Case Report

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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 HIVseropositive 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.

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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

Fig. 1. Scaly, erythematous, papular and pustular eruption on the cheeks, chin, forehead, eyelids and nose.

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

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

| Table 1. Demodicidosis | associated with HIV | infection rep | ported in the literatur | re |
|------------------------|---------------------|---------------|-------------------------|----|
|------------------------|---------------------|---------------|-------------------------|----|

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 folliculorum* 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

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single dose of $200 \ \mu g/kg$ body weight. A dramatic response was obtained within 2 weeks after initiation of treatment. To prevent reinfestation, 5% permethrin cream once weekly was given after ivermectin. No recurrence has been observed after a period of at least 1 year.

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, be-

References

- Nutting WB: Hair follicle mites (Acari: Demodicidae) of man. Int J Dermatol 1976;15: 79–98.
- 2 Bonnar E, Eustace P, Powell FC: *Demodex* mite in normal skin. Lancet 1991;337:1168.
- 3 Forton F, Seys B: Density of *Demodex folliculorum* in rosacea: A case-control study using standardized skin surface biopsy. Br J Dermatol 1993;128:650–659.
- 4 Bonnar E, Eustace P, Powell FC: The *Demodex* mite population in rosacea. J Am Acad Dermatol 1993;28:443–448.
- 5 Marks R, Harcourt-Webster JN: Hiostopathology of rosacea. Arch Dermatol 1969;100:683– 691.
- 6 Ramelet AA, Perroulaz G: Rosacea: Histopathologic study of 75 cases. Ann Dermatol Vénéréol 1988;115:801–806.
- 7 Roihu T, Kariniemi AL: *Demodex* mites in acne rosacea. J Cutan Pathol 1998;25:550– 552.

sides pityriasis folliculorum [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 (recurrent 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] furthers the occurrence of *Demodex* infestation. In addition, demodicidosis in association with AIDS is reported in the literature. The first record 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 $200 \mu g/$ 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 immunorestoration.

- 8 Ayres S Jr: Pityriasis folliculorum (*Demodex*). Arch Dermatol Syphilil 1930;21:19–24.
- 9 Miskjian HG: Demodiciodis (*Demodex* infestation of the scalp). Arch Dermatol 1951;63: 282–283.
- 10 Purcell SM, Hayes TJ, Dixon SL: Pustular folliculitis associated with *Demodex folliculorum*. J Am Acad Dermatol 1986;15:1159–1162.
- 11 Ayres S, Ayres S III: Demodectic eruptions (demodicidosis) in the human: Thirty years' experience with two commonly unrecognized entities: Pityriasis folliculorum (*Demodex*) and acne rosacea (*Demodex* type). Arch Dermatol 1961;83:816–824.
- 12 Ecker RI, Winkelmann RK: *Demodex* granuloma. Arch Dermatol 1979;115:343–344.
- 13 Aydingoz IE, Mansur T, Dervent B: *Demodex* folliculorum in renal transplant patients. Dermatology 1997;195:232–234.

- 14 Sahn EE, Sheridan DM: Demodicidosis in a child with leukemia. J Am Acad Dermatol 1992;27:799–801.
- 15 Ivy SP, Mackall CL, Gore L, Gress RE, Hartley H: Demodicidosis in childhood acute lymphoblastic leukemia: An opportunistic infection occurring with immunosuppression. J Pediatr 1995;127:751–754.
- 16 Castanet J, Monpoux F, Mariani R, Ortonne JP, Lacour JP: Demodicidosis in an immunodeficient child. Pediatr Dermatol 1997;14: 219–220.
- 17 Nakagawa T, Sasaki M, Fujita K, Nishimoto M, Takaiwa T: *Demodex* folliculitis on the trunk of a patient with mycosis fungoides. Clin Exp Dermatol 1996;21:148–150.
- 18 Dominey A, Rosen T, Tschen J: Papulonodular demodicidosis associated with acquired immunodeficiency syndrome. J Am Acad Dermatol 1989;20:197–201.

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- 19 Ashack RJ, Frost ML, Norins AL: Papular pruritic eruption of *Demodex* folliculitis in patients with acquired immunodeficiency syndrome. J Am Acad Dermatol 1989;21:306– 307.
- 20 Banuls J, Ramon D, Aniz E, Jorda E, Torres V: Papular pruritic eruption with human immunodeficiency virus infection. Int J Dermatol 1991;11:801–803.
- 21 Girault C, Borsa-Lebas F, Lecomte F, Humbert G: Eruption papulo-nodulaire: démodécie au cours du syndrome d'immunodéficience acquise. Press Méd 1991;20:177.
- 22 Sanchez-Viera M, Hernanz JM, Sampelayo T, Gurbindo MD, Lecona M, Soto-Melo J: Granulomatous rosacea in a child infected with the human immunodeficiency virus. J Am Acad Dermatol 1992;27:1010–1011.
- 23 De Jaureguiberry JP, Carsuzaa F, Pierre C, Arnoux D, Jaubert D: *Demodex* folliculitis: A cause of pruritus in human immunodeficiency virus infection. Ann Méd Interne (Paris) 1993; 144:63–64.
- 24 Redondo Mateo J, Soto Guzman O, Fernandez Rubio E, Dominguez Franjo F: *Demodex*attributed rosacea-like lesions in AIDS. Acta Derm Venereol 1993;73:437.
- 25 Barrio J, Lecona M, Hernanz JM, Sanchez M, Gurbindo MD, Lazaro P, et al: Rosacea-like demodicosis in an HIV-positive child. Dermatology 1996;192:143–145.
- 26 Sarro RA, Hong JJ, Elgart ML: An unusual demodicidosis manifestation in a patient with AIDS. J Am Acad Dermatol 1998;38:120– 121.
- 27 Patrizi A, et al: Demodicidosis in a child infected with acquired immunodeficiency virus. Eur J Pediatr Dermatol 1999;9:25–28.
- 28 Jansen T, Kastner U, Kreuter A, Altmeyer P: Rosacea-like demodicidosis associated with acquired immunodeficiency syndrome. Br J Dermatol 2001;144:139–142.

- 29 Brown KR, Ricci FM, Ottesen EA: Ivermectin: Effectiveness in lymphatic filariasis. Parasitology 2000;121:S133–146.
- 30 Currie B, Huffam S, O'Brien D, Walton S: Ivermectin for scabies. Lancet 1997;350:1551.
- 31 Usha V, Gopalakirshnan Nair TV: A comparative study of oral ivemectin and topical permethrin cream in the treatment of scabies. J Am Acad Dermatol 2000;42:236–240.
- 32 Paasch U, Haustein UF: Treatment of endemic scabies with allethrin, permethrin and ivermectin: Evaluation of a treatment strategy. Hautarzt 2001;52:31–37.
- 33 Forstinger C, Kittler H, Binder M: Treatment of rosacea-like demodicidosis with oral ivermectin and topical permethrin cream. J Am Acad Dermatol 1999;41:775–777.

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