teeth and some evidence of osteosclerosis. OSCC histopathologically presents as a very dysplastic surface epithelium with elongated rete ridges invading

**Table 1.** List of pathologies included in this study with information on age range and gender distribution, as well as the arch and region predilection for each pathology

| Diagnosis (N=218) | No. of Cases | (%) | Age range (years old) | | | | | | | Gender | | Arch predilection | | Region predilection | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | <20 | 20-30 | 31-40 | 41-50 | 51-60 | >60 | N/A | female | male | mandi | maxi | anterior | posterior |
| Pyogenic granuloma | 106 | 48.62 | 27 | 10 | 7 | 18 | 16 | 23 | 5 | 71 | 35 | 54 | 51 | 63 | 43 |
| Squamous cell carcinoma | 65 | 29.82 | 0 | 0 | 0 | 3 | 11 | 49 | 2 | 47 | 18 | 47 | 18 | 44 | 21 |
| Peripheral ossifying fibroma | 19 | 8.72 | 1 | 2 | 4 | 2 | 4 | 3 | 3 | 14 | 5 | 11 | 8 | 9 | 10 |
| Fibrous epulis | 15 | 6.88 | 2 | 1 | 3 | 3 | 2 | 2 | 2 | 8 | 7 | 9 | 5 | 12 | 3 |
| Ameloblastoma | 3 | 1.38 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 1 | 2 | 3 | 0 | 3 | 0 |
| Metastatic carcinoma to the gingiva | 3 | 1.38 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 2 | 3 | 0 | 3 | 0 |
| Non-Hodgkin's lymphoma | 2 | 0.92 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 1 | 1 | 1 |
| Squamous papilloma | 2 | 0.92 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 1 | 1 | 1 | 1 |
| Myxofibroma | 1 | 0.46 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 |
| Neurofibroma | 1 | 0.46 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 1 |
| Peripheral odontogenic fibroma | 1 | 0.46 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 0 |
| *TOTAL* | *218* | *100* | *32* | *13* | *16* | *26* | *34* | *84* | *13* | *146* | *72* | *130* | *86* | *138* | *80* |

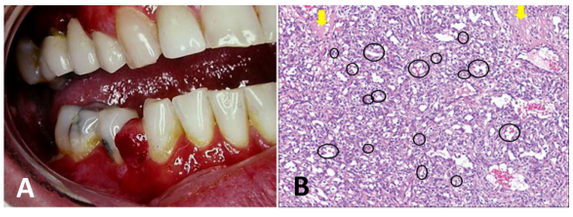


**Figure 1.** A. The clinical picture of a pyogenic granuloma showing a bright red exophytic growth due to high vascularity; B. Photomicrograph showing the connective tissue containing numerous small channels lined by endothelial cells with red blood cells within the channels (*black circles*). It also contained a fibrous part (*yellow arrows*) (hematoxylin & eosin, ×40).

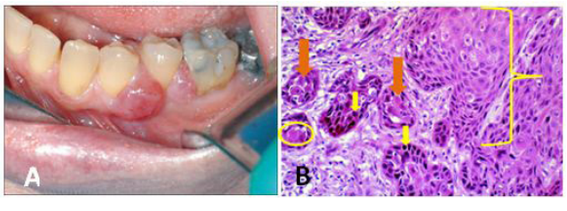


**Figure 2.** A. The clinical picture of a gingival squamous cell carcinoma that appears to be a localized gingival overgrowth in the gingiva; B. Photomicrograph shows a very dysplastic surface epithelium with elongated rete ridges (*yellow bracket*). There is invasion of the underlying connective tissue as islands or cords (*orange arrows*). The cells (*yellow arrows*) are pleomorphic, with prominent nucleoli, nuclear hyperchromatism, and mitotic activity. Keratin pearls (*yellow circle*) can also be observed in several islands of the tumor (hematoxylin & eosin, ×40).

the underlying connective tissue as islands or cords. The cells are pleomorphic, with prominent nucleoli, nuclear hyperchromatism, and mitotic activity.

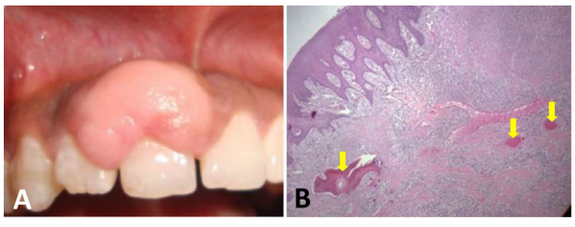


**Figure 3.** A. The clinical picture of peripheral ossifying fibroma, which appears paler than that of a pyogenic granuloma with a relatively smooth surface; B. Photomicrograph showing calcifications (*yellow arrows*) within the cellular stroma (hematoxylin & eosin, ×40).

Keratin pearls are present in addition to the dense lymphoplasmacytic infiltrate in the connective tissue (Figure 2B).[10]

POF was the third most commonly occurring LGO in Northeast Thailand and is one of the most common lesions occurring on the gingiva.[3] These lesions are paler than that of a PG and the surface of the lesion is relatively smooth unlike OSCCs, which show a granulated or irregular surface (Figure 3A). If the number and degree of calcification of bone spicules or cementum-like materials in the lesion are adequately formed, these can be detected through intraoral radiography. A POF tends to be more cellular than a peripheral fibroma and has reduced vascularity compared to PG (Figure 3B).[3]

The cases of LGOs presented in this study have a female bias. This, in general, is consistent with previous reports from the literature on the pathological lesions mentioned in this study, including GSCC. [2,8,9]

Although the reason for this remains unclear, it has been hypothesized that hormones, particularly female hormones, affect the LGOs. For example, exposure of inflamed gingiva to progesterone and estrogen in the bloodstream and saliva is hypothesized to be a contributory factor in the etiopathogenesis of PG during pregnancy, suggesting a relationship between hormones and gingival lesions, but further studies are needed to support this hypothesis.[8] There is still no agreement on this matter among different authors.

In general, the LGOs in this study were commonly found in the older age group (≥60 years). This is in contrast to previous studies showing that the highest incidence occurs within the second to fourth decade of life.[8,12-14] However, GSCC occurs in patients ≥ 50 years old.[9] Thus, LGOs occurring in older patients should be checked thoroughly because of the possibility for GSCC.

The LGOs in this study had a mandibular predilection. This result is in contrast with previous studies reporting that the common LGOs are slightly more prevalent in the upper arch.[7,15] However, GSCC is most prevalent in the mandible[9], while Kfir et al.[12] reported no predilection for the mandible or maxilla. In the present study, the most common region of occurrence was the incisor-canine region of either the maxilla or mandible. This agrees with literature findings[2,5,15], and these lesions are usually located more on the facial aspect rather than on the lingual aspect[7]. However, GSCC is more commonly occurs in the premolar-posterior region[9], while Kfir et al.[12] reported no predilection to the anterior or posterior part.

Some unusual cases of soft tissue counterparts of some benign odontogenic tumors have been reported, such as peripheral ameloblastoma, peripheral odontogenic fibroma, myxofibroma, neurofibroma, and some metastatic carcinomas to the gingiva with no evidence of bone invasion observed in this study. Metastatic carcinomas (MCs) to the gingiva are rare, but they can clinically mimic the more common LGOs, such as PG, and are often underdiagnosed[16] until they become worse. MC to the gingiva occurs in older patients and can originate from primary lesions of several vital organs, such as the thyroid, kidneys, prostate, lungs, and breasts. A confirmed diagnosis of a metastatic gingival lesion is usually graded as stage IV carcinoma. Routine intraoral radiographs should be taken to assess the degree of bone destruction and to detect intra-osseous changes. Furthermore, chest X-rays may be beneficial to detect evidence of lung metastasis.

The possibility that some lesions not being reported due to patient factors, such as negligence or the inability to have the lesion checked, cannot be excluded even if the Oral Pathology Laboratory of KKU is the only oral pathology center in the region. Regular reports of documentation, including other areas or centers in the country, should be performed to expand the LGO databank.

## CONCLUSION

The three most common LGOs in Northeast Thailand were PG, GSCC, and POF. This study provides baseline data on the prevalence of LGOs in Northeast Thailand. The results indicate that age and gender distribution, as well as the location of the lesion, can be used to narrow down or specify the diagnoses, but most importantly, a thorough case history, as well as clinical, and histopathological examinations are needed, particularly because some malignant and metastatic pathologies mimic the most common benign LGOs. This study should be broadened to obtain national data for Thailand.

## ACKNOWLEDGMENT

Special thanks to Ms. Pawinee Wisetsak and the rest of the staff of the Oral Pathology Laboratory, Division of Oral Diagnosis, Department of Biomedical Sciences, Faculty of Dentistry, Khon Kaen University, Thailand for all of their assistance. Thank you very much for all your support.

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(Received October 3, 2019; Accepted February 22, 2020)