SKIN

BRIEF ARTICLE

Enterococcal Infection-Provoked Generalized Pustular Psoriasis in the Absence of Preexisting Psoriasis: A Novel Case Report

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ABSTRACT

A 50-year-old female with a history of cervical cancer, chemoradiation-induced arteritis, peripheral artery disease, and multiple vascular surgeries presented for an extensive pruritic and painful rash on her abdomen, trunk, and extremities. A physical exam revealed well-defined, thick plaques with silvery and micaceous scales on her right lower leg, left knee, stomach, back, groin, bilateral elbows, distal dorsal fingertips, and dorsal hands. Her right-sided axillary femoral bypass site, placed for her peripheral artery disease, had an exposed polytetrafluoroethylene (PTFE) graft with purulent, malodorous discharge. The laboratory work-up showed elevations in acute inflammatory markers, hypoalbuminemia, hypoproteinemia, and hypocalcemia. Skin biopsy revealed mounds of parakeratosis with intracorneal neutrophilic aggregates, large intraepidermal aggregates of neutrophils, and exocytosis of neutrophils into the epidermis with stuffing of the dermal papilla. Wound cultures from the right groin fold were positive for *Enterococcus faecium* and *E. faecalis.* Based on the characteristic findings of the rash and biopsy results, a diagnosis of generalized pustular psoriasis (GPP) secondary to an enterococci infection was made. To our knowledge, this is the first reported case of GPP caused by *Enterococci* spp. infection.

INTRODUCTION

Generalized pustular psoriasis (GPP) is a rare, severe form of pustular psoriasis associated with systemic inflammation. Several infections have been linked to GPP flares, including *Streptococcus* spp., *Trichophyton rubrum*, cytomegalovirus, Epstein–Barr virus, and varicella zoster virus.[1] We report the first case of *Enterococci* spp. infection as the trigger for GPP, and discuss multiple treatment considerations.

CASE REPORT

A 50-year-old female with a history of cervical cancer status-post chemoradiation complicated by arteritis and peripheral artery disease (PAD) requiring multiple vascular bypasses and surgeries presented to the emergency department for suspected graft infection and a pruritic, painful rash on her abdomen, trunk, and extremities. She reported that her right-sided axillary femoral bypass site, placed for her PAD, began draining malodorous discharge shortly before the rash erupted one week prior. The patient denied any changes to her medications, exposures, or any personal or family history of psoriasis. She endorsed diffuse joint pain, subjective fevers, chills, malaise, and was

hemodynamically unstable. She was not immunosuppressed upon admission.

Examination revealed well-defined, thick erythematous plaques with silvery and micaceous scale on her right lower leg, left knee, abdomen, back, groin, bilateral elbows, distal dorsal fingertips, and dorsal hands (**Figure 1**). There were diffuse, tiny pustules overlying erythema on her bilateral thighs, breasts, left lower leg, bilateral upper extremities, and back. Her right groin fold, at the right-side axillary femoral bypass site, had an exposed polytetrafluoroethylene (PTFE) graft with purulent malodorous discharge (**Figure 2**).

The right groin fold wound culture grew *Enterococcus faecium* and *E. faecalis*. Bacterial, acid-fast bacilli (AFB), and fungal tissue cultures from a pustule demonstrated no growth. Blood cultures were intermittently positive on admission; however, subsequent cultures were negative. Labs revealed hypoalbuminemia (2.1 g/dL), hypoproteinemia (3.9 g/dL), hypocalcemia (4.7 mg/dL), leukocytosis, and elevated levels of C-reactive protein (CRP), beta-D-glucan, creatinine, and alkaline phosphatase (ALP).

A punch biopsy from the left mid-upper arm revealed mounds of parakeratosis with intracorneal neutrophilic aggregates, large intraepidermal aggregates of neutrophils (spongiform pustules of Kogoj), and exocytosis of neutrophils into the epidermis with stuffing of the dermal papilla (**Figure 3**).

The patient was diagnosed with generalized pustular psoriasis (GPP). The right femoral graft site wound infection was identified as the trigger, based on the timeline between infection onset and rash appearance. Initial antibiotics included cefepime, metronidazole, and fluconazole, then later escalated to linezolid, piperacillin-tazobactam, and micafungin for broader coverage. Daptomycin was briefly used but discontinued due to elevated creatine phosphokinase levels. Dermatology initiated 25 mg of acitretin daily. Topical corticosteroids and keratolytics were added as adjunctive therapy. Due to her damaged skin barrier, supportive care was provided to maintain adequate hydration, nutrition, and temperature regulation. Insurance approval of spesolimab was attempted. The patient's GPP began to show significant improvement and a promising response to acitretin treatment within three days of initiation.

The patient then underwent explant surgery of the presumed source of sepsis, the infected right axillofemoral graft. Unfortunately, she remained unstable postoperatively and developed septic shock, multi-organ failure, disseminated intravascular coagulation, and pulmonary hemorrhage. Following a goals-of-care discussion, she was terminally extubated and expired.

DISCUSSION

Generalized pustular psoriasis (GPP) is a rare, severe form of pustular psoriasis associated with systemic inflammation. The exact pathophysiology has not yet been elucidated; however, several genetic, infectious, and environmental risk factors have been associated with GPP. Genetic factors include mutations in genes involved in the regulation of immune and inflammatory pathways, such as IL-36RN (interleukin 36 receptor antagonist) and CARD14 (caspase recruitment domain-containing protein 14).[1,2]

Additionally, numerous psoriasis subtypes are known to be exacerbated by infections.[3] Streptococcal tonsillitis or pharyngitis is a

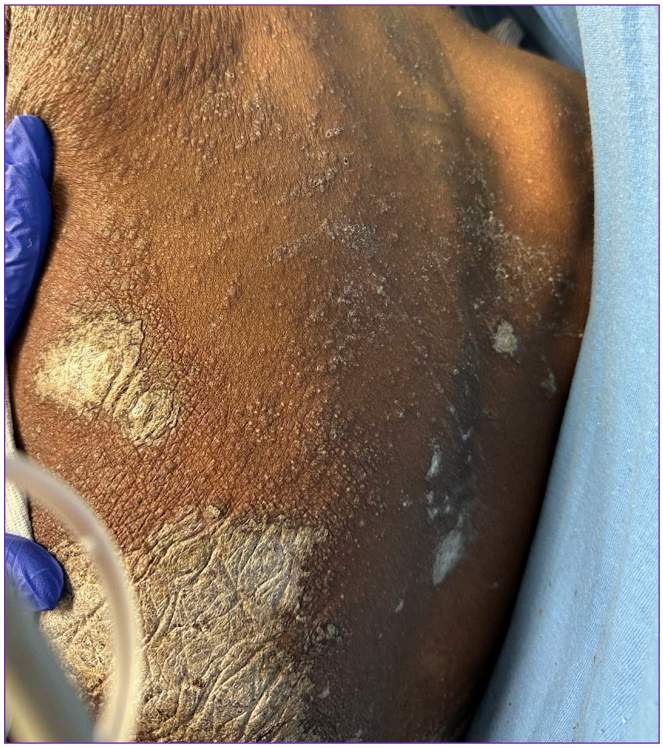

Figure 1: Thick plaques with silvery and micaceous scale and crops of pustules on the back.

Figure 2: Thick plaques with silvery and micaceous scales on the abdomen, right groin, distal dorsal fingertips, and hands. Exposed PTFE graft with purulent malodorous discharge.

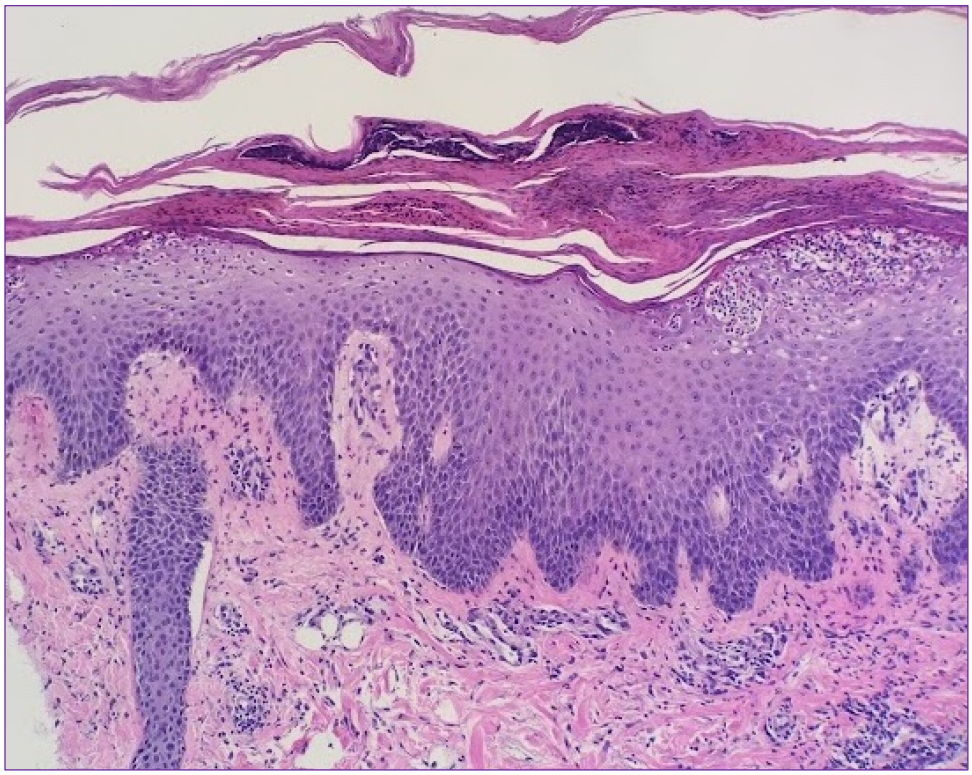

Figure 3: Parakeratosis with intracorneal neutrophilic aggregates, spongiform pustules of Kogoj, and exocytosis of neutrophils into the epidermis with stuffing of the dermal papilla (H&E, 20x).

well-known trigger for guttate psoriasis. Human immunodeficiency virus, Candida infection, and *Staphylococcus aureus* superantigens have been reported to exacerbate plaque psoriasis.[3] Regarding GPP, *Streptococcus* spp., *Trichophyton rubrum*, cytomegalovirus, Epstein–Barr virus, and varicella zoster virus are among the most reported infectious triggers.[1] *Enterococci* spp. is a gram-positive bacterium that naturally inhabits the gut flora but may become an opportunistic pathogen in an immunocompromised individual. To our knowledge, this is the first reported case of psoriasis triggered by *Enterococci* spp.

Patients with GPP present with acute onset of widespread, sterile pustules overlying painful or pruritic, erythematous skin. Mucosal findings may include a geographic or fissured tongue, cheilitis, and ocular involvement. The differential diagnosis of GPP includes acute generalized exanthematous pustulosis (AGEP), Sneddon-Wilkinson disease, and infectious causes.[1,2] Accurate diagnosis relies on clinical examination, laboratory tests, and histopathology. Laboratory work-up may demonstrate leukocytosis with neutrophilia, elevated erythrocyte sedimentation rate (ESR), CRP, hypoalbuminemia and hypoproteinemia, hypocalcemia, and hypozincemia, elevated blood urea nitrogen and creatinine, and elevated liver function enzymes.[2]

A skin biopsy is recommended to differentiate GPP from AGEP. Histopathologic features of GPP include parakeratosis, neutrophilic exocytosis, epidermal spongiosis, and acanthosis.[2] Other classic features include hyperkeratosis, elongation of rete ridges, diminished stratum granulosum, and capillary dilation in the dermal papillae.[2]

Systemic retinoids, such as acitretin, are the most frequently used non-biologic therapies for GPP. The precise mechanism by which acitretin works in GPP is not fully understood, but it's thought to be via regulation of keratinocyte differentiation, proliferation, and apoptosis.[4] In addition to retinoids, other reported treatments for GPP include cyclosporine, methotrexate, and biologic agents targeting tumor necrosis factor-alpha, interleukin (IL)-17A or IL-17 RA (receptor), and IL-23.[5] A recent advance is FDA approval of spesolimab. This biologic agent targets the IL-36 pathway, demonstrating efficacy in patients with GPP.[5] This marks the beginning of a new era of targeted therapy for GPP. It's essential to understand that treatments can alleviate symptoms of GPP, but they're not curative. Treatment aims to help patients manage symptoms and improve their quality of life.

CONCLUSION

Medical literature reporting the relationship between *Enterococci* spp. and psoriasis is scarce. To our knowledge, this is the first reported case of GPP caused by *Enterococci* spp. infection. Further contributing to the novelty of this case is the lack of family or personal history of psoriasis, as GPP typically occurs in patients with pre-existing psoriasis. The patient's positive response to acitretin treatment underscores the importance of early recognition and aggressive therapy in managing this condition.

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