**Pharmacology and therapeutics**

**Pyoderma gangrenosum following isotretinoin therapy for acne nodulocystic**

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A 19-year-old man presented with nodulocystic acne lesions predominantly involving his face and trunk; he was put on a regimen of isotretinoin therapy (0.3 mg/kg/d). A month later having already begun medication, he noticed the development of superficial hemorrhagic pustule lesions located on his pubis and inguinal area. Nevertheless, he omitted this fact to his physician, and the regimen was scaled up to 0.5 mg/kg/d. One week after starting this new dose regimen, the lesions changed from pustules into well-delimited ulcerated lesions with cribriform pattern located on the inguinal and pubis area (Fig. 1). Not withstanding, he sought medical attention only after 15 d. At this time, he presented himself with widespread ulcerated lesions, including the primary ulcers, as well as, well-defined ulcerated lesions on his left arm, right leg, left shoulder, and on his left calf (Fig. 1). Because these lesions exhibited a violaceous hue on the undermined borders, a biopsy was performed on the pubis lesion and revealed an unspecified inflammation and absence of leukocytoclastic vasculitis.

The patient also developed a pustule (pathergy) on a puncture site (Fig. 1), and a diagnosis of pyoderma gangrenosum was proposed.

Other underlying diseases were excluded through complementary exams including full blood count, serum immunoelectrophoresis, urinary κ and λ light chain, hepatitis B surface antigen, HIV (Human immunodeficiency virus) serology, liver function tests, a collagen screen, chest x-ray, and colonoscopy, which were all negative. Cultures from lesions swabbed, nasal nare, tissue biopsy, and blood cultures were negative. He denied any disease on his past medical history.

Oral steroid was initiated (prednisone 1 mg/kg/d). Based on the possible diagnosis of pyoderma gangrenosum associated with isotretinoin therapy, the latter was withdrawn. The lesions began to heal with a cribriform pattern corroborating the diagnosis of pyoderma gangrenosum.

After 4 months on steroid therapy, a normal G6PD level was obtained and dapsone was started (100 mg daily); prednisone was tapered and the patient was maintained only with dapsone daily.

In a 10-month follow-up all lesions healed (Fig. 2), no underlying disease developed and no new lesions appeared after isotretinoin therapy withdrawn and after prednisone and dapsone initiation.

Including our patient, five individuals with isotretinoin-induced pyoderma gangrenosum have been described and their features are summarized in Table 1. Although the pathogenesis for pyoderma gangrenosum following the initiation of isotretinoin therapy remains to be established, we postulate a mechanism in which isotretinoin alters adhesion molecule requirements for acute neutrophil emigration.

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**Abstract**

A 19-year-old man with nodulocystic acne on baseline was treated with isotretinoin therapy. After 1 month on the medication, he developed pyoderma gangrenosum on his pubis area, arms and legs, and pathergy on a puncture site. Possible underlying diseases were excluded. The patient was started on steroids (prednisone 1 mg/kg/d) and isotretinoin therapy was withdrawn. Later the prednisone was tapered and dapsone 100 mg/daily was initiated. After 10 months of follow-up all lesions had healed and no underlying diseases developed.
Figure 1 Primary ulcer, a well-delimited ulcerated lesion with cribriform pattern and a violaceous hue on the undermined border located on the pubis area (a). Ulcerated lesions on his left arm (b) and on his left calf (c). The patient developed a pustule (pathergy) on a puncture site (d).

Figure 2 (a) Primary pubis lesion (b) 1 month after isotretinoin therapy withdrawn and prednisone initiation (c) 4 months follow-up with dapsone and tapering prednisone, (d) 9 months follow-up only with dapsone.
Table 1 Clinical features of five pyoderma gangrenosum cases associated with isotretinoin therapy

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Days between IT initiation and onset of PG</th>
<th>Multiple or single lesions</th>
<th>Distribution of lesions</th>
<th>Associated medical problems</th>
<th>Treatment of PG</th>
<th>Response to therapy</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>Male</td>
<td>21 d</td>
<td>Single</td>
<td>Thigh</td>
<td>Acne flare-up and no other underlying disease</td>
<td>Cephalotin, prednisone 40 mg/d and dapsone 200 mg/d</td>
<td>Gradual improvement</td>
<td>6 months, with only two active acne lesions</td>
</tr>
<tr>
<td>19</td>
<td>Male</td>
<td>3 years</td>
<td>Multiple</td>
<td>Trunk</td>
<td>Myelodysplastic syndrome, severe acne and folliculitis</td>
<td>Topical steroid (beclomethasone 0.025% cream) and prednisolone 40 mg/d</td>
<td>Recurrence after topical steroid and gradual improvement after prednisolone initiation</td>
<td>6 months with a maintaining dosage of 20 mg/d of prednisolone</td>
</tr>
<tr>
<td>14</td>
<td>Male</td>
<td>14 d</td>
<td>Single</td>
<td>Trunk (internal area)</td>
<td>Acne and no other underlying disease</td>
<td>Hidrocortisone 800 mg/d initially and afterwards</td>
<td>Gradual improvement</td>
<td>4 years with no recurrence</td>
</tr>
<tr>
<td>30</td>
<td>Female</td>
<td>30 d</td>
<td>Multiple</td>
<td>Pubis and inguinal area, leg, calf, arm, and shoulder</td>
<td>Acne nodulocystic, diabetic nephropathy, and mycophenolate mofetil 3 g/d</td>
<td>Nonadherent dressings, topical tacrolimus 0.1% ointment and prednisone 30 mg/d. The latter was then changed to mycophenolate mofetil 3 g/d and prednisone was tapered</td>
<td>Recurrence after topical steroid and gradual improvement after prednisolone initiation</td>
<td>6 months with a maintaining dosage of 20 mg/d of prednisolone</td>
</tr>
<tr>
<td>30</td>
<td>Male</td>
<td>30 d</td>
<td>Multiple</td>
<td>Pubis, inguinal area, leg, calf, arm, and shoulder</td>
<td>Acne nodulocystic and no other underlying disease</td>
<td>Prednisone 60 mg/d. Afterwards, dapsone 100 mg/d and prednisone was tapered</td>
<td>Gradual improvement</td>
<td>10 months with no recurrence although dapsone was maintained (100 mg/d)</td>
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References


