



## Case Report

## 23-Year-old male with multiple giant facial pyogenic granulomas being treated with combined topical timolol and steroid: A case report

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## ABSTRACT

**Introduction and importance:** Pyogenic Granuloma (PG) commonly presents as a solitary, erythematous, non-tender, skin lesion, usually not exceeding 2.5 cm. Although Surgical excision is the first-line treatment, conservative treatments are recently developing. Solitary PG is well documented unlike multiple PGs, as the latter is rarely described in terms of its presentations and treatments.

**Case presentation:** This interesting case report describes a 23-year-old male who developed multiple PGs on the nasal area (2cmx2cm) and mandibular area (10cmx2cm) after sutures removal secondary to a recent history of trauma. The lesions regressed after successfully treated with two months of timolol drops and topical corticosteroids. Subsequently, intralesional corticosteroids injections were given once-per-month for two months, with residual fibrosis of the regressed lesion.

**Clinical discussion:** While the most common site for multiple PGs is the interscapular region, this case reports giant, facial, multiple PGs followed suture removal. Although  $\beta$ -blockers were reported to successfully treat solitary PG, only a few cases were raised to discuss this treatment in terms of multiple PGs. This case completes the series and reports successfully-treated multiple PGs using a combination of topical timolol and steroid.

**Conclusion:** This case supports the need to consider multiple PGs as a differential diagnosis following sutures removal even when it reaches rarely reported diameters. Also, it suggests topical timolol and steroids as an effective conservative treatment in similar cases of multiple giant PGs. Notably, the treatment failed to sidestep scar formation.

## 1. Introduction

Pyogenic granuloma (PG) refers to a benign, non-neoplastic vascular tumor that arises in skin and mucous membranes [1]. The lesion usually presents as a minuscule, solitary, erythematous papule [1]. Regardless of its name, PG is not associated with pus production since it is not infection-induced [1]. Also, the term PG is considered a misnomer as in the past PGs were thought to be an exaggerated granulomatous reaction to an infectious or pyogenic insult, which resulted in the use of the terms “pyogenic granuloma” or “granuloma pyogenicum” [1]. While the pathogenesis of PG remains unclear, one study reported an involvement of the proto-oncogene BRAF mutation in most of their patients, resulting in enhanced angiogenesis and an imbalance between pro-angiogenic

and anti-angiogenic factors [2].

PG is a common acquired skin lesion that may affect all ages [3]. Trauma-induced PG is thought to stimulate the formation of one-third of the lesions. Other contributing factors also involved hormones, vascular anomalies and drugs including oral contraceptives, antiretrovirals, retinoids and Immunosuppressive agents [1,3]. Notably, PG is classified as a benign non-neoplastic vascular tumor, also known as lobular capillary hemangioma (LCH). As its name indicates, LCH consists of a collection of small vessels with a feeding vessel in its center [3]. Furthermore, the histological features of this benign tumor can be divided into LHC and non-LHC (NLCH) [1]. However, the clinical differences between these two histological types are not of a statistical significance [4].

PG can be clinically classified into mucosal and cutaneous lesions in

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terms of affected sites. It can also be classified into solitary and multiple in terms of number of lesions. Gingivae, lips, tongue, and buccal mucosa were reported to be the most common mucosal sites of PG lesions [5]. While trunk, as well as extremities, formed the most commonly reported cutaneous sites [6]. The most common site for multiple cutaneous PGs was reported to be the trunk, the interscapular region, in particular [6]. Also, previous studies reported the male predominance in cutaneous PG occurrence especially among children [7]. This is reversed in terms of mucosal lesions, as females are more affected, especially during pregnancy [8].

Differential diagnosis of PG includes Kaposi's sarcoma, squamous cell carcinoma, angiosarcoma, bacillary angiomatosis and hemangioma [9]. These differentials can be ruled out following clinical and histopathological findings [10].

Although surgical excision is the first-line treatment [1], many PG cases regress spontaneously upon follow-up only, with mild chances of scars formation [11]. Therefore, recent studies suggested a 6 weeks follow-up protocol alongside the appliance of topical  $\beta$ -blockers [12]. A recent review also suggested topical steroids and timolol as an efficient treatment, especially in cases of young ages and sites of cosmetic issues [13]. However, only few cases presented the efficacy of such treatment in multiple PGs. Our case completes the series and presents a giant, facial, multiple PGs condition that was treated with topical timolol alongside corticosteroid cream.

## 2. Case presentation

A 23-year-old Syrian male self-presented to the dermatology clinic complaining of large swellings on the nasal and left lower jaw region. He noticed that these swellings started immediately after suture removal following a road traffic accident. Physical examination revealed two giant lesions that measured on the nasal area (2cmx2cm) and left mandibular area (10cmx2cm). The lesions were firm, erythematous, ulcerated with lobular texture and painless to palpation (Fig. 1). Detailed medical history revealed no relevant familial or drug information. The patient was immunocompetent and had no prior history of diabetes or Human immunodeficiency virus.

The differential diagnosis was narrowed as Iododerma following the application of Povidone-iodine, Pyogenic Granuloma, Kaposi's sarcoma, angiosarcoma, bacillary angiomatosis and hemangioma. A histological biopsy was required to confirm the diagnosis. Histological report revealed the proliferation of vascularized granulation tissue with dense neutrophils and scattered lymphocytic plasma cells as well as areas of capillary proliferation and surface ulceration (Fig. 2). The histopathological pattern alongside the clinical presentation narrowed the diagnosis to Pyogenic Granuloma.

The patient's young age and facial lesions required a treatment with least aggressiveness. Accordingly, a two-month topical timolol drop and Triamcinolone cream 7.5 mg/ml were applied resulting in the regression of the lesion, leaving areas of fibrosis. Fibrosis formation was followed by two intralesional corticosteroid injections that were applied in monthly intervals (Fig. 3). The patient was clinically followed-up for one year with no signs of recurrence. This case has been reported in line with the SCARE 2020 criteria [14].

## 3. Discussion

Although the mechanism of solitary PG formation is not clear, the etiology of multiple PGs is yet less understood. Burns are well documented precipitating factors for multiple PGs [10], especially in cases of hot milk burns [10]. Which raised the assumption of the relation between milk proteins and the occurrence of multiple PGs. However, our case represents giant multiple PGs following sutures removal, supporting the fact that such giant lesions must be taken into considerations following similar conditions. It is noteworthy that PGs etiology is not trauma- or infection-related, rather, it is attributed to a loss balance



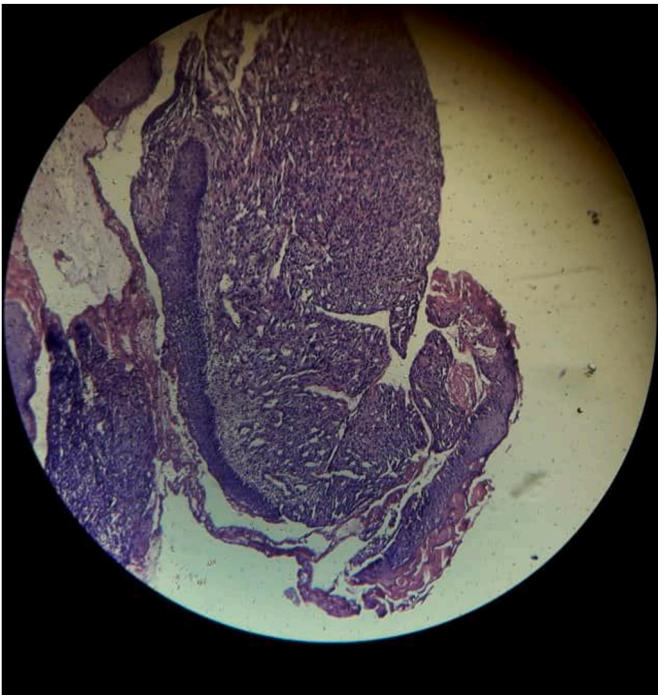
Fig. 1. Appearance of multiple pyogenic granulomas on the nasal.

between pro-angiogenic and anti-angiogenic factors, resulting in different growth factors release [10].

PG typically presents as a red, non-tender, rapidly proliferative, and easily bleeding skin or mucosal lesion. Solitary PG develops upon the location of previous injuries and rarely presents with a diameter larger than 2.5 cm [3]. However, multiple PGs are less described [3]. They usually present in three forms. Either as satellite lesions following the original lesion removal, or as an eruptive disseminated PG. Lastly, similar to our case, it can present as multiple disseminated PGs following widespread trauma [15]. Noting that trunk is the most common site for multiple PGs [6]. Interestingly, our case presents a giant facial multiple PGs condition, where the mandibular-located lesions measure 10 cm in diameter while the nasal lesion measured 2 cm.

Histopathological report is mandatory for the confirmation of PG diagnosis [8]. Differential diagnosis for PG includes Kaposi's sarcoma, squamous cell carcinoma, angiosarcoma, bacillary angiomatosis and hemangioma [9]. Kaposi's sarcoma can mimic a number of lesions; thus, a microscopic investigation is required to confirm its diagnosis, which shows extravasated erythrocytes and intracellular hyaline globes, not of





**Fig. 2.** Histological examination: Ulcerated surface replaced by inflammatory granulation tissue, vascular proliferation of capillaries with central branching vessels separated by.

which are seen in PG [16]. Angiosarcoma can also be distinguished from PG by the lobular and vascular pattern as well as its cytological features. Similar to our case, PG histopathological report would show capillary-sized vascular proliferation [8].

First-line treatments for PG include full-thickness excision [3]. Excision of the PGs followed by primary closure resulted in minimum recurrence among 408 patients [8]. Since this method of management requires general or local anesthesia and has a high rate of scar formation, new methods of conservative treatments were recommended [3].

In our case of giant facial lesions, surgical removal of the lesion would mostly have resulted in scar formation. Thus, a conservative treatment with the lowest rates of recurrence was more applicable. Accordingly topical treatment using timolol alongside Triamcinolone was applied. Topical corticosteroids affect the pathogenesis of PG in several ways, including vasoconstriction and inhibiting proangiogenic agents.  $\beta$ -blockers effectiveness was reported in terms of solitary PG lesions regression [12]. Although  $\beta$ -blockers have a gradual effect in treating PGs and the period of treatment would take more than 6 weeks, it can avoid the adverse effects of other treatments including scar formation [17].  $\beta$ -blockers also reduce the need to use local or general anesthesia [18]. Topical treatments using  $\beta$ -blockers or corticosteroids are discussed in terms of solitary PG [13,19]. However, this method of conservative treatment is rarely documented in terms of multiple cutaneous PGs. Thus, our case bridges the gap and illustrates the efficacy of a combination of topical  $\beta$ -blockers and corticosteroids in a multiple PGs condition. Although we expected our treatment to sidestep scar formation, it failed to achieve the expected outcomes.

#### 4. Conclusion

To our knowledge this is the first case to report giant facial multiple PGs with one of the lesions reaching  $10 \times 2$  cm in diameter. Also, this case highlights the need to investigate multiple PGs following sutures removal. Furthermore, it suggests a successfully treated multiple PGs condition using topical steroids and timolol. However, it is noteworthy that this protocol failed to sidestep scar formation. We emphasize the



**Fig. 3.** Regression of the lesions accompanied fibrosis formation after the treatment.

need to confirm the efficacy and investigate the side effects of this conservative treatment protocol using a case series study design.

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#### Author contribution

KK, HK, HM drafted the manuscript. RN supervised the patient's examination, treatment, and follow-up. All authors have read and approved the final manuscript.

## Registration of research studies

Name of the registry: N/A.

Unique Identifying number or registration ID:

Hyperlink to your specific registration (must be publicly accessible and will be checked):

## Guarantor

Rasha Nabhan, MD, Derm.

## Consent of patient

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Provenance and peer review

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## Declaration of competing interest

The authors declare that they have no conflict of interests.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104544>.

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