Multiple Erythematous Nodules: An Intriguing Entity

Abstract

Pyogenic granuloma (PG), also called a lobular capillary hemangioma, is a benign vascular proliferation of skin or mucous membrane. It classically presents as a solitary friable nodule over the face or distal extremities. Multiple disseminated PG is a rare form generally reported after trauma such as burn injury. We report two cases of spontaneous development of multiple localized PGs in immunocompetent individuals.

Keywords: *Eruptive pyogenic granuloma, multiple erythematous papulo-nodules, spontaneous*

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Introduction

Pyogenic granuloma (PG, also known as granuloma pyogenicum, lobular capillary hemangioma, or telangiectatic granuloma) is a benign vascular proliferation of the skin and mucous membranes. It is a misnomer as it is neither infectious nor granulomatous.[1] Although PG may occur over normal skin, it is considered as a reactive hyper proliferative vascular response to minor trauma. Although the development of PG after trauma to the skin is very common, spontaneous development of multiple PG have been rarely reported in the literature.

Case 1

A 66-year-old female patient presented with multiple reddish raised lesions over right forearm of 6 months duration. Initially, she developed a single reddish raised lesion which gradually increased in size with the appearance of new lesions in the vicinity of the initial lesion. She gave a history of intermittent bleeding on trivial trauma. She denied history of any drug intake, preexisting skin lesion since birth, trauma prior to the onset of lesions, or any previous treatment taken for the same. She did not have any other cutaneous or systemic findings. On cutaneous examination, there were multiple erythematous, soft to firm, non tender, sessile nodules ranging from size 6 mm to 15 mm and ulceration with crusting at places, present over the extensor aspect of the right forearm [Figure 1a]. In addition, there were multiple erythematous papules with satellite lesions [Figure 1b]. On the basis of history and cutaneous examination, differential diagnoses of PG, angiokeratoma, bacillary angiomatosis, and Kaposi's sarcoma were considered. Dermoscopy was performed using 3 Gen Dermlite DL4 (CA, USA) in 10× polarized mode. Dermoscopy of nodular lesions revealed homogenous reddish areas with rail lines with ulceration at places surrounded by white collarette suggestive of PG, which was further confirmed on histopathology [Figure 2a-c]. Histopathological examination of nodule over the forearm revealed multiple lobules of proliferating capillaries in the dermis and deeper tissues with focal inflammatory infiltrate, suggestive of pyogenic granuloma (PG) [Figure 3a and b]. Warthin–Starry stain was done to rule out bacillary angiomatosis and revealed no organism. No underlying arteriovenous malformation was detected on local ultrasonography. General and systemic examination was normal. Routine hematological investigations such as complete hemogram, liver, and renal function tests were within normal limits. Serology for HIV was nonreactive. On the basis of clinical, dermoscopic, and histopathological findings, a final diagnosis of localized multiple eruptive PGs was reached. The patient was treated with cryosurgery using liquid nitrogen as the cryogen. There was a significant resolution

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of nodular lesions after three sessions of cryotherapy, given 2 weeks apart [Figure 4a and b].

Case 2

A 27-year-old male presented with 3 months' history of multiple reddish raised lesions over the forehead. He gave a history of intermittent bleeding during combing or manipulation. On cutaneous examination, there were multiple erythematous, soft to firm, nontender, smooth-surfaced nodules ranging from size 10–20mm present over the right half of forehead [Figure 5a and b]. On the basis of history and cutaneous examination, differential diagnosis of PG, angiokeratoma, and bacillary angiomatosis was considered. Histopathological examination of nodule over forehead revealed multiple dilated vascular clefts in the dermis separated by septae and myxoid stroma, suggestive of PG [Figure 6a and b]. Warthin–Starrystain of the section did not reveal any organism. No underlying arteriovenous malformation was detected on local ultrasonography and Doppler study. General and systemic examination was normal. Routine hematological investigations such as complete hemogram, liver, and renal function tests were within normal limits. On the basis of history, clinical, and histopathological findings, a diagnosis of multiple localized eruptive PGs was reached. The patient was referred to surgery for excision considering the size of the lesion.

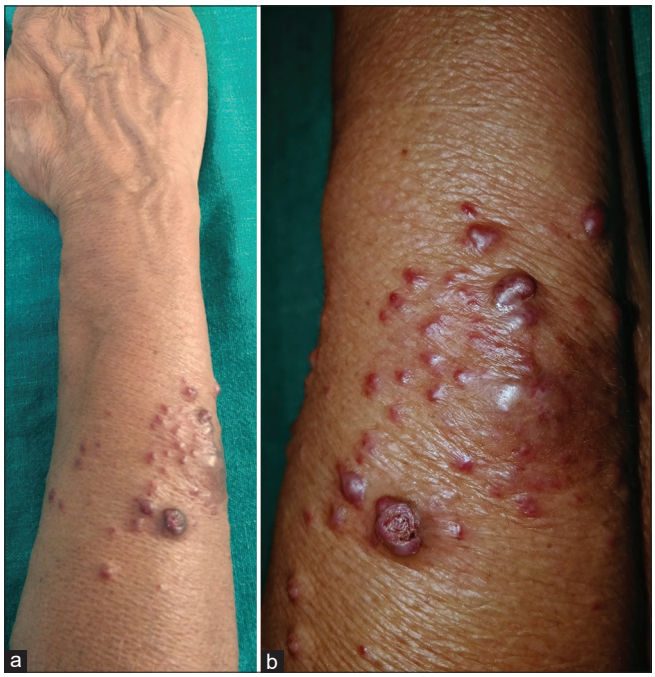

Figure 1: (a and b): Multiple erythematous, soft to firm, nontender, sessile nodules ranging from size 6 mm to 15 mm and ulceration with crusting at places over the extensor aspect of right forearm (a). Multiple erythematous papules and satellite lesions (b)

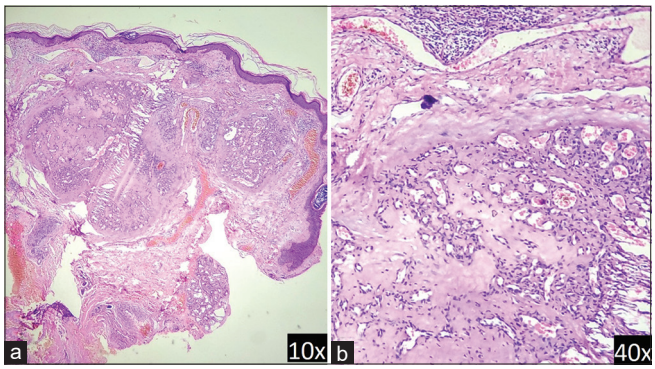

Figure 3: (a and b): Histopathological examination of nodule over forearm revealed multiple lobules of proliferating capillaries in the dermis and deeper tissues with focal inflammatory infiltrate, suggestive of PG [H and E, (a: 10× and b: 40×)]

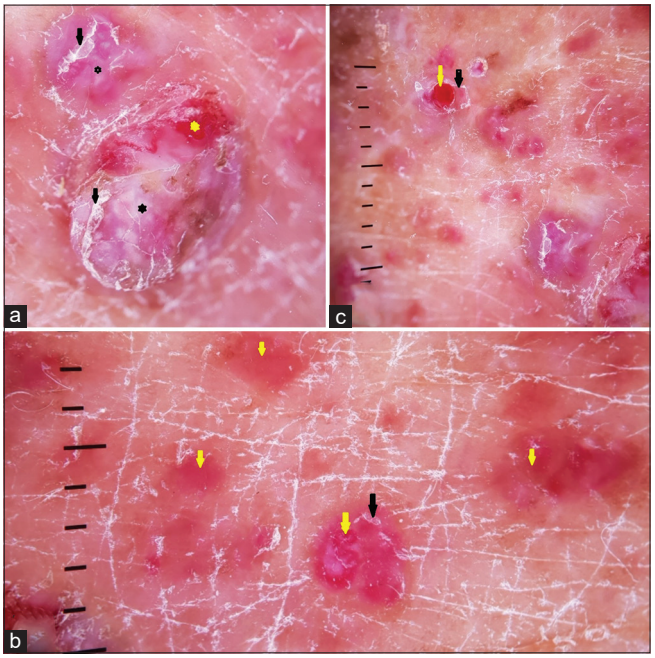

Figure 2: (a-c): Dermoscopy (3 Gen Dermlite DL4 (CA, USA) 10× polarized mode) of nodular lesions revealed rail lines (black star), ulceration (yellow star), and white collarette (black arrow)(a), homogenous reddish areas (yellow arrow) surrounded by white collarette (black arrow)(b), ulceration (yellow star) and white collarette (black arrow) (c), suggestive of PG

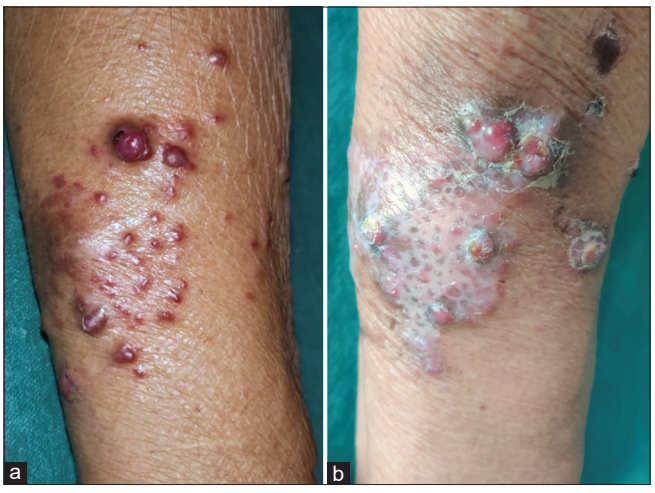

Figure 4: (a and b): Pre (a) and post treatment images (b) of nodular lesions in case 1 after 3 sessions of cryotherapy

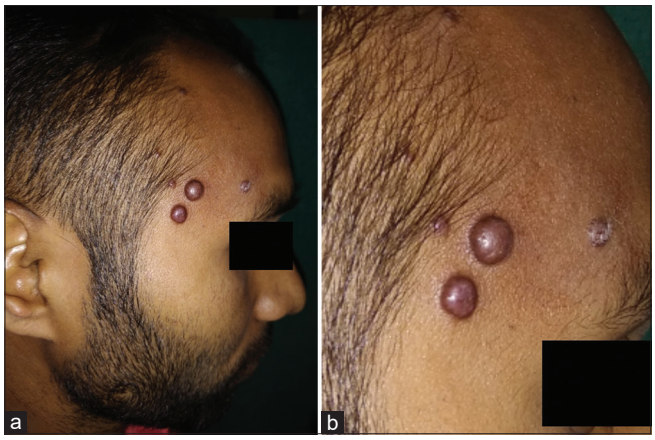

Figure 5: (a and b): Multiple erythematous, soft to firm, nontender, smooth-surfaced nodules ranging from size 10–20 mm present over right half of forehead

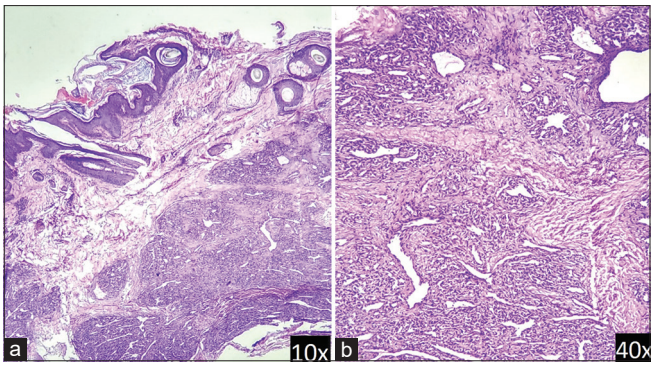

Figure 6: (a and b): Histopathological examination of nodule over forehead revealed multiple dilated vascular clefts in the dermis separated by septae and myxoid stroma, suggestive of PG [H and E, (a: 10× and b: 40×)]

Discussion

PG is a common acquired benign angiomatous proliferation of the skin and mucous membranes that develops spontaneously. It was first described by Poncet and Dor in 1897. It usually affects children and young adults, sometimes pregnant women, and rarely elderly individuals.[2] The commonest sites of involvement are face, especially lips and extremities, mainly fingers, upper trunk, head, and perianal area.[3] Our first case is a 65-year-old female with multiple PGs over forearm, while second case is a 24-year-old male with multiple PGs over the forehead. It usually starts as a friable papule eventually growing over weeks to months, finally stabilizing into an erythematous nodule. The friable structure is prone to bleeding and ulceration. Occasionally, nodules may spontaneously involute.[4] The size varies between 5 mm and 10 mm, sometimes even reaching up to 50 mm. It is considered as a reactive hyper proliferative vascular response to a variety of stimuli such as infection, trauma, increased levels of female sex hormones, viral oncogenes, microscopic arteriovenous anastomosis, and growth factors. Local trauma or tissue injury is followed by sequential phases of wound healing with the activation of early inflammatory phase leading to the release of cytokines and growth factors that include vascular endothelial growth factor (VEGF).[5] It is followed by a proliferative phase, with the formation of granulation tissue and remodeling phase in which the granulation tissue is replaced by a scar. Godfraind *et al*.[6] suggested that PG may result from tissue injury or local trauma, followed by a dysregulated wound healing process, during which vascular growth is driven byFLT4 (VEGF signaling) and nitric oxidepathways.[6] Retinoids, antineoplastic, and antiretroviral medications have also been implicated in the pathogenesis.[7] It usually presents as a solitary papule, but multiple lesions and satellitosis, although unusual, might be present. Other theories focus on an imbalance between angiogenic promoters and inhibitors which leads to capillary overgrowth. There maybe overexpression of phosphorylated ATF2 and stat 3.[8] Eruptive PG can be classified as localized occurring in specific regions and disseminated or widespread.[9] Localized eruptive PG have been reported at sites of trauma, burns, within port wine stain, particularly after treatment with pulsed dye laser. The disseminated eruption is characterized by the acute appearance of multiple widespread lesions either spontaneously[10] or in the context of retinoid therapy, burn injury, pregnancy, or presence of antiphospholipid antibodies.[11] They have also been reported in association with malignancies like multiple myeloma, Hodgkin's disease, chronic lymphocytic leukemia, and disseminated melanoma.[12,13] In both of our cases, the spontaneous occurrence of multiple and satellite lesions is an interesting feature. In the first case, lesions were confined to the right forearm, while the second case had multiple smaller lesions over the right frontal area, in which combing of hair might have triggered the development of satellite lesions. PG is dermoscopically characterized by homogenous reddish or white-red areas, whitish rail lines surrounded by whitish collarette in majority of the case.[14] Similar observations were reported in our case. Reddish homogenous areas may be attributed to the presence of numerous small capillaries or proliferating vessels in a myxoid stroma. White collarette is a ring shaped or arcuate squamous structure that corresponds to the hyperplastic adnexal epithelium that partially or totally embraces the lesion at the periphery.[15] White rail lines correspond histologically to fibrous septa that surround the capillary lobule in advanced cases. The vascular patterns described in PGs are linear, regular, dotted, or polymorphous atypical vessels. The differential diagnoses of such lesions include bacillary angiomatosis, disseminated atypical mycobacterial infections, and Kaposi's sarcoma which can be ruled out by histopathological and/or microbiological cultures [Table 1]. The lesions often resolve spontaneously within months to years. Treatment options include excision, curettage, electrodessication, laser surgery, sclerotherapy, and cryotherapy.[16] Our first case has shown significant resolution after treatment with cryotherapy without any complication. Multiplicity or satellite lesions of PG are

Table 1: Differential diagnoses of multiple pyogenic granulomas

	Examination	Dermoscopy	Histopathology
Pyogenic granuloma	Usually single or rarely multiple reddish or skin-colored papulo-nodules	White/red homogenous stuctureless area, white rail lines, ulceration, white collarete	Vascular proliferation in lobular fashion. Fibrous septations, inflammation and edema.
Bacillary angiomatosis	Mutiple reddish or brown papules or subcutaneous lumps Dramatic response after antibiotic therapy	-	Single or multinodular proliferations of capillaries with inflammatory infiltrate. Extracellular deposits of hemotoxylin grain material. Leucocytoclasis seen.
Kaposi's Sarcoma (nodular)	Numerous dome shaped skin colored or erythematous nodular lesions	Bluish reddish coloration, polychromatic rainbow pattern with surface scales and brown clods.	Honey comb like network of blood filled spaces/slits closely associated with spindle cells woven between delicate vascular spaces.
Angio-keratoma	Single or multiple reddish, bluish-black keratoticpapulo-nodules	Red lacunae, dark blue lacunae, whitish veil	Acanthosis, hyperkeratosis, multiple blood-filled ectatic, and congested thin-walled blood vessels in papillary dermis with normal deep dermis and subcutaneous tissue

uncommon and if multiple lesions appear, they develop around the site of recently treated lesions, more as a phenomenon of recurrence. They may develop after treatment with excision, shave excision, electrodesiccation, ligation, curettage, cautery, and CO_2laser. Multiple eruptive with satellite PGs have also been rarely reported in patients with skin trauma, after burns, its treatment, and lightning injuries.[17-20] However, there is a paucity of literature describing the spontaneous occurrence of multiple PGs. Sethuraman *et al*.[3] reported two patients of PG with the spontaneous occurrence of multiple and satellite lesions. Thus, we report these two cases because of its rarity. Our report also highlights the utility of dermoscopy, which helps in the diagnosis of such lesions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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