

# Recalcitrant Papulopustular Rosacea in an Immunocompetent Patient Responding to Combination Therapy With Oral Ivermectin and Topical Permethrin

Kattie J. Allen, MD; Carrie L. Davis, MD; Steven D. Billings, MD; Nico Mousdicas, MB ChB, MMed

*A 68-year-old healthy man presented with papulopustular rosacea (PPR) recalcitrant to multiple therapies, including permethrin cream 5%. Histologic examination detected the presence of chronic folliculitis and numerous Demodex organisms. A diagnosis of rosacealike demodicidosis was rendered, and the patient was treated with oral ivermectin and permethrin cream 5%, resulting in resolution of the folliculitis. Demodex infestation should be considered in any patient with rosacealike dermatitis resistant to conventional rosacea therapies. If infestation is demonstrated in these patients, oral ivermectin in combination with topical permethrin is a safe and effective therapeutic option.*

*Cutis.* 2007;80:149-151.

**D***emodex folliculorum* is a common ectoparasite of pilosebaceous follicles with a prevalence of nearly 100% in the adult population.<sup>1</sup> The mite may be pathogenic as its density increases above normal levels ( $\geq 5$  mites/cm<sup>2</sup>), and demodicidosis has been implicated in several diseases, such as pityriasis folliculorum, papulopustular rosacea (PPR), and pustular folliculitis. Elevated mite densities have been detected in patients with PPR compared with healthy controls.<sup>1</sup> Although *Demodex* has been implicated in rosacea and rosacealike demodicidosis, the use of ivermectin in such patients rarely has been

documented in the literature.<sup>2-4</sup> We echo the finding of Forstinger et al<sup>2</sup> with the second reported case of clinical resolution of a rosacealike dermatitis in an immunocompetent patient following treatment with oral ivermectin and topical permethrin.

## Case Report

A 68-year-old healthy man presented with a 6-year history of PPR recalcitrant to multiple therapies, including topical and oral metronidazole, doxycycline, and erythromycin. The patient reported occasional pruritus but no flushing. He had been treated unsuccessfully with permethrin cream 5%, and skin scrapings from prior examinations revealed *Demodex* infestation. Physical examination demonstrated numerous erythematous papules and pustules with associated scale on his face, ears, and upper neck (Figure 1A). Skin biopsy showed acute and chronic folliculitis with numerous *Demodex* organisms (Figure 2). A diagnosis of rosacealike demodicidosis was rendered. Because of the previously failed response to permethrin monotherapy, a combination of oral ivermectin 12 mg once weekly for 2 weeks and permethrin cream 5% applied 3 times weekly was prescribed. The permethrin cream was continued for 3 months for maintenance. The patient misunderstood the dosage instructions and actually took 3 mg daily of oral ivermectin for a total dose of 24 mg. At 3-month follow-up, he showed marked improvement and sustained this response for at least 9 months (Figure 1B).

## Comment

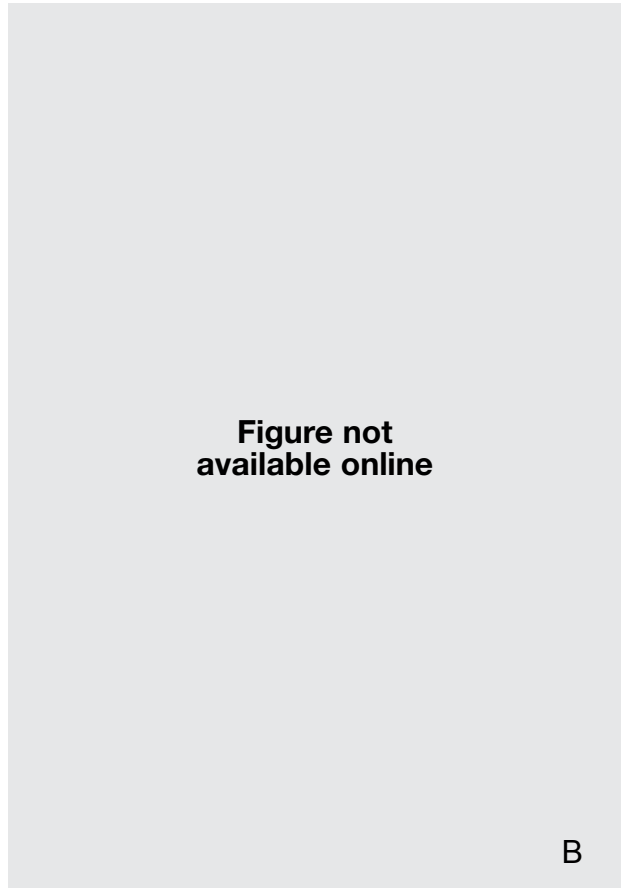
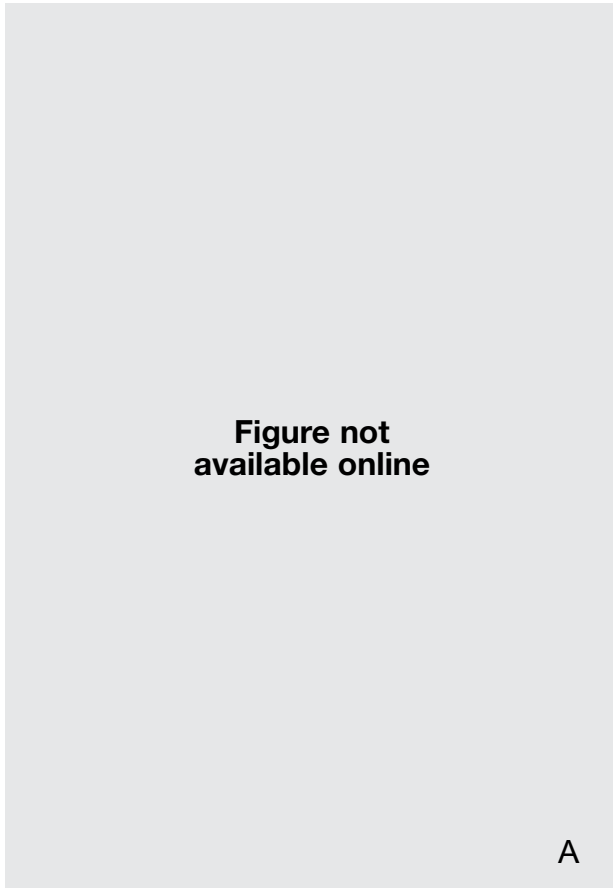
Rosacealike demodicidosis presents with erythema, scaling, and papulopustules, which can clinically resemble PPR, but pruritus, perifollicular scaling, or an asymmetrical distribution also have been

Accepted for publication April 26, 2007.

From Indiana University School of Medicine, Indianapolis.

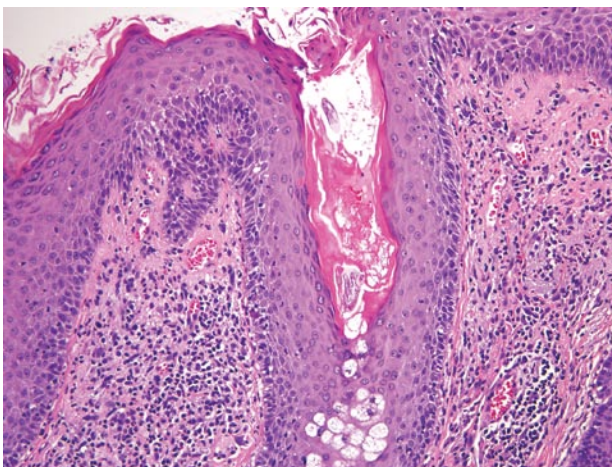
The authors report no conflict of interest.

Reprints: Nico Mousdicas, MB ChD, MMed, Indiana University Department of Dermatology, 550 N University Blvd, Suite 3240, Indianapolis, IN 46202 (e-mail: nmousdic@iupui.edu).



**Figure 1.** Extensive erythematous papules and pustules (A). Three months after treatment with oral ivermectin and permethrin cream 5% (B).

described.<sup>1,5</sup> Definitive diagnosis of *Demodex* infestation can be made by confirming the presence of mites in skin scrapings, standardized skin surface biopsy, or punch biopsy. The pathogenic role of



**Figure 2.** Chronic folliculitis characterized by a perifollicular lymphocytic infiltrate and numerous *Demodex* organisms within the follicular orifice (H&E, original magnification  $\times 200$ ).

*D folliculorum* in rosacea is controversial and a clear separation between rosacealike demodicidosis and rosacea exacerbated by *Demodex* infestation often is difficult to establish.<sup>1,5</sup> In our patient, however, the diagnosis of demodicidosis mimicking rosacea is more appropriate. The presence of pruritus and perifollicular scaling, lack of flushing, demonstration of *Demodex* organisms with associated folliculitis on histopathology, and the patient's dramatic response to antimitic therapy after several conventional rosacea therapies were unsuccessful all support the diagnosis of rosacealike demodicidosis.

*Demodex* infestation has been treated with multiple different agents, including permethrin cream 5%, lindane, topical metronidazole, crotamiton, benzyl benzoate, and sulfur compounds.<sup>3,4</sup> For refractory cases of demodicidosis, as seen in our patient, oral ivermectin may be a successful treatment option.<sup>2,4</sup> Ivermectin is an acaricidal agent that has been successful in the treatment of scabies, lice, and helminthic infections, but is not US Food and Drug Administration approved for use in human mite infections. Similarly, permethrin cream 5% has been shown to be

effective in the treatment of PPR and more effective than metronidazole gel in decreasing *Demodex* density, though it is not approved for this indication.<sup>6</sup>

### Conclusion

Our patient was recalcitrant to multiple therapies, including permethrin cream 5%; however, the combination of oral ivermectin and topical permethrin resulted in substantial clinical improvement of his rosacealike demodicidosis. When *Demodex* infestation is demonstrated in a patient with PPR and the patient is recalcitrant to standard rosacea therapy or permethrin monotherapy, oral ivermectin in combination with permethrin cream 5% should be considered as a safe and effective therapeutic option.

### REFERENCES

1. Forton F, Germaux M, Brasseur T, et al. Demodicosis and rosacea: epidemiology and significance in daily dermatologic practice. *J Am Acad Dermatol.* 2005;52:74-87.
2. 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.
3. Aquilina C, Viraben R, Sire S. Ivermectin-responsive *Demodex* infestation during human immunodeficiency virus infection: a case report and literature review. *Dermatology.* 2002;205:394-397.
4. Damian D, Rogers M. *Demodex* infestation in a child with leukaemia: treatment with ivermectin and permethrin. *Int J Dermatol.* 2003;42:724-726.
5. Baima B, Sticherling M. Demodicidosis revisited. *Acta Derm Venereol.* 2002;82:3-6.
6. Koçak M, Yağlı S, Yahapoğlu G, et al. Permethrin 5% cream versus metronidazole 0.75% gel for the treatment of papulopustular rosacea: a randomized double-blind placebo-controlled study. *Dermatology.* 2002;205:265-270.