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Single Case

The First Case of Eruptive Pyogenic Granuloma following COVID-19 Vaccination

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Keywords

Pyogenic granuloma · Lobular capillary hemangioma · Eruptive pyogenic granuloma · Oral propranolol · COVID-19

Abstract

Introduction: Pyogenic granuloma presents clinically as a rapidly growing, friable, red papule of skin or mucosa, commonly measuring less than 10 mm with frequent bleeding due to ulceration. Angioproliferative diseases including pyogenic granuloma and cherry angioma have been reported during COVID-19 infection or following COVID-19 vaccination. ***Case Presentation:*** Here, we report a 52-year-old female patient who developed diffuse skin eruptions 3 weeks after the second dose of COVID-19 vaccination. ***Conclusion:*** As per our knowledge, this is the first case of eruptive PG following COVID-19 vaccination. Oral propranolol and PDL laser therapy were administered after obtaining inconvenient results from electro-cautery, and there was a good response within 6 weeks of starting therapy, defined by the cessation of new lesion formation and a decrease in the size of large lesions.

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Introduction

Pyogenic granuloma (PG) presents clinically as a rapidly growing, friable, red papule of the skin or mucosa, commonly measuring less than 10 mm, with frequent bleeding due to ulceration. Histologically, it is a benign reactive neovascularization occurring in all ages but commonly in children and young adults. The term "PG" is a misnomer; it is neither infectious in etiology nor granulomatous histologically. PG usually presents as a solitary skin papule and rarely as an intravascular, subcutis mass, or very rarely as an eruptive disseminated pattern. In one-third of patients, PG develops after minor trauma, but an association with pregnancy and some medications like systemic retinoids, indinavir, and EGFR inhibitors has been reported [1]. Angioproliferative diseases, including PG and cherry angioma, have been reported with SARS-CoV-2 infection or following COVID-19 vaccination [2, 3]. The pathogenesis of PG in COVID-19 vaccination and SARS-CoV-2 infection is unknown; a possible explanation is an imbalance between anti-angiogenic and pro-angiogenic factors leading to capillary proliferation and neovascularization. In addition to angioproliferative diseases, it is not unusual to observe that many patients attribute their dermatological complaints to either SARS-CoV-2 infection or COVID-19 vaccination, or observing deterioration of chronic dermatological condition in relation to SARS-CoV-2 infection or COVID-19 vaccination. New-onset lichen planus has been reported following COVID-19 vaccination and many inflammatory skin lesions such as psoriasis, hidradenitis suppurativa, atopic dermatitis, and lichen planus were reported to be worsened after COVID 19 vaccination [4, 5]. Also it seems that vaccination for COVID-19 might exacerbate patients with autoimmune blistering diseases, especially pemphigus vulgaris [6].

Here, we report a 52-year-old female patient who developed diffuse skin eruptions 3 weeks after the second dose of the COVID-19 vaccination (Sinopharm COVID-19 vaccine). The multifaceted nature of the lesions, recurrences, and pain related to cauterization rendered electrocautery inconvenient and shifted the management toward a combination of oral propranolol 40 mg daily and PDL laser therapy. A good response was observed within 6 weeks of starting therapy, defined by the cessation of new lesion formation and a decrease in the size of large lesions.

Case Report

A 52-year-old female, a known case of hypothyroidism, presents with multiple red-colored skin lesions involving the head, trunk, and extremities for 2 years. The lesions exhibited an eruptive nature, with a tenth of them developing within 1 month. Subsequently, there was a gradual increase in size and number over 2 years, reaching more than one hundred and varying in size from 3 mm to 12 mm. She developed the cutaneous eruption just 3 weeks after having the second dose of the COVID-19 vaccination without reporting similar lesions with her first-dose vaccination. She denied having symptoms like pruritus, a burning sensation, or pain but stated that the lesions occasionally bled when traumatized or during wearing clothes. Multiple sessions of cauterization were conducted over 2 years, but the result was inconvenient for the patient as the lesions increased in number, and there was a recurrence of the previously cauterized lesions. This prompted the patient to visit Razi Dermatology Hospital for further management.

Skin examination revealed diffuse, discrete, red to bright red-colored papules and papulonodules on the scalp, neck, trunk, and extremities shown in Figure 1a–d, but ulcerated papules were not observable at the time of examination. There was no oral or genital mucosal involvement. The lesions were not tender upon palpation, and there were no significant findings on systemic examination. Dermoscopy of the lesions revealed a central homogenous reddish area and a white collarette formed by a white keratinized edge shown in Figure 2a–d. Initial laboratory test was performed with normal biochemical test, normal serum vascular

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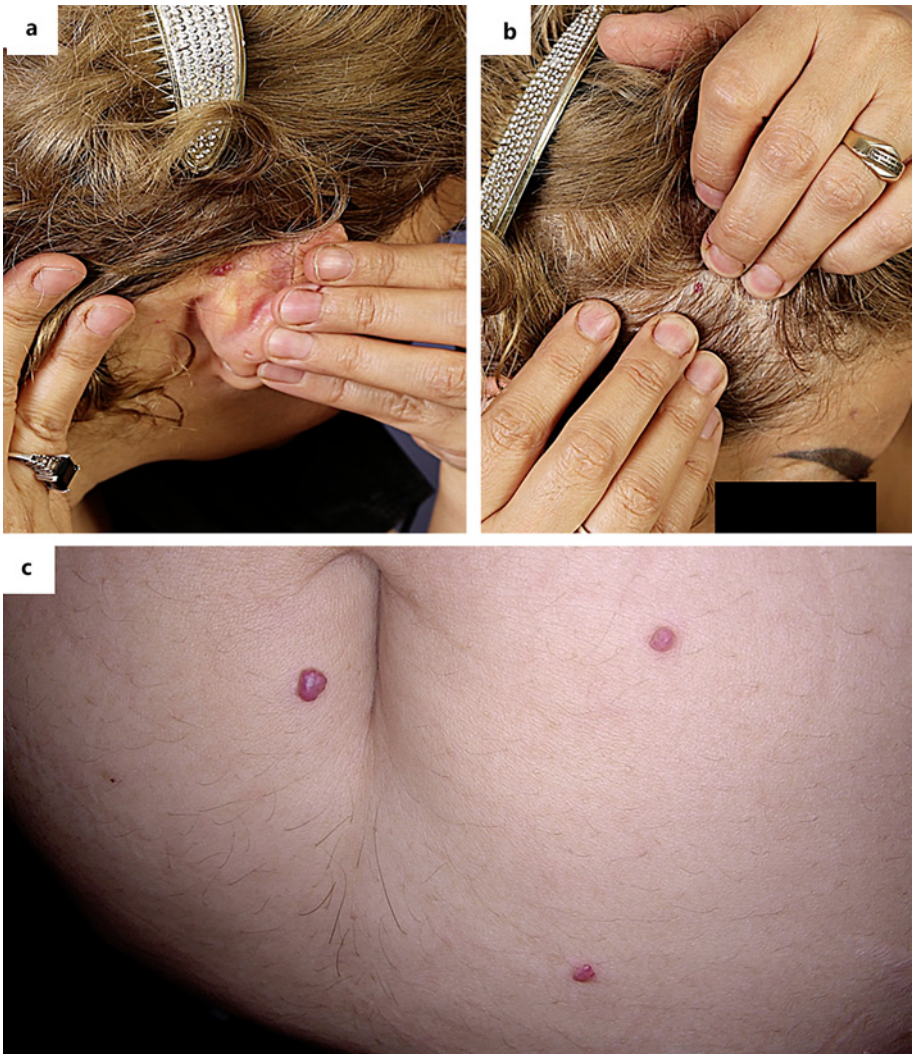

Fig. 1. Multiple bright red papules with slight scales on right post-auricular (**a**), right parietal (**b**), and anterior abdomen (**c**).

endothelial growth factor, and normal lactate dehydrogenase. Viral screening was also negative for hepatitis and HIV. Neck, axillary, and inguinal ultrasound probes did not reveal lymphadenopathy. Biopsy of one of the red papules from the left leg skin confirmed the diagnosis of PG shown in Figure 3a–b. She was started on treatment with propranolol 20 mg twice daily with titration up to 40 mg twice daily, and PDL laser therapy with a good response within 6 weeks of starting therapy, defined by the cessation of new lesion formation and a decrease in the size of large lesions (Table 1).

Discussion

Eruptive disseminated PG is a rare variant of PG that has been reported in association with oral isotretinoin in the setting of severe nodulocystic acne and granulocyte colony-stimulating factor in immunosuppressed patients [11]. Recently, with the era of the COVID-19 pandemic, various dermatological manifestations have been observed in

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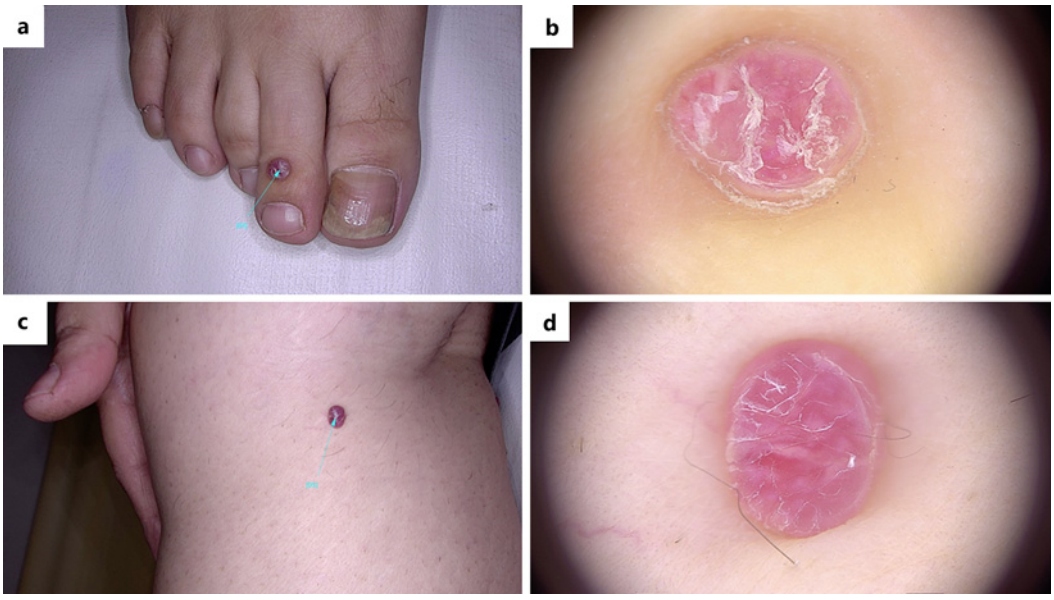

Fig. 2. a Bright red papule with slight scale with dermoscopic homogenous redness and white linear rail lines (**b**). **c** Red papule in left leg, with dermoscopic finding of red homogenous area and very slight white scale (**d**).

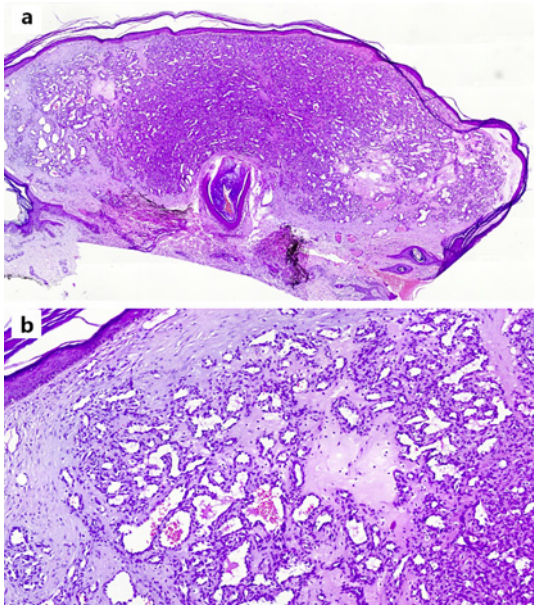

Fig. 3. Skin biopsy showing epidermal thinning and orthokeratosis. Dermal small vessel proliferation with lobular configuration and dermal fibrosis (hematoxylin and eosin stain. ×10 [**a**], ×40 [**b**]).

patients with SARS-CoV-2 infection and after COVID 19 vaccination. Although the most common skin finding was reported to be a non-specific maculopapular rash, PG and other angioproliferative dermatoses have been reported as very rare skin findings in association with SARS-CoV-2 infection and COVID 19 vaccination. The early reported angioproliferative cases were eruptive pseudoangiomatosis and eruptive cherry angioma-like lesions in patients with COVID-19. The diagnosis was clinical and lacked histopathological confirmation [15, 16]. To our knowledge, the only case of eruptive pyogenic granuloma (EPG) in association with COVID-19 is reported by Maronese et al. [2]. They

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Table 1. Reported variants of PG

Variant of PG	Main association	Common site
Trauma-induced PG	PG is associated with trauma. In one-third of cases [1], another study suggested less than 25% association with trauma [7]	In general gingiva, fingers, lips, face, and tongue [1], other study reports propensity for trunk and extremities [8]
PG gravidarum	Estrogen and other sex hormones accentuate the inflammatory response of the gingival tissue [9]	Gingiva and buccal mucosa
Disseminated PG	Rare, occur in association with oral isotretinoin in the setting of severe nodulocystic acne [10] or granulocyte colony-stimulating factor in immunosuppressed patients [11], 1 case of disseminated PG after oral contraceptive pill also has been reported [12]	No predilection for any specific site, any site may be involved
Disseminated PG in association with COVID-19 vaccination	Only 1 case of PG has been reported due to SARS-CoV-2 infection [2] Our patient will be the first case to have disseminated PG due to COVID-19 vaccine. PG due to other vaccinations has not been reported	No predilection for any specific site
Peri-ungual PG	Commonly associated with medications such as isotretinoin, indinavir, and EGFR inhibitors [13]	Lateral or proximal nail fold, multiple digits may be involved
Intra-oral PG	Associated with cyclosporine and tacrolimus intake in patients who underwent HSCT [13]	Buccal, tongue, and gingiva
PG associated with vascular malformation	Occasionally, PG arises within port-wine stain or arterio-venous malformation [1]	Site of vascular malformation
Satellite PG	Very rare, arise secondarily around the primary PG lesion due to trauma or excision of the primary lesion	No predilection for specific site of the body
Gastrointestinal PG	Rarely, PG may occur in the gastrointestinal tract and might cause iron deficiency anemia due to chronic bleeding [14]	PG has been reported to occur throughout the intestine with no predilection for specific site [14]
Post-burn PG	Develop at the sites of previous burn	Sites of previous burn

reported a 25-year-old female patient who developed EPG 1 month after contracting COVID-19. They demonstrated that subsequent COVID-19 vaccination, given 5 months after the onset of the disease, did not induce new lesions [2]. Our patient was in good health when she received the second dose of the COVID-19 vaccination (Sinopharm COVID-19 vaccine). Three weeks after the vaccination, she developed eruptive red-colored papules and papulonodules on the head, then the trunk, and finally the

extremities. Although cases of eruptive pseudoangiomatosis and eruptive cherry angioma have been reported in association with different COVID-19 vaccinations. [17, 18], but, to our knowledge, our case is the first case of EPG to be reported following COVID-19 vaccination. The PG in this patient could not be attributed to other causes as she had no known medical condition except hypothyroidism and was not receiving any medication other than levothyroxine. Although levothyroxine has been reported to be associated with multiple eruptive peri-ungual PG, she had been on this medication for years before experiencing the skin eruptions [19].

The clinical differential diagnosis of disseminated EPG includes bacillary angiomatosis, eruptive cherry angioma, and Kaposi sarcoma. Eruptive cherry angioma might be associated with an underlying systemic disease [20]. But the pathology was typical for PG, and initial laboratory tests, probe ultrasound for lymphadenopathy were normal. Perhaps the most important clinical differential diagnosis of solitary PG is amelanotic melanoma and poroma. The typical dermal small vessel proliferation with a lobular configuration and dermal fibrosis were enough to differentiate it from amelanotic melanoma and poroma. While it is convenient to treat a solitary lesion with surgical excision, electrocautery, or radiofrequency, the treatment of disseminated eruptive PG needs alternative options like oral propranolol or laser therapy, with the rate of recurrence being the lowest in patients undergoing excision [21]. Electrocautery has the disadvantage of recurrence, and it is inconvenient for disseminated lesions. Laser therapy has been reported to be effective in resolving disseminated PG associated with COVID-19 [2]. Lasers that have been reported to be effective in the treatment of PG include CO2 laser, PDL, and long-pulsed 1,064 nm Nd:Yag laser [22]. The multiple patterns of lesions, recurrence, and pain related to cauterization rendered cautery inconvenient and made oral propranolol an alternative option in this case. Oral propranolol has been reported to be an effective modality in treating EPG with a dose of 60 mg twice daily; a complete resolution of symptoms was reported within 16 weeks of starting treatment [23]. In children, oral propranolol seems to be an effective option for disseminated PG. Ebrahimi et al. [24] reported successful treatment of post-burn PG in children with oral propranolol.

We believe that our case is the first instance of disseminated PG following COVID-19 vaccination. She had a good response to a combination of oral propranolol, starting with an initial dose of 20 mg daily that was titrated to 40 mg twice daily, along with PDL laser therapy for large lesions. There was a decrease in the size of large lesions, and no new lesion formation was observed after 6 weeks of initiating treatment. The patient was satisfied with the result and continued oral propranolol, with planned further follow-up in the upcoming weeks.

Conclusion

In this study, we reported a 52-year-old female patient with diffuse, EPG following the second dose of the COVID-19 vaccination (Sinopharm). To our knowledge, this is the first case of eruptive PG following COVID-19 vaccination. Oral propranolol and PDL laser therapy were administered after obtaining inconvenient results from electrocautery for nearly 2 years, and there was a good response within 6 weeks of starting the therapy. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000539849).

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Statement of Ethics

Ethical approval is not required for this study in accordance with local guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Saman Al Zahawi: writing – original draft and writing – review and editing. Alireza Ghanadan: supervision and visualization. Fatemeh Saberi: writing – review and editing. Kamran Balighi: conceptualization and supervision. Zahra Razavi: conceptualization, supervision, and writing – review and editing.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy reasons but are available from the corresponding author upon request.

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