Ocular rosacea and treatment of symptomatic Helicobacter pylori infection: a case series

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SUMMARY

Rosacea is a chronic inflammatory skin disease characterized by recurrent episodes of facial flushing, erythema, papules, pustules, and telangiectasia. More than half of all rosacea patients may have ocular symptoms. Rosacea is associated with certain digestive diseases, such as gastritis, hypochlorhydria, or a number of jejunal mucosal abnormalities, and many patients have *Helicobacter pylori* infection. The role of *Helicobacter pylori* has often been a subject of investigation; these studies show conflicting results. Here we present results of the effects of treatment given for *H. pylori* eradication in seven patients with ocular rosacea that, at the same time, had clinical and serological evidence of *H. pylori* infection. Six weeks after completion of the treatment, all patients experienced improvement of their rosacea symptoms. Ocular disease responded better than cutaneous rosacea.

KEY WORDS

rosacea, ocular rosacea, *Helicobacter pylori*, treatment

Introduction

Rosacea is a chronic inflammatory skin disease characterized by recurrent episodes of facial flushing, erythema, papules, pustules, and telangiectasia (1). More than half of rosacea patients may also have ocular symptoms, and the frequency of this condition peaks between the ages of 30 and 50 (2). The manifestations of ocular rosacea include blepharoconjunctivitis, meibomitis, episcleritis, recurrent chalazia, iritis, corneal vascularization, corneal scarring, and keratitis (1–4). Burning or stinging, itching, photophobia, and foreign body sensation are frequent symptoms (1, 2). Ophthalmic complications of rosacea are independent of the severity of facial rosacea. Although ocular signs and symptoms may precede cutaneous disease by a number of years, concurrent presentation of eye findings and skin signs is more often observed (4).

The cause of rosacea remains unknown. Among many theories, the role of *Helicobacter pylori* has often been a subject of investigation (1). These studies show conflicting results; some demonstrated clinical improvement of rosacea after eradication therapy for *H. pylori*, whereas others found that the treatment had no effect (1, 5–9). A recent systematic review of rosacea treatments showed that reliable evidence concerning thera-

peutic efficacy exists only for topical metronidazole and azelaic acid, whereas oral metronidazole and tetracyclines, though effective, require further clinical trials (10).

The aim of this report is to present results of the effective treatment given for *H. pylori* eradication in seven patients with ocular rosacea who, at the same time, had clinical and serological evidence of *H. pylori* infection.

Case series

Among 79 patients with rosacea seen at our outpatient dermatology services over a 6-month period, 23 reported some of the ocular symptoms: redness, mild morning discharge, lacrimation, photophobia, stinging, itching, burning, and foreign body sensation. The patients had already been on topical treatment for their ocular symptoms with 0.75% metronidazole gel, wet compresses, and artificial tears for more than 3 months, but with only slight or no improvement at all. Of the 23 patients, 11 had gastrointestinal symptoms such as epigastric abdominal pain, heartburn, or halitosis. They underwent serologic testing for *H. pylori* infection (ELISA kit, Euroimmun AG, Germany). Seven patients, all males, age 58–64 years with ocular rosacea and concomitant gastrointestinal complaints, had serologic evidence of *H. pylori* infection: increased titers of IgA (> 1.1 reference units) and of IgG (> 15 reference units) antibodies to *H. pylori*. All the patients had the erythematotelangiectatic form of rosacea with various degrees of erythema and telangiectasia. Ophthalmologic examination was performed by two experienced ophthalmologists. Diagnostic criteria for ocular rosacea were Meibomian gland dysfunction, blepharitis, lid margin telangiectasia, punctate superficial keratopathy, and conjunctival hyperemia with or without inferior corneal vascularization. Schirmer's test and the tear film breakup time (TBUT) were measured at 1 and 6 weeks after completion of the treatment. Cutaneous (erythema, swelling) and ocular signs (blepharoconjunctivitis, meibomitis) were scored by investigators at the first and follow-up visits semiquantitatively: 1 = very mild, 2 = mild, 3 = moderate, 4 = severe. The response to treatment was rated at the follow-up visit on a 5-point scale: 0 = no improvement, 1 = mild improvement, 2 = moderate improvement, 3 = significant improvement, 4 = cleared.

All patients completed a standard two-week course of treatment for *H. pylori* infection, which included metronidazole, 500 mg orally BID, clarithromycin 500 mg orally BID, and ranitidine 150 mg orally BID. They were permitted to continue their topical ophthalmologic treatment.

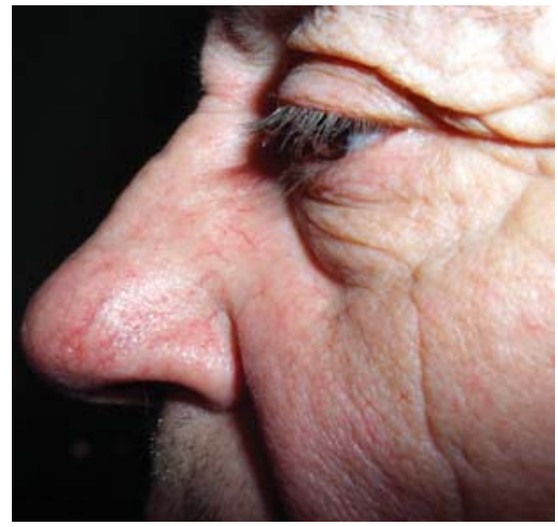

Figure 1. Rosacea: dilated capillaries and reddish skin of the nose and adjacent sites; slightly edematous and reddish eyelids.

All patients had mild to moderate erythemotelangiectatic rosacea, and patient 4 also had moderate midfacial edema. Ocular findings included blepharitis, conjunctivitis, meibomitis (Figure 1), and, in patients 6 and 7, dry eye syndrome. The patients had significantly bilaterally reductions in both Schirmer's test and TBUT. Six weeks after completion of the treatment, all patients experienced improvement of their rosacea symptoms . The improvement was more obvious concerning ocular signs and symptoms than cutaneous symptoms. Post-treatment titers of anti-HP IgA antibodies were negative in three patients, whereas titers of IgG antibodies, although lower compared to pretreatment levels, were still positive in all patients (above 16 RU). No side effects of the treatment were recorded.

Discussion

Almost 50% of patients with facial rosacea experience ocular symptoms (2–4). These are frequently missed if the patient does not express significant ocular complaints. Ocular manifestations are essentially confined to the eyelids and ocular surface with eyelid

telangiectasia, blepharitis, Meibomian gland dysfunction, chalazia, and chronic conjunctivitis. Corneal damage may induce keratopathy, infiltrates, neovascularization, opacification, keratitis with corneal thinning, sterile ulceration, perforation, and finally blindness (2).

The association between rosacea and certain digestive diseases, such as gastritis, hypochlorhydria, or a number of jejunal mucosal abnormalities, is well established (11). Dyspepsia, constipation, diarrhea, and abdominal discomfort have all been described among symptoms associated with rosacea.

The mainstay treatments of ocular rosacea are topical metronidazole and oral tertracyclines administered over several months. Given the possible but contentious association of *H. pylori* infection and rosacea, we examined the effects of therapy for this infection on ocular rosacea signs. Five patients had typical lesions consisting of blepharoconjunctivitis and meibomitis, and 2 of them had complaints of dry eyes with shortened Schirmer's test and TBUT. Although changes in Meibomian gland secretion and its lipid composition as well as unstable tear film seem to be common in ocular rosacea (12, 13), five of our patients had normal TBUT. All participants experienced moderate or significant improvement in their eye disease 6 weeks after the completion of a 2-week treatment course. Of note, cutaneous signs responded to a lesser degree. It seems that papulopustular rosacea responds better to the *H. pylori* treatment than the erythematotelangiectatic variety (6). As expected, gastrointestinal manifestations disappeared in all patients, and titers of IgA and IgG anti-*H. pylori* antibodies were either negative or decreased. Though serology alone cannot be the sole criterion to judge either the activity of infection or the eradication of *H. pylori*, it does indicate that the treatment was effective. Because the patients had applied topical metronidazole to their eyes for at least 3 months prior to inclusion in the study without clear benefit, this treatment might be considered a failure. Thus, the effects of *H. pylori* therapy are even more encouraging. Just as in the cutaneous variant, the efficacy of oral tetracyclines in ocular rosacea is not backed by firm clinical evidence (14), and so further research is needed.

The investigation has a few obvious drawbacks: there was no control group, and the number of participants is small. Considering the favorable therapeutic results, however, a controlled trial may be worth trying, possibly with a larger number of carefully selected patients.

REFERENCES

1. Crawford GH, Pelle MT, James WD. Rosacea: I. Etiology, pathogenesis, and subtype classification. J Am Acad Dermatol. 2004;51:327–41.

2. Tanzi E, Weinberg J. The ocular manifestations of rosacea. Cutis. 2001;68:112–4.

3. Kligman A. Ocular rosacea. Arch Ophthalmol. 1993;111:228–30.

4. Akpek EK, Merchant A, Pinar V, Foster CS. Ocular rosacea: patient characteristics and follow up. Ophthalmology. 1997;104:1863–7.

5. Szlachcic A. The link between *Helicobacter pylori* infection and rosacea. J Eur Acad Dermatol Venereol. 2002;16:328–33.

6. Boixeda de Miquel D, Vázquez Romero M, Vázquez Sequeiros E, Foruny Olcina JR, Boixeda de Miquel P, López San Román A, et al. Effect of *Helicobacter pylori* eradication therapy in rosacea patients. Rev Esp Enferm Dig. 2006;98:501–9.

7. Diaz C, O'Callaghan CJ, Khan A, Ilchyshyn A. Rosacea: a cutaneous marker of *Helicobacter pylori* infection? Results of a pilot study. Acta Derm Venereol. 2003;83:282–6.

8. Bamford JTM, Tilden RL, Blankush JL, Gangeness DE. Effect of treatment of Helicobacter pylori infection on rosacea. Arch Dermatol. 1999;135:659–63.

9. Gedik GK, Karaduman A, Sivri B, Caner B. Has *Helicobacter pylori* eradication therapy any effect on severity of rosacea symptoms? J Eur Acad Dermatol Venereol. 2005;19:398–9.

10. Van Zuuren EJ, Gupta AK, Gover MD, Graber M, Hollis S. Systematic review of rosacea treatments. J Am Acad Dermatol. 2007;56:107–15.

11. Marks R, Beard RJ, Clark ML, Kwok M, Robertson WB. Gastrointestinal observations in rosacea. Lancet .1967;1:739–43.

12. Zengin N, Gunduz K, Okudan S, Balevi S, Endogru H. Meibomian gland dysfunction and tear film abnormalities in rosacea. Cornea. 1995;14:144–6.

13. Quarterman MJ, Johnson DW, Abele DC, Lesher Jr JL, Hull DS, Davis LS. Ocular rosacea. Signs, symptoms, and tear studies before and after treatment with doxycycline. Arch Dermatol. 1997;133:49–54.

14. Stone DU, Chodosh J. Oral tetracyclines for ocular rosacea: an evidence-based review of the literature. Cornea. 2004;23:106–9.

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