Is Topical Monotherapy Effective for Localized Pyoderma Gangrenosum?

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Clinical Question: Is topical treatment alone effective for localized pyoderma gangrenosum (PG), and if yes, is one more effective than the others?

Background

In May 2008, a 32-year-old woman was seen with a painful infiltrated erythematous lesion 11 cm in diameter, studded with purulent necrotic pits, on the anterior right shin (Figure, A). It had started as an erythematous infiltrated lesion 3 months previously and had been stable for 1 month. Pyoderma gangrenosum was diagnosed based on the clinical appearance, negative findings on bacterial culture, and histologic examination of a skin biopsy specimen. No systemic underlying disease was found during investigations, including a colonoscopy.

There is little evidence on the efficacy of PG treatment because there is only 1 randomized controlled trial to date comparing the effects of infliximab vs placebo.1 Systemic corticosteroids and cyclosporine are usually recommended as first-line treatments.2 Given the stability of this solitary lesion, we decided to consider the option of topical monotherapy for our patient. The objective of this article was to determine from the available evidence whether a topical agent would be an effective and safe treatment in this setting.

Literature Search

We searched MEDLINE and the Cochrane Controlled Trials Register for each topical agent cited in reviews and textbooks on PG treatment, including hyaluronic acid, becaplermin, topical corticosteroids, clobetasol, betamethasone, intralesional corticosteroids, topical cyclosporine, mesalamine, topical nitrogen mustard, sodium cromoglycate, benzoyl peroxide, pimecrolimus, tacrolimus, and pyoderma gangrenosum. We selected all trials, case series, and case reports describing PG treatment with a topical agent as monotherapy. In addition, we searched for relevant publications in each article's reference list.

Appraisal of the Evidence

We found no randomized controlled trial. Except for topical corticosteroids and calcineurin inhibitors, we found 1 to 10 reported cases for each topical or intralesional treatment. We considered these data too limited to conduct a valuable analysis.

We found 16 publications on PG treatment with topical tacrolimus or topical corticosteroids without an associated systemic treatment:

<table>
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<tr>
<th>A</th>
<th>B</th>
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<tbody>
<tr>
<td>Figure. The patient’s pyoderma gangrenosum lesion before treatment (May 2008) (A) and after topical treatment (September 2008) (B).</td>
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Table. Characteristics of Pyoderma Gangrenosum (PG) Lesions and Their Outcomes by Topical Agent Prescribed

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Corticosteroids (n=46)</th>
<th>Tacrolimus (n=26)</th>
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<tbody>
<tr>
<td>Peristomal PG</td>
<td>40 (1.1)</td>
<td>14 (1.1)</td>
</tr>
<tr>
<td>Nonperistomal PG</td>
<td>6 (0.6)</td>
<td>12 (0.6)</td>
</tr>
<tr>
<td>Lesion size, mean (SD), cm</td>
<td>2.4 (1.1)</td>
<td>3.6 (0.6)</td>
</tr>
<tr>
<td>Patients with complete healing, No./Total No.</td>
<td>29/46</td>
<td>18/26</td>
</tr>
<tr>
<td>Peristomal PG with complete healing, No./Total No.</td>
<td>24/40</td>
<td>10/14</td>
</tr>
<tr>
<td>Other site PG with complete healing, No./Total No.</td>
<td>5/6</td>
<td>8/12</td>
</tr>
<tr>
<td>Time to healing, mean (SD), wk</td>
<td>9.8 (10.8)</td>
<td>5.8 (1.6)</td>
</tr>
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</table>

Topical tacrolimus: 2 prospective case series and 4 case reports.

Topical corticosteroids: 2 retrospective series and 7 case reports, and

One trial comparing topical clobetasol propionate treatment with topical tacrolimus treatment.

One case report was excluded because it lacked information on treatment dosage and disease response.

Comment

Although case series are subject to patient selection bias and case reports preferentially describe positive outcomes, they often provide preliminary evidence for efficacy of new treatments. We analyzed 4 case series and 10 case reports using a checklist for quality assessment of these types of communications.

Diagnostic criteria were clearly identified and met by patients in 9 articles of 14. Although an institutional review board approved 1 prospective case series, patient consent was not documented in any of the publications. No reference to the natural course of the disease or its outcome based on standard treatment was clearly stated in any study. The clinically important outcome of complete healing was mentioned in all publications.

The aesthetic appearance of the scar and the patient’s perception of the treatment outcome, which are also important, were not mentioned in any of the publications. Potential risks and adverse effects of treatment were discussed in only 1 article. The authors abstained from unfounded claims about safety or efficacy in 12 of 14 reports. In the case series, inclusion and exclusion criteria were not given, nor was it stated whether all consecutive cases were included or what were reasons for noninclusion.

The open-label nonrandomized trial compared clobetasol, 0.05%, (n=13) with tacrolimus, 0.3%, (n=11) for treatment of peristomal PG. However, the study design did not allow statistical comparison between treatments. Patients recruited initially were treated with clobetasol, whereas those recruited later were treated with tacrolimus. There was no discussion of comparability between groups at study inclusion, nor were any clear inclusion criteria listed for the choice of topical vs systemic treatment.

Together, among the open-label trial and the aforementioned 15 other relevant publications, 26 patients received topical tacrolimus, and 46 patients received topical corticosteroids. Twelve patients received tacrolimus, 0.3%, once a day, and 7 patients received tacrolimus, 0.1%, once a day, whereas 7 patients had neither the dosage nor the number of applications specified. Among patients who used topical corticosteroids, 24 received clobetasol, 11 betamethasone dipropionate, 2 triamcinolone acetonide paste, 4 hydrocortisone, and 1 acetonide; the type of topical corticosteroid used was unspecified for 4 patients.

All 18 cases of nonperistomal PG were localized, and an underlying disease was present in 8 of 18. Characteristics of lesions and responses to topical treatment are summarized in the Table. Serum tacrolimus levels were available in 17 patients and were always below the therapeutic range. However, the daily amount of tacrolimus used was not reported for any patient. Other than exuberant granulation tissue in 11 patients and burning sensation in 1 patient, no adverse effects were reported. For topical corticosteroid outcomes, the authors of 1 case series reported that there were no adverse effects, whereas the other publications mentioned neither the presence nor the absence of adverse effects.

The absence of adverse effects should be balanced by 2 reported cases of PG with serum tacrolimus levels higher than the therapeutic range. These occurred with topical treatment of high tacrolimus dosages (7.5 g/d or 15 g/d).

Limitations of the Critically Appraised Topic

Our search was limited to MEDLINE and the Cochrane Controlled Trials Register. A relevant clinical case published in German was excluded. Our conclusions are based on a small open trial and on 15 aforementioned case reports.

Clinical Bottom Line

Among local therapies (hyaluronic acid, becaplermin, topical corticosteroids, intralesional corticosteroids, topical cyclosporine, mesalazine, topical nitrogen mustard, sodium cromoglycate, benzoyl peroxide, pimecrolimus, and tacrolimus) reported as potential treatment for PG, our analysis of the literature showed that the best evidence is available for topical corticosteroids and tacrolimus. Most analyzed cases involved peristomal PG, and the others involved localized PG with or without an underlying disease. No apparent differences in complete healing rates were seen between peristomal and nonperistomal PG, with no clear evidence that one type of topical treatment is better than another.

Despite limited available evidence, topical monotherapy with corticosteroids or tacrolimus is a reasonable treatment option for localized and limited PG. However, there is insufficient evidence to advise the frequency of topical application, class of topical corticosteroids, tacrolimus dosage, or use of occlusive dressing. Furthermore, the risk of systemic absorption has to be considered.
What Happened to Our Patient?

We decided to commence topical monotherapy in our patient and chose a topical corticosteroid based on a better risk profile and the lower cost. Clobetasol propionate ointment, 0.05%, was applied once daily for 1 month and every other day for 1 month. At the end of this period, the ulceration was partially healed. The patient was concerned about the development of cutaneous atrophy and depigmentation, and 2 new erythematous nodules had developed on the treated area. Topical tacrolimus has no atrophogenic potential, so we switched treatment from topical clobetasol to topical tacrolimus, 0.1%, ointment once daily without occlusion. The remaining part of the lesion healed completely after 6 weeks (Figure, B). The patient had reported a burning sensation after application during the 2 first weeks of treatment. A recurrence appeared 7 months later on the upper left part of the scar, was again treated with tacrolimus, 0.1%, ointment once daily, and disappeared completely in 2 weeks.

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REFERENCES


