Remission of refractory pyoderma gangrenosum, severe acne, and hidradenitis suppurativa (PASH) syndrome using targeted antibiotic therapy in 4 patients

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Pyoderma gangrenosum, severe acne, and suppurative hidradenitis (PASH) syndrome can prove refractory to treatment and is characterized by relapses and recurrences. The combination of antibiotic therapy and surgery can produce success in the management of the syndrome. Acute treatment is required, but maintenance therapy is also necessary to prevent disease relapse. The response to antibiotic therapy is hypothesis generating, raising the issue of a modified host response. To date, anecdotal reports support the use of surgery and medical therapy, but controlled investigations with extended follow-up are necessary to substantiate preliminary data observed with individual cases. (J Am Acad Dermatol 2015;73:S66-9.)

Key words: acne fulminans; antibiotic therapy; hidradenitis suppurativa; microbiome host disease; PASH syndrome; pyoderma gangrenosum; remission; severe acne.

Pyoderma gangrenosum, severe acne, and suppurative hidradenitis (PASH) syndrome is characterized by the association of pyoderma gangrenosum (PG), severe acne (A), and hidradenitis suppurativa (HS).[1] PG and HS are both therapeutic challenges.[2-4]

We report the remission of PG and HS in 4 patients with refractory PASH syndrome who were treated with a combination of prolonged targeted antibiotic (PTA) therapy and surgery.

Abbreviations used:

IV:	intravenous
NSAID:	nonsteroidal anti-inflammatory drug
PASH:	pyoderma gangrenosum, severe acne, and hidradenitis suppurativa syndrome
PG:	pyoderma gangrenosum
PTA:	prolonged targeted antibiotherapy
HS:	hidradenitis suppurativa

CASE REPORTS

Within a cohort of 800 patients with HS, 4 patients with severe PASH syndrome were treated with the PTA protocol used in our center to treat HS, based on the microbiology of lesions.[5-8] Clinical remission (CR) was defined by the absence of any inflammation in all HS and PG areas. Intravenous (IV) ceftriaxone and oral metronidazole or IV ertapenem were first administered for 3 to 6 weeks. Thereafter, an oral consolidation treatment combining 2 to 3 antibiotics

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(eg, rifampin, moxifloxacin, metronidazole, amoxicillin, and/or linezolid) was given in 4- to 6-week cycles. If HS recurred, a new cycle of IV antibiotics was administered before surgery. With remission achieved, maintenance treatment with cotrimoxazole was proposed; relapses were treated with pristinamycin with or without metronidazole for 3 weeks. Topical antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and steroids were stopped before treatment. Three patients were smokers, and no patients stopped smoking. No patients had diabetes or were overweight.

CAPSULE SUMMARY

- The syndrome of pyoderma gangrenosum, severe acne, and hidradenitis suppurativa represents a therapeutic challenge to clinicians.
- Treatment modalities such as surgery and prolonged targeted antibiotic therapy have shown some success.
- The efficacy of antibiotic therapy suggests that host microbiome dysregulation is involved in both pyoderma gangrenosum and hidradenitis suppurativa.

Patient 1

Patient 1 was a 37-year-old man with familial HS and acne fulminans, active PG, and Hurley stage III HS for 20 years in spite of 4 wide excision surgeries for HS. The use of PTA obtained remission of PG and axillary and groin HS in 5 months; HS on his buttocks remitted after 18 months with wide excisional surgery and PTA therapy. There was no PG relapse for 4 years. After 12 months of remission, inguinal HS relapses responded to pristinamycin with metronidazole in 3 weeks.

Patient 2

Patient 2, the brother of patient 1, was a 26-year-old man with Hurley stage II HS for the past 11 years who had previous severe acne and PG. Oral antibiotics, NSAIDs, isotretinoin, and 30 drainages failed to heal his HS. The use of PTA therapy led to remission of HS in 3 months, which was sustained for 9 months. A loss to follow-up of 2 years resulted in an HS relapse, with new remission obtained in 2.5 months with the use of PTA therapy.

Patient 3

Patient 3 was a 23-year-old who previously had acne fulminans and active Hurley stage III HS for 11 years. NSAIDs, steroids, antibiotics, and several drainages failed to improve his PASH symptoms for 6 years. PTA therapy healed PG in 6 months (Fig 1) and HS in 18 months. After a loss to follow-up for 1 year, 2 stage III HS and PG relapses were successfully treated with PTA therapy in 6 months. No new relapses of PG or HS occurred for 2 years with the use of cotrimoxazole.

Patient 4

Patient 4 was a 29-year-old woman who was a nonsmoker and who had Hurley stage III HS for the past 18 years. Previous treatments failed to improve PASH, including steroids, NSAIDs, isotretinoin, colchicin, etanercept, adalimumab, and 12 excisions. The use of PTA resulted in inguinal and axillary remission of HS within 4 months, with softening of PG scars without any relapse since 2010. HS lesions on the buttocks required 3 wide excisions (Fig 2). A 6-month remission after the last excision was followed by a Hurley 1 relapse in a scar, which was treated with pristinamycin for 3 weeks.

DISCUSSION

PG and HS are recalcitrant conditions with no therapeutic consensus.[2-4] This is reflected by multiple previous therapeutic failures in these 4 patients. However, both PG and HS responded to our combined PTA therapeutic protocol,[5-7] allowing surgery in 2 previously inoperable patients. Patients 1, 3, and 4 were severely handicapped, constantly flaring in several areas for many years without any remission. Both the severity of their PASH symptoms and the previous treatment failures justified PTA therapy, which is based on HS microbiology data showing a polymorphous anaerobic flora, including strict anaerobes, Streptococci of the Milleri group, and anaerobic actinomycetes.[8]

The favorable response to PTA therapy—the disappearance of HS flares and healing of PG within 3 to 6 months—had never been obtained for years with any treatment. In Hurley stage II HS, remission is often achieved in 3 months with PTA therapy,[5] as was the case with patient 2. But Hurley stage III HS usually requires surgery, as was the case for patients 1 and 3, in whom buttocks resistance to PTA justified surgery to avoid a prolonged antibiotic therapy with a risk of resistance emergence. With the use of PTA therapy, PG lesions healed in patients 1 and 3 within 5 to 6 months, but PG scars also faded and softened in patient 4.

Spontaneous regression or a placebo effect is unlikely because the disease permanently flared for many years in spite of many therapeutic attempts. The occurrence of relapses with the lack of maintenance treatment supports this hypothesis, as do new remissions obtained when treatment was resumed.