Healing discordance revealing squamous cell carcinoma within a chronic pyoderma gangrenosum lesion

Pyoderma gangrenosum (PG) and cutaneous squamous cell carcinoma (SCC) can present with overlapping clinical features, namely as chronic, non-healing, painful ulcerations that are inflammatory in appearance. This overlap poses a diagnostic challenge and may delay recognition of malignant transformation, particularly in patients receiving long-term immunomodulatory therapy. While SCC arising within chronic wounds is well described, SCC developing within a PG lesion has been reported only once previously in the literature. This case reports an 84-year-old man who initially presented with lower leg lesions of 4 months' duration. The lesions were eventually diagnosed as PG during 2 years of treatment. All lesions healed with treatment, aside from one anterior tibial lesion that was biopsied and confirmed as SCC. This case highlights the importance of a low threshold for biopsy in chronic inflammatory lesions given the possibility for malignant transformation.

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Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis that presents with painful ulcers with purple, rolled edges and peripheral erythema (Maverakis et al, 2020). It is suspected to be an autoimmune disorder, is often associated with other immune-mediated diseases and is challenging to diagnosis, given it is a diagnosis of exclusion. The chronic and recurrent course of PG ulcers can lead to prolonged inflammation, immunosuppression as a result of treatment and pathergy contributing to delayed wound healing and possible complications. Squamous cell carcinoma (SCC) is not only the second most common type of skin cancer, but it has also increased in incidence up to 200% in the past three decades (Hale and Hanke, 2025). SCC most commonly occurs in skin exposed to ultraviolet radiation and can also develop in scars, skin sores or areas of skin injury, typically appearing as a scaly patch, open sore, or raised wart that crusts and bleeds. Malignant transformation of chronic ulcers into Marjolin ulcers is recognised in wounds such as burn scars or venous stasis ulcers, but SCC arising in PG lesions is rare and to our knowledge, has only been reported once in the literature (Bazaliński et al, 2017; Morrison et al, 2022). This case report presents a rare case of SCC arising within a chronic, longstanding PG ulcer, highlighting the importance of further work-up in patients with non-healing lesions.

Case report

An 84-year-old man with a history of bilateral extremity venous insufficiency, bilateral knee osteoarthritis, left knee replacement, hyperlipidaemia, and previous malignant fibrous histiocytosis of the right knee was referred to the wound clinic for recurrent venous stasis ulcers of the right and left lower extremities that had been present for approximately 4 months. He had stage IIIB malignant fibrous histiocytosis of the right knee treated with local excision, neoadjuvant continuous intravenous infusion of cyclophosphamide + adriamycin + dacarbazine, definitive surgical resection and radiation 20 years earlier.

At wound clinic presentation, vascular ultrasound suggested small vessel disease and clinical picture fit most consistently with venous stasis ulcerations with likely contributions from osteoarthritis and posterior pressure from limited mobility. He was seen weekly for a year at the wound clinic and despite many advanced topical therapies, he had an overall poor response. Therapies included periwound topical steroids, debridement as needed, absorptive foam antimicrobial dressings, multilayer compression wraps and cellular grafting (intact fish skin grafts). During the first 10 months of this treatment year, he experienced periods of clinical improvement with decreased pain and drainage, as well as some healing of ulcerations. However, new ulcerations and increased swelling, drainage and pain at the end of this initial year of treatment led to concern for other aetiologies.

A biopsy was performed, which showed a mixed inflammatory infiltrate and dermatology

Figure 1. Right lower-leg pyoderma gangrenosum lesions upon re-presentation to the wound care clinic following 5 months of immunomodulating therapy (17.09.2024)

Figure 2. Right pretibial PG lesion. All other PG lesions of the leg healed. (27.05.2025)

Figure 3. Right pretibial PG lesion. All other PG lesions of the leg healed. Punch biopsy and deep swab for microbiology performed at this visit (03.06.2025)

Figure 4. Right pretibial PG lesion positive for superficially invasive SCC (11.06.2025)

Figure 5. Right pretibial wound s/p SCC resection (07.07.2025)

Figure 6. Right pretibial wound, healed (08.12.2025)

was consulted. He was treated in the dermatology clinic for over a year, during which his wounds were considered a result of radiation dermatitis and mostly treated with gentian violet. During this time, he also started on trental, prednisone, methotrexate, and calcium/Vitamin D supplementation.

Given the patient's positive response to immunomodulating therapy, another biopsy was performed 10 months after the initial biopsy and demonstrated features consistent with pyoderma gangrenosum. After continuing immunomodulating therapy for 5 more months, which resulted in stabilised inflammation, the patient returned to the wound clinic for weekly management of his lower-extremity wounds. At that time, the patient had scattered shallow wounds on the right lower leg with a surface area of 567 cm^2 [Figure 1].

Over the next 8 months, the wounds were treated with weekly debridement as needed, absorptive foam antimicrobial dressings, multilayer compression wraps and eight cellular grafts (cryopreserved placental membrane). Efforts were made to improve skin hygiene with weekly dressing changes and cleaning using soap/water and 3-WEA (sodium tetradecyl sulfate) keratolytic solution. After 8 months of weekly treatment, the lateral ulcer present on the patient's right leg was healed while the medial ulcer was decreasing in size. Four weeks later, all right leg wounds were healed except for the medial ulcer that remained fairly unchanged [Figure 2]. The persistence and poor progress of this wound suggested the need for additional workup. Three 3 mm punch biopsies were performed, as well as a deep swab after debridement for microbiology [Figure 3]. Pathology demonstrated superficially invasive SCC [Figure 4].

The patient was referred to dermatology for excision and treatment. The tumour-containing tissue was removed using Mohs micrographic surgery [Figure 5]. Follow-up after excision demonstrated healing, healthy granulation tissue with no signs of infection. Treatment with cellular grafting (cryopreserved placental membrane) facilitated complete healing in 22 weeks [Figure 6].


Figure 1


Figure 2

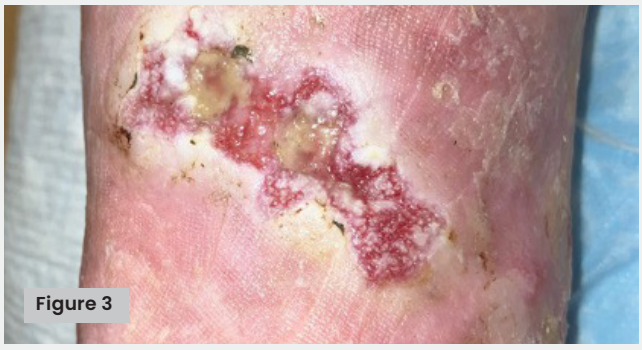

Figure 3


Figure 4


Figure 5


Figure 6

Discussion

We described a case of SCC arising in a PG lesion of the lower leg present that was present for over 2.5 years. The patient's PG was diagnosed by dermatology following a biopsy initiated after a positive response to immunomodulating therapy. After return to the wound clinic and standard wound care treatment, all PG lesions were healed aside from a medial leg lesion prompting biopsy that confirmed SCC.

To our knowledge, there is only one reported case of SCC arising in a PG lesion (Morrison et al, 2022). Morrison et al. reported an instance of invasive SCC of verrucous type in a 57-year-old man with a chronic, non-healing PG lesion present on the lateral tibia for 13 years. This patient had a history of Crohn's disease, colon cancer, bilateral deep vein thrombosis and venous stasis. Imaging showed no evidence of distant metastasis and the patient was managed with radiation therapy, given the risk of surgical management in triggering proliferation of PG.

There is more extensive literature describing SCC arising in chronic wounds. SCC can arise in non-healing diabetic foot ulcers (DFUs), pressure ulcers and venous leg ulcers (VLUs). Three cases of SCC arising in a non-healing diabetic foot ulcer in older men have been published (Scatena et al, 2016; Larijani et al, 2017; Luo et al, 2024). Two of the cases resulted in surgical excision and successful treatment, while one case demonstrated systemic dissemination and the patient died shortly after diagnosis.

Kasai et al (2021) reported a case of SCC within an ischial pressure ulcer in a middle-aged man that was initially believed to be necrotising soft tissue infection. Eventual biopsy showed well-differentiated metastasised SCC that ultimately led to the patient's death.

There are many potential mechanisms by which chronic ulcers can undergo malignant transformation into SCC, also known as Marjolin ulcers (Kuraitis and Murina, 2024). Constant extrinsic inflammation leads to proinflammatory cytokines and recruitment of inflammatory cells. Malignant transformation can occur because of this chronic inflammation and persistent cellular damage, leading to increased mitotic activity and local toxin encouraging mutagenesis.

Additionally, immunosuppressive treatment used to manage PG can increase the risk of developing cancer. A recent case control study identified that patients taking methotrexate are 1.61 times more likely to develop cutaneous SCC in a dose-response manner (Polesie et al, 2023). This may have played a role in our patient's pathogenesis, given that he had been taking methotrexate for over a year at SCC diagnosis.

SCC and PG pose a diagnostic challenge as both conditions can present similarly and can be misdiagnosed for one another. While both Marjolin ulcers and PG are rare conditions, the presence of one condition should not lower clinical suspicion for other possible mechanisms of chronic ulceration.

The key clinical sign prompting our biopsy was a stall in healing of one PG lesion while other lesions healed. While there is no absolute timeframe, guidelines from the Society of Vascular Surgery and American Venous Forum published in 2014 emphasise the importance of leg ulcer biopsy within 4-6 weeks of lack of responsiveness to standard treatment for VLUs, as well as time-independent biopsy of lesions suspicious for another aetiology (O'Donnell et al, 2014), which is also supported by a more recent VLU algorithm (James et al, 2022).

We encourage clinicians to have a low threshold for biopsy of suspicious lesions and encourage collaboration with wound care, dermatology, pathology and oncology in treating these challenging-to-diagnose skin conditions.

Limitations of this case report include its lack of generalisability.

Conclusion

In patients with PG, healing discordance — when one lesion stalls while others resolve — should prompt immediate biopsy. Given the possibility of malignant transformation in PG, as well as in any chronic wound, continuous surveillance is a key feature of management.

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