Pyogenic Granuloma

Richie L. Lin, MD; Camila K. Janniger, MD

GOAL

To recognize, diagnose, and treat pyogenic granuloma (PG)

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Understand the etiology and pathogenesis of PG.
2. Recognize and diagnose PG.
3. Effectively treat PG.

CME Test on page 251.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: September 2004.

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Albert Einstein College of Medicine and Quadrant HealthCom, Inc. Albert Einstein College of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Albert Einstein College of Medicine designates this educational activity for a maximum of 1 category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only that credit that he/she actually spent in the activity.

This activity has been planned and produced in accordance with ACCME Essentials.

Drs. Lin and Janniger report no conflict of interest. The authors report no discussion of off-label use. Dr. Fisher reports no conflict of interest.

Pyogenic granuloma (PG) is an acquired vascular lesion of the skin and mucous membranes common to the pediatric age group. PG appears as a solitary red nodule on the head or neck. The nodule is prone to hemorrhage, and bleeding is often refractory to pressure. The etiology of PG is unknown, but proposed agents include trauma, infection, and preceding dermatoses. Several surgical treatments are available with variable cosmetic results and recurrence rates.

Cutis. 2004;74:229-233.

Accepted for publication January 13, 2004.

Dr. Lin is an intern at St. Mary's Hospital in San Francisco, California. Dr. Janniger is Clinical Professor and Chief, Pediatric Dermatology, UMDNJ-New Jersey Medical School, Newark.

Reprints: Camila K. Janniger, MD, Dermatology, UMDNJ-New Jersey Medical School, 185 S Orange Ave, Newark, NJ 07103-2714 (e-mail: janniger@yahoo.com).

Pyogenic granuloma (PG) is a common vascular hyperplasia of the skin and mucous membranes that occurs in children and young adults.[1-3] It is usually found on the face, trunk, and limbs. There are also subcutaneous[4] and intravenous[5,6] variants. PG is often solitary, but multiple satellite lesions may occur.[7]

PG was identified over a century ago and has been associated with minor trauma, chronic irritation, hormonal factors, and viral infections. To date, however, no significant causative relationships have been verified. The etiologic hypotheses have led to a number of terms used to describe PG that suggest a causative agent; these terms include *botryomycosis hominis*,[8] *granuloma telangiectodes*,[9] and *granuloma pediculatum*.[10] The term *pyogenic granuloma* was adopted in 1925 because it was considered descriptive of the underlying process.[10] Recently, the term *lobular capillary hemangioma* has been suggested because of the histologic appearance of the lesions.[11]

Epidemiology

PG is common in children and young adults. In children, the mean age of onset is 6.7 years; 42% of cases occur by 5 years of age, 12% occur before 1 year of age, and 1.1% are present at birth.[2] Cutaneous PG has no gender predisposition and accounts for 0.5% of all skin nodules in children.[12] The incidence of oral mucosal nodules peaks in the second or third decade of life[13]; oral mucosal nodules occur in a 2:1 female-male ratio and are associated with pregnancy and oral contraceptive use.[13] Multiple PGs usually occur in young adults but have been reported in children.[13,14]

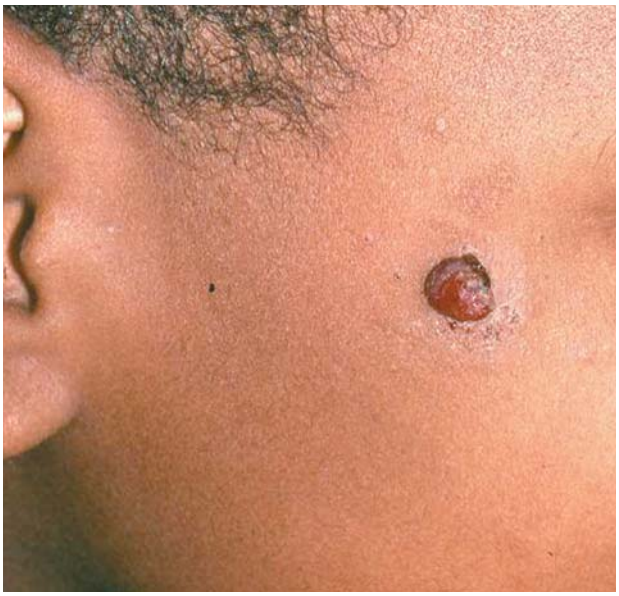
Etiology and Pathogenesis

The etiology of PG is unknown, but because PG regresses when potential initiating stimuli are removed, it qualifies as a vascular hyperplasia.[3] Possible predisposing factors include trauma, chronic irritation, increased levels of female sex hormones, infections, viral oncogenes, and microscopic arteriovenous anastamoses.

As many as 50% of individuals with PG have a history of local trauma.[10,15,16] Further, multiple PGs often develop following surgical manipulation of primary nodules.[7] It has been postulated that excessive production of an angiogenic factor following trauma may be responsible for the vascular hyperplasia.[17-19] However, some studies report little association between trauma and PG.[2]

Female sex hormones also may play a role in the pathogenesis of PG. Oral mucosal nodules occur at an increased frequency in pregnant women and in women who use oral contraceptives.[13,20-22] This increased occurrence is thought to be due to an imbalance between angiogenesis enhancers and inhibitors.[23] A recent study demonstrated that female sex hormones enhance the expression of angiogenic factors, including vascular endothelial growth factor, basic fibroblast growth factor, and interleukin 1β.[21] A decreased rate of endothelial cell apoptosis also was seen. Recurrence of an excised nodule is not uncommon during pregnancy, and conversely, lesions tend to resolve after childbirth.[20,22,24] There is no relationship between sex hormones and cutaneous PG.

Bacterial infection is another suspected cause of PG, yet no etiologic agents have been found. *Bartonella* infection may manifest as a spectrum of lesions, ranging from solitary PG to widespread bacillary angiomatosis.[25,26] There was a statistically significant association between PG and seropositivity for *Bartonella*.[26] Gram-positive bacilli have also been observed on microscopic examination of PG tissue samples.[25]



A nodular pyogenic granuloma 3 cm lateral to the palpebral fissure of an African American child.

Viral oncogenes might lead to sudden and uncoordinated growth of the dermal papillae, resulting in PG. It is hypothesized that viral infection leads to disregulation of gene repression in papillary fibroblasts.[27]

PG nodules may have a propensity to develop at sites of microscopic arteriovenous anastomoses.[28] Consistent with this idea is the observation that the frequency of PG and the density of cutaneous vascularity is greatest in the head and neck, followed by the trunk and limbs (with vascularity greater in the upper limbs than in the lower).[2,29] In addition, PGs have occurred within a nevus flammeus (port-wine stain), a type of vascular malformation.[30-33]

Clinical Features

Commonly recognized variants of PG include cutaneous, oral mucosal (granuloma gravidarum), satellite, subcutaneous, intravenous, and congenital types. Cutaneous PG often arises as a painless, red, and crusted or ulcerated papule on the skin surface (Figure). The mean diameter of a cutaneous PG is 6.5 mm.[2] The lesion develops over weeks, and growth typically stabilizes over several months.[2,11,15] Eventually, it shrinks to become a fibrotic "angioma."[2] Some nodules spontaneously infarct and involute. Solitary cutaneous PGs are commonly located on the head and neck (62.5%), trunk (19.7%), or limbs (17.9%), with the upper limbs involved more often than the lower.[2,13]

Oral mucosal nodules account for up to 70% of PGs in women.[13] These lesions may develop on the gingiva, lips, or buccal mucosa.[13,23] Lesions

often arise during the second or third trimester of pregnancy or with the use of oral contraceptives.[13,20-23] PG on the oral mucosa has a higher rate of recurrence than cutaneous PG if excised during pregnancy and often resolves spontaneously after childbirth. Mucosal PG also has been reported on the tongue,[34] in the larynx,[35] and on the glans penis.[16,36]

Satellite PGs are rare, usually occurring after treatment or manipulation of a solitary nodule.[7,25,37] Spontaneous occurrence is rare.[7,38] Satellite lesions are smooth, red, sessile papules that range in diameter from 1 to 10 mm. Unlike solitary PGs, satellite PGs most commonly appear on the trunk.[7,39]

Subcutaneous PGs also are uncommon and appear as nonspecific subcutaneous nodules.[4,11,40] Because the clinical appearance of this tumor is quite different from that of cutaneous PG, subcutaneous PG is often difficult to diagnose based on clinical features. It is sometimes mistaken for a hemangioma or an epidermal cyst. Biopsy results readily distinguish it from granulation tissue or from other vascular entities.

Intravenous PGs may appear as subcutaneous nodules with nonspecific features, most commonly developing on the upper limb.[6,41] Intravenous PG also may be evident as a red-brown polyp.[41] Clinical diagnosis of intravenous PG can be difficult, as it can be mistaken for an organizing thrombus.

Congenital PG is an uncommon disseminated variant.[2,42] Multiple lesions, similar in appearance to the cutaneous form, are present at birth. The condition appears to follow a benign course, with spontaneous resolution over 6 to 12 months.

Differential Diagnosis

The differential diagnosis of PG should include amelanotic melanoma,[43] angiosarcoma, basal cell carcinoma, squamous cell carcinoma, Kaposi sarcoma,[44] hemangioma, bacillary angiomatosis,[45-47] metastatic visceral malignancies,[48] and granulation tissue. A case of hepatocellular metastases to the gingiva mimicking PG also has been reported.[49]

Histology

Early PG is histologically identical to granulation tissue, appearing as highly vascularized connective tissue with capillaries and venules in an edematous matrix.[2,3] As the lesion matures, a fibromyxoid stroma separates the lesions into lobules containing aggregates of capillaries and venules with plump endothelial cells.[3] By this point, the edema has resolved. The epidermis exhibits inward growth at the lesion base, forming a so-called epidermal collarette and causing slight pedunculation. Extensive fibrosis signifies the final stage of regression.

Treatment and Prognosis

Various treatment modalities have been used to remove PG. Effective means include excision, shave excision, laser surgery, sclerotherapy, electrodesiccation, curettage, ligation, or a combination of methods.

Excision with linear closure offers the lowest recurrence rate and allows histologic examination of a tissue sample. Closure, however, leaves a linear scar.[50] Shave excision followed by argon laser photocoagulation is an effective therapeutic alternative that minimizes scar formation while preserving the ability to confirm the diagnosis with histologic examination.[50]

More conservative methods such as 585-nm flashlamp-pumped pulsed-dye laser surgery are beneficial but require multiple treatments and can only be used for small lesions.[51] A 100% cure rate was observed with ethanolamine oleate sclerotherapy on both large and small lesions.[52] Recurrence rate with shave excision plus cauterization or cauterization alone has been reported to be 43.5%.[2] None of these tissue-preserving methods allows histologic examination. The lack of histologic confirmation should not pose a problem for experienced dermatologists or in clinically obvious cases. However, in one series, 18% of PGs were incorrectly diagnosed.[50]

Surgical debulking of cutaneous lesions followed by cauterization with silver nitrate has been advocated as an effective yet inexpensive treatment. Follow-up should occur weekly, with repeat cauterization as needed. This regimen results in an 85% resolution rate in an average of 1.6 treatments.[53]

Peduncular PGs may be ligated at the base using absorbable suture.[54] The tumor is lifted with forceps and ligated at the base with tight suture knots. The tumor will become necrotic and fall off over several days. The procedure is atraumatic and inexpensive and requires no anesthesia or special equipment. Persistence or recurrence can be treated with excision or laser surgery. However, the procedure does not allow histologic examination.

Conclusion

PG is an acquired vascular neoplasm of considerable interest.[55-60] Its friability often produces an enhanced level of clinical concern. PG needs to be distinguished from Kaposi sarcoma, melanoma, and metastatic carcinoma, as well as an important systemic bacterial infection, bacillary angiomatosis.

REFERENCES

1. Mooney MA, Janniger CK. Pyogenic granuloma. *Cutis*. 1995;55:133-136.
2. Patrice SJ, Wiss K, Mulliken JB. Pyogenic granuloma (lobular capillary hemangioma): a clinicopathologic study of 178 cases. *Pediatr Dermatol*. 1991;8:267-276.
3. Requena L, Sangueza OP. Cutaneous vascular proliferations, part II: hyperplasias and benign neoplasms. *J Am Acad Dermatol*. 1997;37:887-920.
4. Cooper PH, Mills SE. Subcutaneous granuloma pyogenicum. *Arch Dermatol*. 1982;18:30-33.
5. Song MG, Kim HJ, Lee ES. Intravenous pyogenic granuloma. *Int J Dermatol*. 2001;40:57-59.
6. Kocer U, Aksoy HM, Tiftikcioglu YO, et al. Intravenous pyogenic granuloma of the hand. *Dermatol Surg*. 2003;29:974-976.
7. Blickenstaff RD, Roenigk RK, Peters MS, et al. Recurrent pyogenic granuloma with satellitosis. *J Am Acad Dermatol*. 1989;21:1241-1244.
8. Poncet A, Dor L. Botryomycose humaine. *Rev Chir*. 1897;18:996.
9. Kuttner H. Über telangiektatische granulome. *Beitr Zur Klin Chir*. 1905;47:1-36.
10. Michelson HE. Granuloma pyogenicum: a clinical and histologic review of twenty-nine cases. *Arch Dermatol Syphil*. 1925;12:492-505.
11. Mills SE, Cooper PH, Fechner RE. Lobular capillary hemangioma: the underlying lesion of pyogenic granuloma. *Am J Surg Pathol*. 1980;4:471-479.
12. Grimalt R, Caputo R. Symmetric pyogenic granuloma. *J Am Acad Dermatol*. 1993;29:652.
13. Harris MN, Desai R, Chuang TY, et al. Lobular capillary hemangiomas: an epidemiologic report, with emphasis on cutaneous lesions. *J Am Acad Dermatol*. 2000;42:1012-1016.
14. Ceyhan M, Erdem G, Kotiloglu E, et al. Pyogenic granuloma with multiple dissemination in a burn lesion. *Pediatr Dermatol*. 1997;14:213-215.
15. Premalatha S, Thambiah AS. Pyogenic granuloma following the trauma of nose-boring. *Br J Dermatol*. 1979;100:455-458.
16. Naimer SA, Cohen A, Vardy D. Pyogenic granuloma of the penile shaft following circumcision. *Pediatr Dermatol*. 2002;19:39-41.
17. Wolf JE, Hubler WR. Origin and evolution of pyogenic granuloma [editorial]. *Arch Dermatol*. 1974;110:958.
18. Arbiser JL, Weiss SW, Arbiser ZK, et al. Differential expression of active mitogen-activated protein kinase in cutaneous endothelial neoplasms: implications for biologic behavior and response to therapy. *J Am Acad Dermatol*. 2001;44:193-197.
19. Shimizu K, Naito S, Urata Y, et al. Inducible nitric oxide synthase is expressed in granuloma pyogenicum. *Br J Dermatol*. 1998;138:769-773.
20. Musalli NG, Hopps RM, Johnson NW. Oral pyogenic granuloma as a complication of pregnancy and the use of hormonal contraceptives. *Int J Gynaecol Obstet*. 1976;14:187-191.
21. Yuan K, Wing LY, Lin MT. Pathogenic roles of angiogenic factors in pyogenic granulomas in pregnancy are modulated by female sex hormones. *J Periodontol*. 2002;73:701-708.
22. Leyden JJ, Master GH. Oral cavity pyogenic granuloma. *Arch Dermatol*. 1973;108:226-228.
23. Yuan K, Jin YT, Lin MT. The detection and comparison of angiogenesis-associated factors in pyogenic granuloma by immunohistochemistry. *J Periodontol*. 2000;71:701-709.
24. Katta R, Bickle K, Hwang L. Pyogenic granuloma arising in port-wine stain during pregnancy. *Br J Dermatol*. 2001;144:644-645.
25. Itin PH, Fluckiger R, Zbinden R, et al. Recurrent pyogenic granuloma with satellitosis—a localized variant of bacillary angiomatosis? *Dermatology*. 1994;189:409-412.
26. Lee J, Lynde C. Pyogenic granuloma: pyogenic again? association between pyogenic granuloma and *Bartonella*. *J Cutan Med Surg*. 2001;5:467-470.
27. Davies MG, Barton SP, Atai F, et al. The abnormal dermis in pyogenic granuloma: histochemical and ultrastructural observations. *J Am Acad Dermatol*. 1980;2:132-142.
28. Fusin LJ, Harrell ER. Arteriovenous fistula: cutaneous manifestations. *Arch Dermatol*. 1976;112:1135-1138.
29. Paysyk VA, Thomas SV, Hassett CA, et al. Regional differences in capillary density of the normal human dermis. *Plast Reconstr Surg*. 1989;83:939-945.
30. Kim TH, Choi EH, Ahn SK, et al. Vascular tumors arising in port-wine stains: two cases of pyogenic granuloma and a case of acquired tufted angioma. *J Dermatol*. 1999;26:813-816.
31. Valeyrie L, Lebrun-Vignes B, Descamps V, et al. Pyogenic granuloma within port-wine stains: an alarming clinical presentation. *Eur J Dermatol*. 2002;12:373-375.
32. Castanedo-Cazares JP, Lepe V, Moncada B. Pyogenic granuloma within port-wine stains [comment]. *Eur J Dermatol*. 2002;12:616.
33. Lee JB, Kim M, Lee SC, et al. Granuloma pyogenicum arising in an arteriovenous haemangioma associated with a port-wine stain. *Br J Dermatol*. 2000;143:669-671.
34. Akyol MU, Yalciner EG, Dogan AI. Pyogenic granuloma (lobular capillary hemangioma) of the tongue. *Int J Pediatr Otorhinolaryngol*. 2001;58:239-241.
35. Irani S, Brack T, Pfaltz M, et al. Tracheal lobular capillary hemangioma: a rare cause of recurrent hemoptysis. *Chest*. 2003;123:2148-2149.
36. Eickhorst KM, Nurzia MJ, Barone JG. Pediatric pyogenic granuloma of the glans penis. *Urology*. 2003;61:644.
37. Kirschner RE, Low DW. Treatment of pyogenic granuloma by shave excision and laser photocoagulation. *Plast Reconstr Surg*. 1999;104:1346-1349.
38. Zayoun ST, Juljulian HH, Kurban AK. Pyogenic granuloma with multiple satellites. *Arch Dermatol*. 1974;109:689-691.
39. Warner J, Jones EW. Pyogenic granuloma recurring with multiple satellites: a report of 11 cases. *Br J Dermatol*. 1968;80:218-227.

40. Park YH, Houh D, Houh W. Subcutaneous and superficial granuloma pyogenicum. *Int J Dermatol.* 1996;35:205-206.
41. Cooper PH, McAllister HA, Helwig EB. Intravenous pyogenic granuloma: a study of 18 cases. *Am J Surg Pathol.* 1979;3:221-228.
42. Nappi O, Wick MR. Disseminated lobular capillary hemangioma (pyogenic granuloma): a clinicopathological study of two cases. *Am J Dermatopathol.* 1986;8:379-385.
43. Harrington P, O'Kelly A, Trail IA, et al. Amelanotic subungual melanoma mimicking pyogenic granuloma in the hand. *J R Coll Surg Edinb.* 2002;47:638-640.
44. Wyatt ME, Finlayson CJ, Moore-Gillon V. Kaposi's sarcoma masquerading as pyogenic granuloma of the nasal mucosa. *J Laryngol Otol.* 1998;112:280-282.
45. Bastug DF, Ness DT, DeSantis JG. Bacillary angiomatosis mimicking pyogenic granuloma in the hand: a case report. *J Hand Surg (Am).* 1996;21:307-308.
46. Schwartz RA, Janniger CK. Bacillary angiomatosis. *J Am Acad Dermatol.* 1991;24:802-803, 807-808.
47. Schwartz RA, Nychay SG, Janniger CK, et al. Bacillary angiomatosis: presentation of six patients, some with unusual features. *Br J Dermatol.* 1997;136:60-65.
48. Hager CM, Cohen PR. Cutaneous lesions of metastatic visceral malignancy mimicking pyogenic granuloma. *Cancer Invest.* 1999;17:385-390.
49. Rim JH, Moon SE, Chang MS, et al. Metastatic hepatocellular carcinoma of gingiva mimicking pyogenic granuloma. *J Am Acad Dermatol.* 2003;49:342-343.
50. Kirschner R, Low D. Treatment of pyogenic granuloma by shave excision and laser photocoagulation. *Plast Reconstr Surg.* 1999;104:1346-1349.
51. Gonzalez S, Vibhagool C, Falo LD Jr, et al. Treatment of pyogenic granulomas with the 585 nm pulsed dye laser. *J Am Acad Dermatol.* 1996;35:428-431.
52. Matsumoto K, Nakanishi H, Seike T, et al. Treatment of pyogenic granuloma with a sclerosing agent. *Dermatol Surg.* 2001;27:521-523.
53. Quitkin HM, Rosenwasser MP, Strauch RJ. The efficacy of silver nitrate cauterization for pyogenic granuloma of the hand. *J Hand Surg (Am).* 2003;28:435-438.
54. Holbe HC, Frosch PJ, Herbst RA. Surgical pearl: ligation of the base of pyogenic granuloma—an atraumatic, simple, and cost-effective procedure. *J Am Acad Dermatol.* 2003;49:509-510.
55. Vega Harring SM, Niyaz M, Okada S, et al. Extramedullary hematopoiesis in a pyogenic granuloma: a case report and review. *J Cutan Pathol.* 2004;31:555-557.
56. van Eeden S, Offerhaus GJ, Morsink FH, et al. Pyogenic granuloma: an unrecognized cause of gastrointestinal bleeding. *Virchows Arch.* 2004;444:590-593.
57. Hung CH, Kuo HW, Chiu YK, et al. Intravascular pyogenic granuloma arising in an acquired arteriovenous malformation: report of a case and review of the literature. *Dermatol Surg.* 2004;30:1050-1053.
58. Kuroda K, Mizoguchi M. Subcutaneous granuloma pyogenicum in patients with antiphospholipid antibodies. *Dermatology.* 2004;208:331-334.
59. Teknetzis A, Ioannides D, Vakali G, et al. Pyogenic granulomas following topical application of tretinoin. *J Eur Acad Dermatol Venereol.* 2004;18:337-339.
60. Tursen U, Demirkan F, Ikizoglu G. Giant recurrent pyogenic granuloma on the face with satellitosis responsive to systemic steroids. *Clin Exp Dermatol.* 2004;29:40-41.