

ORIGINAL ARTICLE

Pyogenic Granuloma: Multiple lesions affecting the pinna. Case report and literature review

Enrique Úraga,* Verónica Úraga,** Alfredo Chávez,** Juan Carlos Garcés,**
Andrea Aguilar****

- * Director of the Dermatological Centre "Dr. Úraga". Director of the UCSG Postgraduate Degree in Dermatology
- ** Dermatologist at the Dermatological Centre "Dr. Úraga" - Guayaquil, Ecuador
- *** Dermatopathologist
- **** Rotation at the Dermatological Centre "Dr. Úraga" - Guayaquil, Ecuador

Corresponding author:
drenriqueuragap@hotmail.com

Key words: Pyogenic granuloma, seborrheic dermatitis, demodicidosis, external auditory canal

Date of receipt: 01-12-2021
Date of acceptance: 12-12-2021
Date of publication:

ABSTRACT

Pyogenic granuloma is a relatively common condition that manifests at all ages and has been associated to trauma, although this does not represent the majority of cases. The case of a patient with long-standing severe facial seborrheic dermatitis is presented. It is accompanied by spinulate demodicosis of the face and neck, as well as one-year multiple tumour-like lesions of the left external auditory canal. The clinical picture is reviewed, as well as the literature.

INTRODUCTION

The term pyogenic granuloma (GP) is a misnomer, as it is neither a true granuloma nor is it of bacterial origin. This injury, also known as telangiectatic granuloma, is currently acknowledged as lobular capillary hemangioma.¹ It is an acquired benign vascular neoplasm, located on the skin in 80% of the cases and on the mucous membranes in 12% of the cases. It is characterized by rapid growth and a very friable surface. It predominates in childhood and early adulthood, between the second and third decades of life. It represents the most common cutaneous location in males and the most prevalent location, involving mucosae, in females. Pregnant patients can present PG in mucosae between 0.9% and 9.6% of the times, especially during the first

five months of gestation. When observed in these circumstances, the PG is also known as pregnancy epulis, granuloma gravidarum or pregnancy granuloma.²

PATHOGENESIS

Regarding its pathogenesis, although, as indicated above, its denomination suggests infectious origin, its cause is actually unknown. PG is an inflammatory vascular lesion of the skin and mucosae. Some define it as a benign vascular tumour while other authors define it as a reactive inflammatory lesion.³ However, the pathogenesis of most sporadic PGs and PGs associated with port wine stains remains difficult to determine. Recently, the BRAF c.1799T>

mutation has been identified as one of the main mutations in the pathogenesis of PG, which would explain the appearance of multiple PGs in patients who are treated with BRAF inhibitors.⁴⁻⁵ Most of the theories about the pathogenesis of PG are focused on hyperplastic neovascular responses to angiogenic stimuli, causing imbalance between promoters and inhibitors. Angiogenic growth factors, such as vascular endothelial growth factor and decorin, transcription factors (pATF2 and pSTAT3), and mitogen-activated protein kinase are overexpressed in PGs, but their exact role is undetermined.⁶

Several reports affirm that the PG may appear as a response to previous injuries. For example, the manifestation of multiple PGs after 3 weeks of an arm burn,⁷ or as a result of piercing the nose with earrings, as in the cases reported by Gosh et al.,⁸ hormonal factors, various drugs or laser treatments, giving rise to the concept of PG being a reactive disease.⁵ Baykal et al. report a case in which the plaster splint produced a slight peripheral nerve injury that, in the short term, led to the interruption of nail growth and the manifestation of multiple PGs that resembled retronychia,⁹ confirming what Tosti et al. discovered in 2001 regarding 9 patients to whom the plaster was removed and revealed onychomadesis and PG of the proximal nail fold.¹⁰

In 2016, Thakur et al. reported a similar case,¹¹ as well as Lopez-Castillo et al. in 2020.¹² All these cases manifested in the hands. Their presence would indicate that they are not isolated cases, but rather a consequence of the pressure of the plaster splint, which must be taken into account as a trigger.

Among the drugs most cited as causative are systemic retinoids, such as acitretin¹³ and isotretinoin¹⁴ that decrease the binding between keratinocytes and have angiogenic properties. Tyrosine kinase and epidermal growth factor receptor inhibitors, such as gefitinib¹⁵ and imatinib with vascular side effects and erlotinib, involving a case of PG localized in the trachea of a patient undergoing treatment for lung cancer,¹⁶ BRAF inhibitors, including vemurafenib, which causes MAPK overexpression. Other me-

dications include levothyroxine, mentioned in the case of multiple oral PGs in a patient with hypothyroidism,¹⁷ along with cyclosporine, tacrolimus, topical and systemic fluoracil¹⁸ with proangiogenic effect, topical imiquimod, among others that have also been cited.⁶

Paradoxically, there is a report on the manifestation of PG in the treatment with angiogenesis inhibitors, such as ramucirumab, a fully humanized monoclonal IgG1 antibody targeting extracellular receptor 2 of vascular endothelial growth factors.¹⁹⁻²⁰

There has been mention of a relation between PG and herpes virus type 1. Hayden et al. report a case that was cured in the span of two weeks with the administration of valanciclovir.²¹ Likewise, its frequency of appearance in pregnant women seems to indicate that hormonal factors play a role in the etiology aspect. However, there are many opponents of this theory.²²

CLINICAL PRESENTATION

It usually starts as a small red papule that then grows rapidly over the span of a weeks or months, presenting easy bleeding until it stabilizes. As for the size, it is unusual for it to exceed one centimetre.

It can be sessile or pedunculated and, at its base, a scallop or collarette of acanthotic epidermis can be observed. Usually, they are formed from apparently normal skin, although their appearance has been reported on vascular malformations or apparent periungual outbreaks.⁶

CLINICAL VARIANTS

According to what it has been previously reviewed, there are clinical variants of PG. Details are found below:

- **Mucosal PG:** Can be solitary or multiple, sessile or pedunculated and presenting with easy bleeding.
- **Multiple and/or disseminated PG and/or with satellitosis:**⁶⁻²³ The latter manifest as multiple lesions and appear spontaneously or following previous treatment.

- **Congenital PG:** Although it is an injury that, as previously indicated, can manifest at any stage of life as acquired, there are reports of appearance at birth. Browning et al.⁵⁸ reported two cases of giant and disseminated congenital PG affecting the face, extremities and vulvar region.
- **Giant PG:** Is very rare with relatively few published cases. Most of them grow less than 2 cm and when they sometimes grow more than 4 cm, they are called giant PG,²⁴ causing great difficulty to differentiate them from malignant tumours. This can occur even with smaller PGs and confusion occurs especially with melanoma.²⁵⁻²⁶
- **Subcutaneous and intravascular PG:** Although PG normally occurs in the superficial dermis, subcutaneous and intravascular lesions are rare, as is the case with these two characteristics reported by Barr et al.²⁷ The intravascular form was reported in 1979 by Cooper et al. presenting a study of 18 patients. In his work, he stated that these cases had to be differentiated from angiosarcoma and angiolymphoid hyperplasia with eosinophilia.²⁸

LOCALIZATION OF LESIONS

Regarding its location, the PG can be located in any area of the body. Most common locations in adults are the trunk or extremities, while in children the lesions are located on the head and neck. The skin is affected to a greater degree than the mucous membranes (86%).⁶

There are reports of unusual locations, such as the urinary meatus,²⁹ tongue, such as a case reported in a pregnant patient and another in a male patient,³⁰⁻³¹ on the vulva³² or penis, such as the curious case of a patient who, after a year of healing from a syphilitic chancre, presented with PG in the spot of the healed chancre.³³ Its location in the scrotum has also been reported.³⁴

There is a curious case that reports the appearance of PG, arising from the empty cavity after dental extraction. The author qualifies this as extremely rare.³⁵

Furthermore, generally, the location on the scalp, fingers and gums (39.64%) are pretty common.³⁶⁻³⁵⁻³⁷

PG can manifest within a capillary vascular malformation,³⁸ such as the port wine stain, either spontaneously or after laser therapy,³⁹ which would support the theory of PG arising from microscopic arteriovenous anastomosis found in capillary malformations and in common sites of PG, such as acral zones and oral and nasal mucosae.⁶ It has also been reported to grow recurrently on a nevus flammeus.⁴⁰

As far as our case is concerned, the location on the pinna is not extremely uncommon, as there are relevant reports. The most frequently cited cases are related to piercing, such as in the case of bilateral PG reported by Dash,⁴¹ Magliulo⁴² or those of Song,⁴³ who also reports bilateral PG in the external auditory canal in a pregnant patient, to which they attributed hormonal origin and that of Hsu with continuous serosanguineous drainage.⁴⁴ For his part, Park reported the first case of PG on a deeper anatomical location (tympanic membrane) on a patient with chronic otorrhea.⁴⁵ Moreover, Rehman reports a case of a giant PG located on the conchae, with the risk obstructing the external auditory meatus.⁴⁶

PATHOLOGY

Histologically, PG is composed of capillaries and venules with epithelial cells arranged in lobes by a fibromyxoid stroma. Its development can be classified into three phases: cellular, capillary or vascular and third (involutional). If the lesion is not treated, there is the possibility of slow fibromatous regression, after a long time. Endothelial cells in PGs express CD34, ICAM-1, VCAM-1 in association with increased microvascular density (47).

DIAGNOSIS

Based on the aforementioned characteristics, it is generally clinical.

Dermoscopy reveals typical characteristics of the condition,⁴⁸⁻⁴⁹ such as:

- Homogeneously pink papules (92%).
- White collarette surrounding the papule (85%)
- Presence of crossed white rail lines on the lesion, representing fibrous septa, seen histopathologically (31%)
- Ulceration (46%)
- Presence of vascular structures
 - Punctiform vessels
 - Comma vessels
 - Hairpin vessels
 - Glomerular vessels
 - Telangiectasias
 - Linear / irregular vessels
 - Polymorphic / atypical vessels
- Presence of fine scales

Oiso and Kawada believe that the dermoscopic examination of PGs should be done with and without pressure because with pressure vascular structures disappear.⁵⁰

In his work, Zaballos⁵¹ recognizes the same dermoscopic characteristics mentioned above, and cites the vascular structures observed. Furthermore, he establishes seven patterns where all structures listed above are combined. Figure 1, from the article by P. Zaballos, exemplifies this.⁵¹

1. Homogeneous net and white collarette (P1)
2. Homogeneous net and white rail lines (P2)
3. Homogeneous net and vascular structures (P3)
4. Homogeneous net, white collarette and white rail lines (P4)
5. Homogeneous net, white collarette and vascular structures (P5)
6. Homogeneous net, white rail lines and vascular structures. (P6)
7. Homogeneous net, white collarette, white rail lines and vascular structures (P7)

In conjunction with dermoscopy, the histopathological examination confirms the diagnosis and makes it pos-

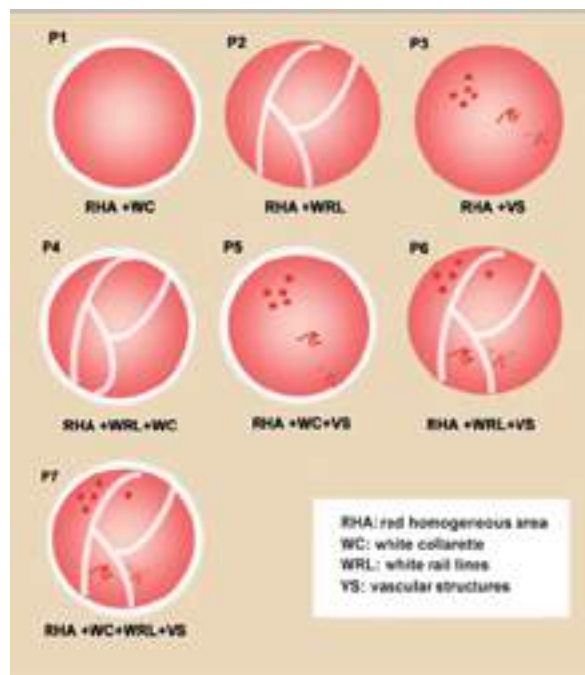


Figure 1. Scheme of combination patterns (taken from the article by Pedro Zaballos Diego⁵¹)

sible to rule out malignant tumours, such as amelanotic melanoma in doubtful cases.

DIFFERENTIAL DIAGNOSIS

Many pathologies have been listed as differential, being those the most cited⁶⁻²²

- Infantile hemangioma
- Spitz nevus
- Glomus tumour
- Common wart
- Amelanotic Melanoma
- Squamous cell carcinoma
- Basal cell carcinoma
- Bacillary angiomatosis
- Angiolymphoid hyperplasia with eosinophilia
- Angiosarcoma
- Irritated melanocytic nevus
- Hemangiomas

TREATMENT

While it is true that spontaneous regression is reported, it is very uncommon and possible bleeding and ulceration requires treatment.

Therapy comparison trials are rare, and there is no agreement for optimal treatments. Many types of treatment are reported and advocated, from surgical to topical and intralesional therapy or even a combination of the same.⁶ If the PG is pedunculated, excision can be performed through cauterization of the base, but in this case the risk of recurrence increases. In a study involving 34 reports of PG therapy carried out by Lee et al where they compared therapies, they concluded that between excision with direct closure (510 cases with 15 recurrences) vs shaving and cauterization of the base (199 cases with 19 recurrences), there was higher percentage of recurrence in the second (2.94%) vs 9.55% respectively. While in non-surgical therapies, cryotherapy with liquid nitrogen was the one that had the lowest percentage of recurrence compared to all other procedures (3 recurrences in 185 cases with a percentage of 1.62%).⁵²

Regarding lesions located in non-cosmetic areas, most authors suggest full-thickness surgical excision to ensure non-recurrence and allow, if necessary, histopathological study.

Among topical and intralesional therapies, sclerotherapy with 0.1ml 3% sodium tetradecyl sulfate is recommended as a safe and economical treatment in adults.⁵³

Imiquimod cream (5%) has been used in 6-month-old to 12-year-old children with facial PG with good results, especially when anaesthesia or sedation is not an option and side effects want to be avoided.⁵⁴

The use of topical beta-blockers, such as BID 0.5% ophthalmic solution timolol⁵⁵ and 4% propranolol gel and 1% ointment have been reported with success.

Lately, the use of table salt has been advocated for the treatment of PG. Paraffin is applied to perilesional skin to avoid irritation. The skin is covered with salt and occluded with surgical adhesive tape. This procedure is repeated every day and results in resolution of the lesion seven and fourteen days after, depending on the location and size of the PG.⁵⁶ Another 2021 report exemplifies treatment in 50 patients with different kinds of PG in the skin and mucosae with 100% success rate, without complications.⁵⁷

CLINICAL CASE

28-year-old patient with no significant history or allergies.

At the time of the consultation, the patient reports two problems: on the one hand, and for some years, intense scaling on the scalp and lesions of the same type on the forehead and midface region accompanied by intense itching; on the other hand, one-year small tumours with occasional bleeding, which had been treated by an ENT specialist with topical corticosteroids. No improvements were observed. The patient reports that these lesions appeared after persistent itching that led to intense scratching.

Examination revealed profuse desquamation of the scalp, scaly erythematous plaques on the forehead, cheeks and the central face region. Presence of acneiform eruptions on the cheeks. (Picture 1)

The neck reveals multiple small whitish projections that can be seen by the naked eye. They suggest spinous demodicosis (Picture 2).

The left pinna reveals multiple rounded pink tumours with scaling on the surface and presence of ulceration. Four lesions were located in the meatus of the external auditory canal and one in the branch of the helix.



Picture 1. Scaly lesions are observed at the edge of the scalp and seborrheic regions.



Picture 2. Multiple whitish projections suggestive of demodex can be seen with the naked eye.

Dermoscopic examination of the lesions on the neck reveals the presence of multiple spicules suggestive of spinulosis demodicosis (Picture 3).



Picture 3. Dermoscopy allows to clearly visualize demodex spicules and tails on the neck.



Picture 4. There are 4 tumours located on the external orifice of the auditory canal (white arrow) and one in the branch of the helix (red arrow). An ulcerated lesion is observed (blue arrow).



Picture 5. Dermoscopic characteristics.



Picture 6. Dermoscopic characteristics.

Dermoscopic examination (pictures 5 and 6) shows pink coloration in all lesions, along with desquamation (white arrow), ulceration (blue arrow and circle). The enlargement shown in picture 7 reveals structures that make it compatible with pattern 7 of Zaballos, including a pink pattern (yellow arrow), white rail lines (white arrow), vascular structures (red arrow), white collarette (blue arrow), as well as ulceration (green arrow) and fine scales (black arrow).



Picture 7. Dermoscopic enlargement that allows observing structures typical of Zaballos pattern 7: pink net, white collar, white lines in rail, vascular structures and also desquamation and ulceration.

Histopathology of lesions was carried out, which reported: Skin with exophytic proliferation of newly formed capillary vessels in arborescent architecture, with swollen and prominent endotheliums. It is partially ulcerated, covered with fibrinopurulent exudate. Presence of epidermal collarette at the periphery. No changes suggestive of malignancy. (Picture 8)

DIAGNOSIS

Shave biopsy for skin tumour of the left ear.

Pyogenic granuloma

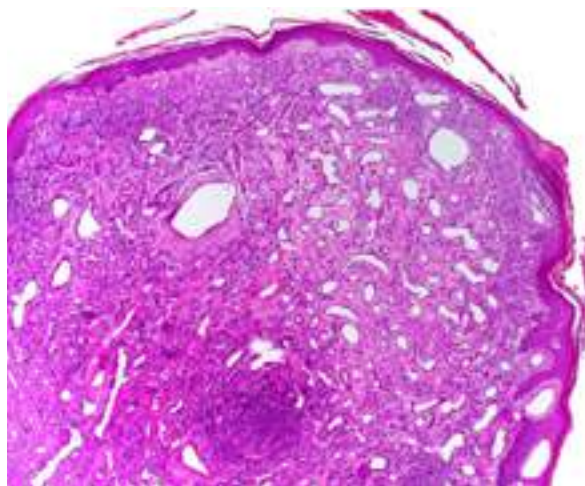
Patient received treatment for her seborrheic dermatitis on both the scalp and face, as well as topical and oral treatment for demodex. Oral antibiotic therapy was prescribed and the lesions were eliminated by cauterization in two sessions. One month after the second session, recurrence of one of the lesions was noted, proceeding to its elimination.

After a year, the patient continues to present seborrheic dermatitis to a lesser degree, but the pinna has no presence of lesions (Picture 9).

DISCUSSION

Originally described by Poncet and Dor in 1897, PG was in fact considered as a botriomycotic infection transmitted from horse to man. Later, it was thought this process was caused by bacteria, such as streptococci and staphylococci, but as time went by, and new research surfaced, no real evidence was found to confirm such theories, determining consequently the name was incorrect. The name of lobular capillary hemangioma was deemed as more appropriate and persists historically. Rather, bacterial infection is considered to be of secondary involvement, rather than the main etiological cause of the process.¹⁷

While PG is a relatively common process, some of the locations we've mentioned are rare and some extremely rare. The one presented by the patient in this



Picture 8. Panoramic view of histopathological study showing capillary proliferation.



Picture 9. A year later, the pinna has no presence of PG lesions.

report falls into the latter group. The PG of the pinna is located in all external and middle anatomical structures, that is, the external orifice, atrial canal and tympanic membrane (Fig.2) and the aforementioned reports, which speak about the limited observation of these cases. The patient was not pregnant. The intense scratching the patient experienced for over a year was identified as the probable cause. This case report is deemed as interesting, both because of the unusual lesional location, as well as the number of lesions and the probable triggers of the pathology (seborrheic dermatitis and demodicosis).



Figure 2. The anatomy of the pinna and locations of the PG cited in the literature. External auditory meatus, atrial channel, tympanic membrane (extracted from the Internet).

REFERENCES

1. Skúladóttir B, Korshø A.R., Wrenfeldt M, Poulsen FR. A capillary hemangioma of lobular subtype (pyogenic granuloma) in the calvarium of a pregnant woman. *Acta Neurochir (Wien)* 2020;12:3001-3004.
2. Qin R, Cohen PR. Concurrent pyogenic granuloma and bullous impetigo of a pregnant woman's finger. *DOJ* 2017;23: 1-4
3. Arciniegas E, Carrillo LM, Rojas H, Pineda J, Ramírez R, Reyes O, Chopite M and Rocheta A. Plump endothelial cells integrated into pre-existing venules contribute to the formation of 'mother' and 'daughter' vessels in pyogenic granuloma: possible role of galectin-1, -3 and -8. *Scars, Burns & Healing*, 2020;6:1-12
4. Wollina U, Langner D, Franca K, Gianfaldoni S, Lotti T, Tchernev G. Pyogenic Granuloma – A Common Benign Vascular Tumor with Variable Clinical Presentation: New Findings and Treatment Options. *Open Access Maced J Med Sci.* 2017; 5(4):423-426.
5. Groesser L, Peterhof E, Evert, Landthaler M, Berneburg M, Hafner C. BRAF and RAS Mutations in Sporadic and Secondary Pyogenic Granuloma. *J Invest Dermatol.* 2016;136(2):481-6.
6. Lawley PL. Pyogenic granuloma (lobular capillary hemangioma) – UpToDate. Last updated: Nov 04, 2020.
7. Krieger Y, Weiss E, Horev A, Melamed R, Shoham Y, et al. Multiple Large Pyogenic Granulomas Overlying a Burn: Case Report and Literature Review. *J Clin Cosmet Dermatol* 2020;4:1-4
8. Ghos SK, Bandyopadhyay D. Granuloma Pyogenicum as a Complication of Decorative Nose Piercing: Report of Eight Cases from Eastern India. *Journal of Cutaneous Medicine and Surgery*, 2012; 16: 197-200
9. Baykal C, Kilic S, Sezer S. Periungual pyogenic granuloma-like lesions following plaster cast immobilization: a case managed with symptomatic therapy. *JDDG* 2018;16:74-75
10. Tosti A, Piraccini BM, Camacho-Martinez F. Onychomadesis and Pyogenic Granuloma Following Cast Immobilization. *Arch Dermatol.* 2001;137:231-232.
11. Thakur BK, Verma S, Mishra J. Pyogenic granuloma with onychomadesis following plaster cast immobilization. *Indian J Dermatol Venereol Leprol.* 2016;82:239-241
12. Lopez-Castillo D, Curto-Barredo L, Sánchez-Schmidt JM, Pujol RM. Multiple Eruptive Pyogenic Granulomas on the Proximal Nail Folds Following Cast Immobilization: A Case Report with Nail Unit Ultrasound Findings. *Acta Derm Venereol.* 2020;100:25-29
13. Thomas M, Shon W, Truong AK. Acitretin-induced periungual pyogenic granulomas and review. *Dermatology Online Journal* 2021; 27:1-4

14. Bellew JG, Taylor C, Daulat J, Mackey VT. Isotretinoin induced nail fold pyogenic granuloma resolution with combination therapy: A case report and review of the literature. *SKIN* 2019;3:1-4
15. Fernandes A, Antunes A, Varela P. Pyogenic Granuloma in a Patient on Gefitinib. *Acta Med Port* 2016;29(6):416-416
16. Putora PM, Benz G, Rodriguez R, Brutsche M, Fruh M. Tracheal granuloma pyogenicum with erlotinib treatment for lung cancer EUROPEAN RESPIRATORY JOURNAL VOLUME 38 NUMBER 5 DOI: 10.1183/09031936.00008411
17. Gutierrez AA. Un inusual caso de granuloma piógeno oral multiple, ¿asociado a tratamiento con levotiroxina? *Rev Estomatol Herediana*. 2020;30(4):294-301
18. Curr N, Saunders H, Murugasu A, Cooray P, Schwarz M, Gin D. Multiple periungual pyogenic granulomas following systemic 5-fluorouracil. *Australasian Journal of Dermatology* 2006; 47, 130-133
19. Ibe T, Hamamoto Y, Takabatake M, et al. Development of pyogenic granuloma with strong vascular endothelial growth factor receptor-2 expression during ramucirumab treatment *BMJ* 2019;12:e231464. doi:10.1136/bcr-
20. Daze RP, Dinkins J, Mahoney MH, Osimertinib and Ramucirumab Induced Pyogenic. Granulomas: A Possible Synergistic Effect of Dual Oncologic Therapy. *Cureus* 2021; 13(5): e15076. DOI 10.7759/cureus.15076
21. Haideri L, Paurobally D, Fassotte MF, Andre J, Arrese JE, Sadzot C, Ruebben A, Nikkels AF. Herpes Simplex Virus Type-I and Pyogenic Granuloma: A Vascular Endothelial Growth Factor-Mediated Association? *Case Rep Dermatol* 2013;5:236-243
22. Sarwal P, Lapumnuaypol K. Pyogenic Granuloma. *StatPearls - NCBI Bookshelf*. Last Update: December 5, 2020.
23. Rana R, Sulugodu S, Chandra U, Aggarwal P, Kajoor J. Recurrent Pyogenic Granuloma With a Satellite Lesion. *CUTIS* 2015;96:e27-e30
24. Polanco-Llanes AS, Amezcua-Gudiño S, Sánchez-Ibarra F, Solorio B, Soria- Orozco M. Granuloma piógeno gigante. *Dermatol Rev Mex*. 2020; 64:313-317
25. Schönlebe J, Wollina U. A Sheep in Wolf's Clothing: Lobular Pyogenic Granuloma Masquerading Nodular Amelanotic Melanoma. *Open Access Maced J Med Sci*. 2019; 7:3015-3017.
26. Tchernev G, Chokoeva AA, Terziev I, Grigorov Y, Lotti T, Wollina U, Cardoso JC, Yungareva I, Lozev I, Maximov GK. Small Dysplastic Congenital Melanocytic Nevi in Childhood as Possible Melanoma Immitators. *Open Access Maced J Med Sci*. 2018; 6:149-151.
27. Barr KL, Vincek V. Subcutaneous Intravascular Pyogenic Granuloma: A Case Report and Review of the Literature. *CUTIS* 2010;86:130-132
28. Cooper PH, McAllister HA, Helwig EB. Intravenous pyogenic granuloma. A study of 18 cases. *The American Journal of Surgical Pathology* 1979;3:2221-228
29. Inakanti Y, Nagaraja A, Peddiredi S, Metikurke V. A case of Pyogenic Granuloma at an Unusual Location. *Egyptian Dermatology Online Journal* 2014;10: 1-6
30. Arunmozhi U, Shanmuga R, Kadshiresan R, Sujatha G, Shasudeen SM. A Large Pregnancy Tumor of Tongue - A Case Report. *Journal of Clinical and Diagnostic Research*. 2016; 10: ZD10-ZD12
31. Gonzaga VL, Gouveia NM, Sanzgiri VB, Khandolkar P, Sukhthankar IR. A Rare Case Report of Pyogenic Granuloma of Tongue. *International Journal of Otolaryngology and Head & Neck Surgery*, 2018, 7, 75-79
32. Vencs M, González M, Figueroa E. Granuloma piógeno en la vulva. *Dermatol Rev Mex* 2018;62(5):423-429
33. Hadzavdic SL, Bartolic L, Doko K, Sherlev M. Pyogenic granuloma of the penis following chancre. *JEADV* 2018, 32, e86-e121
34. Sánchez L. Tumoración nodular exofítica eritematosa escrotal. *Dermatol Perú* 2020;30:160-162
35. Iijima Y, Nakayama N, Kashimata L, Yamadan M, Kawano R, Hino S, Kaneko T, Horie N. A Rare Case of Pyogenic Granuloma in the Tooth Extraction Socket. *Case Reports in Dentistry Volume* 2021, Article ID 5575896, 5 pages <https://doi.org/10.1155/2021/5575896>
36. Suárez M, Acosta A. Lesión exofítica en el cuero cabelludo de un niño. *Diagnóstico y comentario. PIEL* 2020;35 (1 0) : 6 6 4 - 6 6 7

37. Ribeiro JL, Moraes RM, Carvalho FC, Nascimento AO, Milhan NV, Anbinder AL. Oral pyogenic granuloma: An 18-year retrospective clinicopathological and immunohistochemical study. *J Cutan Pathol*. 2021;48:863–869.
38. Rancan A, Boscarelli A, Codrich D, et al. Pyogenic granuloma arising within capillary malformations in children: A case report and literature review. *Dermatol Rep* 2021;13:9115.
39. Liu S, Yang C, Xu S, Yuan C, Yang S, Zhang X. Pyogenic Granuloma Arising as a Complication of 595 nm Tunable Pulsed Dye Laser Treatment of Port-Wine Stains: Report of Four Cases *Dermatol Surg* 2010;36:1341–1343
40. Shruti S, Siraj F, Ramesh V, Ramesh V. Recurrent pyogenic granuloma over nevus flammeus. *Indian J Dermatol Venereol Leprol* 2019;85:236.
41. Dash S, Kain R. A case of bilateral ear pyogenic granuloma following ear piercing. *Our Dermatol Online*. 2018;9(4):462–463
42. Magliulo G, Iannella G, Gianno F, Re M. Lobular Capillary Hemangioma and External Auditory Canal. *Otology & Neurology*, 2014;35: e213–e214.
43. Song K, Lee J, Park MJ, Lee HY. A Case of Bilateral External Auditory Canal Pyogenic Granuloma in a Pregnant Woman. *J Audiol Otol* 2018;22(4):244–247
44. Hsu CH, Chen HC, Wang CH. Bilateral external auditory canal pyogenic granuloma. *Otolaryngology–Head and Neck Surgery* 2008; 139: 596–597
45. Park HW, Lee SH, Hur DG, Ahn SK (2016) A Case of Pyogenic Granuloma Arising from the Tympanic Membrane. *Ann Otolaryngol Rhinol* 3(8): 1126.
46. Rehman S, Loizou P, Singh PK. Obstruction of the external auditory meatus secondary to a giant pyogenic granuloma. *BMJ Case Rep* 2015. doi:10.1136/bcr-2015-211196
47. Wollina U, Langner D, Franca K, Gianfaldoni S, Lotti T, Tchernev G. Pyogenic Granuloma – A Common Benign Vascular Tumor with Variable Clinical Presentation: New Findings and Treatment Options. *Open Access Maced J Med Sci*. 2017; 5(4):423–426.
48. Carneiro CG, Leroy AK, Bresciani C, Tavares L. Brito A, Simao R, Tinoco G. Dermatoscopia do Granuloma Piogénico. *Revista SPDV* 2016;74:99–100
49. Teyssiere S, Thomas L, Dalle S. Dermatoscopie du botryomycome. *Annales de Dermatologie et de Vénéréologie* 2016;143:567–568
50. Oiso N, Kawada A. Dermoscopy of pyogenic granuloma on the lip: the differing appearances of vascular structures with and without pressure. *EJD* 2011;21:441
51. Zaballos P, Carulla M, Zalaudek I, Bañuls J, Puig S, Argenziano G, Malhevy J. Dermoscopy of pyogenic granuloma: a morphological study. *BJD* 2010;163:1229–1237
52. Lee J, Sinno H, Tahiri Y, Gilardino MS. Treatment options for cutaneous pyogenic granulomas: A review *Journal of Plastic, Reconstructive & Aesthetic Surgery* (2011) 64, 1216e1220
53. Ravishankar D, Kusagur MS. Therapeutic vanish in pyogenic granuloma: a case series. *Int J Res Dermatol* 2020;6:553–5.
54. Tritton SM, Smith S, Chuen L, Zagarella S, Fischer G. Pyogenic Granuloma in Ten Children Treated with Topical Imiquimod. *Pediatric Dermatology* Vol. 26 No. 3 269–272, 2009
55. Hoyer P, Ly P, Ross L, Wilkerson M. Timolol for Treatment of Recalcitrant Pyogenic Granulomas: a Case Report and Review of the Literature. *The National Society for Cutaneous Medicine* 2017;1:150–155.
56. Burzin S, Dhurat RS. A pinch of salt is all it takes! The novel use of table salt for the effective treatment of pyogenic granuloma *J Am Acad Dermatol* 2020;83:e107–8.
57. Daruwalla SB, Ghate S, Dhurat R. Establishing the efficacy and safety of the novel use of common salt for the treatment of pyogenic granuloma. *Clinical and Experimental Dermatology* 2021; 46: 1243–1247
58. Browning JC, Eldin. KW, Kozakewich HP, Mulliken JB, Bree AF. Congenital Disseminated Pyogenic Granuloma. *Pediatric Dermatology* 2009;26 :323–327, 2009