

# Thalidomide as Treatment of Lip's Pyogenic Granuloma

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**Abstract:** Pyogenic granuloma (PG) is a benign vascular tumor that can be challenging to treat, particularly in aesthetically sensitive areas. We report a case of a 32-year-old man with a PG on the upper lip that did not respond to conventional treatments, including glucocorticoid injections and long-pulse 1064 nm laser therapy. Due to aesthetic concerns and the lack of response to these treatments, the patient was administered oral thalidomide at a nightly dose of 75 mg for 5 months, which resulted in complete regression without recurrence over a 3-year follow-up. This case suggests thalidomide's potential as an effective alternative treatment for PG in sensitive areas.

**Keywords:** pyogenic granuloma, thalidomide, treatment, lip

## Introduction

Pyogenic granuloma (PG), also known as lobular capillary hemangioma, is a common benign vascular proliferation. It is characterized by rapidly growing, erythematous nodules that can bleed easily.<sup>1</sup> Pyogenic granuloma predominantly occurs in the head and neck regions, including the oral gingiva and lips, and can also affect the limbs.<sup>2</sup> The pathogenesis of PG is not fully understood but is thought to be associated with trauma, infection, hormonal imbalances, and certain medications.

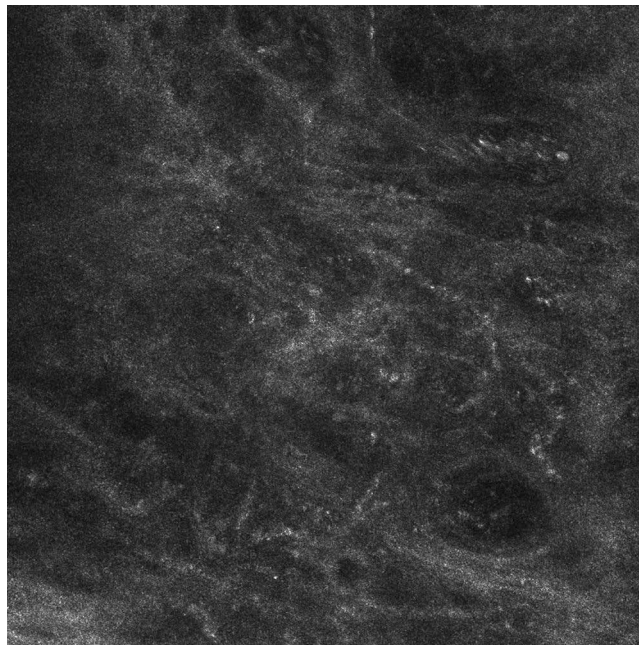
Treatment of PG mainly includes surgical and non-surgical methods. The former has high efficiency, low recurrence rate, and feasible histopathological examination, which is the main choice for the treatment of pyogenic granuloma at the present stage. However, it can be costly and may result in scarring, especially in sensitive areas such as oral gingiva and lips. Non-surgical treatments such as laser therapy, cryotherapy, glucocorticoid injections, and local administration of anticancer drugs are less invasive but may have variable efficacy. Glucocorticoid injections can lead to atrophy, hyperpigmentation and hypopigmentation, while anticancer drug injections may cause local ulceration and scarring. Moreover, some clinical studies demonstrated that the diode laser can achieve effective treatment and superior aesthetic outcomes with minimal complications in oral and maxillofacial surgical ablation.<sup>3,4</sup>

## Materials and Methods

We report a case of an otherwise-healthy 32-year-old man who presented with a single painless red nodule on the middle of the upper lip for 2 months. Initially, the nodule was a corn-sized papule that bled easily upon touch and was not initially treated due to lack of discomfort. Physical examination: a solitary, hemispherical, red nodule measuring approximately 8 mm in diameter, with a smooth, moist surface, telangiectasia, clear boundaries, and a soft texture that bled easily (Figure 1). And we conducted a reflectance confocal microscopy(RCM) examination (Figure 2). Excisional biopsy was the most common treatment modality of PG, and this can eliminate the lesion and provide a definitive



**Figure 1** The red arrow indicates a pyogenic granuloma located on the middle of the upper lip of a 32-year-old man before the treatment with thalidomide. The lesion presents as a solitary, hemispherical, red nodule, measuring approximately 8 mm in diameter, with a smooth, moist surface, telangiectasia, clear boundaries, and a soft texture that bled easily.



**Figure 2** Reflectance Confocal Microscopy(RCM) findings revealed extensive proliferation of capillaries within the dermis, with abundant blood flow. Some capillary lumens were markedly dilated, containing erythrocytes, and a small number of inflammatory cells were observed around the vessels.

diagnosis based on histopathologic assessment. Considering the location of the skin lesion on the middle of the upper lip and the patient's concern about cosmetic outcomes, we did not proceed with the histopathological examination. We diagnosed the condition as pyogenic granuloma by these typical clinical manifestations (hemispherical, red nodule, prone to bleeding, rapid growth), the RCM findings and differentiating it from other similar diseases (Table 1).

Despite local injection of compound betamethasone (Shanghai Schering-Plough Pharmaceutical Co., Ltd., SFDA Approval No. HJ20130188, Specification: 1mL contains betamethasone dipropionate 5mg and betamethasone sodium phosphate 2mg) and four times of long-pulse 1064 nm laser therapy (once a week), the lesion showed no significant improvement within six months. Given the PG's location and the patient's aesthetic concerns, we opted for oral thalidomide treatment (75 mg per dose, once nightly for a total of 5 months). After five months, the lesion had flattened

**Table 1** The Differential Diagnosis of Pyogenic Granuloma.<sup>1,5-8</sup>

Features	Pyogenic Granuloma	Cherry Angioma	Cutaneous Sarcoidosis	Trichofolliculoma	Basal Cell Carcinoma
<b>Age</b>	Any age, often in children and young adults, particularly pregnant women	Older individuals	Often in the third to fourth decades	Individuals aged 18 to 49 years	Middle-aged to older adults
<b>Location</b>	Commonly on the head, neck, hands, and lips	Trunk and extremities	Face, trunk, and extremities	Head and neck	Head, neck, and trunk
<b>Lesion Characteristics</b>	Erythematous nodules, prone to bleeding	Asymptomatic, small, bright-red papules	Numerous, firm, papules, color in flesh-colored, red-brown, purple-brown	Flesh-colored, an umbilical-shaped depression is observed in the center	Pearly papule with rolled borders and arborizing vessels
<b>Growth Rate</b>	Rapid growth	Slow growth	Slow and recurrent	Slow	Slow but locally aggressive

and decreased in volume, with only a faint scar remaining (Figure 3). During this period, patients experienced only mild xerostomia without any other adverse effects. A three-year follow-up confirmed complete healing with no recurrence (Figure 4), and the patient was satisfied with the treatment.

## Discussion

In the extant medical literature, there is a paucity of evidence to support the use of thalidomide in the treatment of pyogenic granuloma. Most studies suggest that PG pathogenesis is related to high expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (FGF).<sup>9</sup> In recent years, immunohistochemical analyses have shown increased expression of cyclooxygenase-2 (COX-2) and Interleukin-10 (IL-10) in PG tissues compared to normal vascular tissue.<sup>10</sup> Some studies have also linked mutations in genes such as BRAF, RAS, and GNAQ to PG pathogenesis.<sup>11</sup> Thalidomide (THD) is a versatile immunomodulatory and anti-angiogenic drug extensively utilized in dermatology for conditions such as erythema nodosum leprosum, cutaneous sarcoidosis, lupus erythematosus, Behcet's disease, pyoderma granulosum, prurigo nodularis, vascular dermatoses and so on. THD serves as an effective treatment for dermatological conditions that are refractory to conventional therapies. It should be noted that the more common and unique side effects of THD are teratogenicity and peripheral neuropathy.<sup>12</sup> THD exerts its therapeutic impact through



**Figure 3** The red arrow indicates the area where the lesion had flattened and decreased in volume after five months of treatment, with only a faint scar remaining.



**Figure 4** The red arrow indicates the middle of the upper lip, where after a three-year follow-up, no visible scar remains.

modulation of vascular and immune responses, demonstrating efficacy in various malignancies. It is recognized for its ability to suppress FGF-2 and VEGF, thereby inhibiting tumor necrosis factor-alpha (TNF- $\alpha$ ) synthesis and attenuating inflammation, angiogenesis, and immune responses.<sup>13</sup> THD also impedes lipopolysaccharide-induced COX-2 expression, destabilizing mRNA and impeding prostaglandin E2 (PGE2) synthesis, further contributing to its anti-tumor and anti-inflammatory effects.<sup>14</sup>

## Conclusion

In this case, the decision to use oral thalidomide was based on the lesion's location where obviously affect appearance and the lack of improvement with local injection and laser treatment. The potential mechanisms of thalidomide in treating PG include inhibiting angiogenesis by suppressing VEGF and FGF, improving microvessel aggregation, and exhibiting anti-tumor effects. It can also degrade COX-2, inhibit tumor growth, and possess anti-inflammatory properties. Thalidomide modulates granulomatous inflammation by promoting immune cell recruitment and activity, while also regulating angiotensin-converting enzyme levels, potentially inhibiting macrophage function.<sup>15</sup> However, the specific mechanism still requires further research.

This case report demonstrates the successful use of thalidomide in treating PG, offering a potential therapeutic option for PG or hemangiomas in specific areas when other treatments have been unsatisfactory.

## Ethical Approval and Consent

Ethical approval is not required to publish the case details in accordance with local or national guidelines. The patient provided written informed consent for the publication of this case report and accompanying images.

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## Disclosure

The authors declare no conflicts of interests for this article.

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