Ivermectin-Responsive Demodex Infestation during Human Immunodeficiency Virus Infection

A Case Report and Literature Review

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Key Words
Demodex - Human immunodeficiency virus - Antiretroviral therapy

Abstract
We report the case of a 56-year-old HIV-seropositive man who presented a facial Demodex infection developed 2 months after initiation of highly active antiretroviral therapy. The Demodex infection was confirmed by scrapings and histopathologic examination and by the dramatic response to antiparasitic treatment with oral ivermectin associated with 5% permethrin cream.

We report herein a case of Demodex infestation simulating a rosacea in an HIV-seropositive man. To our knowledge, this is the first case of an association of Demodex infestation occurring during AIDS which responded dramatically to ivermectin.

Observation
A 56-year-old man had been diagnosed as having AIDS 1 year before consultation. He was asymptomatic (stage 1). Because the CD4 cell count was 150/mm³ and HIV RNA was 200,000 copies/ml, an antiviral regimen was prescribed which consisted of stavudine 40 mg twice a day, didanosine 400 mg once a day and nevirapine 200 mg twice a day. He had a rapid virologic response with undetectable viral load and an increase in CD4 cell count to 210/ml within 1 month of therapy. Two months after the beginning of the antiretroviral treatment, the patient developed a progressively extending facial eruption resembling rosacea. The skin eruption consisted of papules and papulopustules which coalesced on the cheeks to form plaques, associated with erythema, variable oedema (fig. 1) and pityriasis-like scales; the lesions were always limited to the face. He had no pruritus. The remainder of the skin surface...
### Table 1. Demodicidosis associated with HIV infection reported in the literature

<table>
<thead>
<tr>
<th>Authors</th>
<th>Sex/age years</th>
<th>Clinical features</th>
<th>Localization</th>
<th>Histology</th>
<th>Treatment for Demodex</th>
<th>Stage of HIV disease</th>
<th>Antiretroviral treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashack et al. [19]</td>
<td>M/45</td>
<td>folliculitis, pruritus</td>
<td>trunk, extremities</td>
<td>numerous <em>Demodex</em></td>
<td>lindane 1%</td>
<td>C</td>
<td>NS</td>
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<td>Dominey et al. [18]</td>
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<tr>
<td>Case 1</td>
<td>M/49</td>
<td>papular, nodular, vesicular, eruption, pruritus</td>
<td>neck, cheek</td>
<td>inflammatory infiltrate with eosinophils; numerous <em>Demodex</em></td>
<td>benzene hydrochloride</td>
<td>NS</td>
<td>AZT/4 weeks</td>
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<tr>
<td>Case 2</td>
<td>M/51</td>
<td>erythema, papular, nodular, pustular eruption, pruritus</td>
<td>face, forehead, neck, temples</td>
<td>perifollicular inflammatory infiltrate with giant cells, numerous <em>Demodex</em></td>
<td>1% permethrin</td>
<td>NS</td>
<td>AZT/6 days</td>
</tr>
<tr>
<td>Banuls et al. [20]</td>
<td>W/24</td>
<td>papular eruption, pruritus</td>
<td>neck, trunk, arms</td>
<td>perifollicular inflammatory infiltrate, numerous <em>Demodex</em></td>
<td>crotamiton</td>
<td>C, CD4 &lt; 200</td>
<td>AZT/30 days</td>
</tr>
<tr>
<td>Girault et al. [21]</td>
<td>M/27</td>
<td>papular, nodular, pustular eruption</td>
<td>face, trunk</td>
<td>numerous <em>Demodex</em></td>
<td>lindane</td>
<td>Kaposi, CD4 129</td>
<td>AZT/2 months</td>
</tr>
<tr>
<td>Sanchez-Viera et al. [22]</td>
<td>W/4</td>
<td>papular, pustular eruption</td>
<td>cheek</td>
<td>tuberculoid, follicular granuloma, numerous <em>Demodex</em></td>
<td>erythromycin per os</td>
<td>oral candidosis, CD4 840</td>
<td>NS</td>
</tr>
<tr>
<td>De Jaureguiberry et al. [23]</td>
<td>M/35</td>
<td>papular nodular, pustular eruption, pruritus</td>
<td>neck, head</td>
<td>inflammatory folliculitis, numerous <em>Demodex</em></td>
<td>Prioderm</td>
<td>Kaposi, pneumocytosis, CD4 21</td>
<td>NS</td>
</tr>
<tr>
<td>Redondo Mateo et al. [24]</td>
<td>W/48</td>
<td>papular, pustular eruption, pruritus</td>
<td>face, chin, neck, trunk</td>
<td>neutrophils and inflammatory foreign-body reaction, numerous <em>Demodex</em></td>
<td>crotamiton</td>
<td>CD4 50</td>
<td>AZT/45 days</td>
</tr>
<tr>
<td>Barrio et al. [25]</td>
<td>M/2</td>
<td>papules</td>
<td>cheeks</td>
<td>perifollicular infiltrate, numerous <em>Demodex</em></td>
<td>erythromycin, topical metronidazole</td>
<td>CD4 1,570</td>
<td>no treatment</td>
</tr>
<tr>
<td>Patrizi et al. [27]</td>
<td>M/7</td>
<td>papules, pustules</td>
<td>neck, neck, shoulders, trunk</td>
<td>not done but numerous <em>Demodex</em> by scotch test</td>
<td>crotamiton</td>
<td>C, CD4/CD8: 0.05</td>
<td>AZT/2 years, then DDI/4 years, then DDC + indinavir/1 year</td>
</tr>
<tr>
<td>Sarro et al. [26]</td>
<td>M/39</td>
<td>area of dry skin</td>
<td>left temple</td>
<td>not done but numerous <em>Demodex</em></td>
<td>topical 3% sulphur</td>
<td>CD4 9</td>
<td>NS</td>
</tr>
<tr>
<td>Jansen et al. [28]</td>
<td>M/35</td>
<td>papules, pustules</td>
<td>face</td>
<td>numerous <em>Demodex</em>, perifollicular lymphocytic inflammatory infiltrate</td>
<td>5% permethrin</td>
<td>C, CD4 240</td>
<td>AZT + saquinavir + delavirdine</td>
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<td>Our case</td>
<td>M/56</td>
<td>papular and pustular eruption</td>
<td>cheek</td>
<td>follicular inflammatory infiltrate, numerous <em>Demodex</em></td>
<td>ivermectin and permethrin</td>
<td>CD4 &gt; 300</td>
<td>D4T + DDI + nevirapine/2 months</td>
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</table>

NS = Not specified; AZT = azidothymidine; DDI = didanosine; DDC = zalutabine; D4T = stavudine;

and the physical examination were normal. The dermatitis did not respond to topical ketoconazole and topical metronidazole. The patient had no history of skin disease: neither had he applied medications or cosmetics nor did he present a long-lasting history of rosacea, facial erythema and flushing. Cultures from pustules for bacteria, dermatophytes or yeast were negative. The diagnosis was suspected by finding numerous *Demodex follicularum* in the skin scrapings. Histologic examination of a facial skin biopsy demonstrated that follicles contained numerous *Demodex* and were surrounded by a dense perifollicular infiltrate in the dermis with neutrophilic exocytosis. Periodic acid-Schiff stain was negative. We diagnosed facial rosacea-like *Demodex* infestation. At that time, the CD4 cell count was above 300/ml with undetectable viral load (<20 copies/ml).

A topical treatment with metronidazole (0.75%) twice a day during 1 month was ineffective as the oral regimen had been. Cyclines were not prescribed because of their harmful interaction with didanosine. Ivermectin (Stromectol®) was attempted with a
Discussion

D. folliculorum is a 0.3-mm-long transparent mite and an obligate, asymptomatic parasite of pilosebaceous follicles. Another species, D. brevis, lives deep in the sebaceous gland and is difficult to observe. The greatest concentration of Demodex is found where sebaceous glands are numerous and sebum production is pronounced (cheeks, nose and eyelids) [1–3]. Demodex is considered by some authors [3, 4] to have an important pathogenic role in the papulopustular phase of rosacea. Because Demodex is found in all healthy individuals, it has been suggested that the mite density (over 5 Demodex/cm²) is much more important than its mere presence in the pathogenesis of rosacea. The prevalence of the mite was studied in classical biopsies by three authors with contradictory results [5–7], but recent studies [3, 4], using a skin surface biopsy technique, have shown that the mean mite density in the skin is significantly higher in patients with rosacea than in normal controls.

Cutaneous disorders heretofore associated with Demodex infestation include, besides pityriasis follicularis [8], papulopustular eruptions [9, 10], rosacea-like lesions [11] and perioral dermatitis [12]. Demodex infestation can be considered as the cause of the clinical presentation of our patient because (a) he had no history of clinical features compatible with rosacea (recurring facial erythema and flushing, papulopustular eruption), (b) presented dry fine whitish follicular scales and papulopustules resembling ‘acne rosacea Demodex’, also named ‘rosacea-like demodicidosis’ described by Ayres and Ayres in 1932 and 1961 [8, 11], (c) histological examination demonstrated large numbers of Demodex and (d) he rapidly responded to acaricidal treatments.

It is remarkable that this inflammatory process, probably induced by the Demodex proliferation, appeared when the immunity of the patient was beginning to be restored. Demodex infestation has been described in immunocompetent individuals. Aydingoz et al. [13] demonstrated that immunosuppressive therapy did not influence D. folliculorum density in renal transplant patients and that there may be other factors than immunosuppression influencing Demodex density. Forton and Seys [3] did not find any increase in D. folliculorum density in a group of patients with HIV infection compared with controls. Nevertheless reports of isolated cases suggest that immunodeficiency induced by leukaemia [14–16] or by mycosis fungoides [17] further the occurrence of Demodex infestation. In addition, demodicidosis in association with AIDS is reported in the literature. The first report of Demodex infestation associated with AIDS was reported by Dominey et al. [18], who described a papulonodular variant seen in 2 HIV-seropositive patients and a dramatic resolution with antiparasitic measures. To our knowledge, today, our case is the thirteenth report [18–28] (table 1). The disease is said to heal with an antiparasitic ointment (permethrin, lindane, crotamiton, malathion), and the usual treatment of rosacea with metronidazole is ineffective in most cases. Unfortunately, the authors did not disclose sufficient immunological (CD4 counts) or virological (HIV RNA) information. In 5 cases at least, the patients were severely immunodeficient [19–21, 23, 24, 26–28], and demodicidosis occurred within 2 months after the beginning of highly active antiretroviral therapy [18, 20, 21, 24].

Our observation is the first case of demodicidosis arising during HIV infection who dramatically responded to a single dose of ivermectin with a very good tolerance. Ivermectin is a highly effective and generally well tolerated microfilaricide treatment [29]. Ivermectin has also been shown to be an effective scabicide in a single dose of 200 µg/kg body weight with a good tolerance [30–33].

In conclusion, in our patient the immunosuppression and the dermatitis became clinically obvious on the occasion of immunorestitution.

References

Demodex Infestation

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