

Oral Azithromycin for Treatment of Intractable Rosacea

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Rosacea is a common chronic cutaneous disorder that primarily occurs on the convex surfaces of the central face and is often characterized by exacerbations and remissions. A case of a 52-yr-old woman visited our clinic in February 2008 complaining typical features of rosacea including multiple pinhead to rice-sized erythematous papules. We applied various conventional treatments including topical benzoyl peroxide and metronidazole as well as oral metronidazole, isotretinoin, and doxycycline. The lesions were not controlled but were rather aggravated by complications from these treatments. Therefore, we prescribed oral azithromycin, which has anti-inflammatory effects and reduces reactive oxygen species. Ten weeks after the administration of oral azithromycin, 500 mg per day for 2 weeks, the lesions had mostly disappeared and no specific side effects related to the azithromycin were noted. Oral azithromycin dosing 500 mg/day for 2 weeks is effective for treatment of intractable rosacea.

Key Words: Azithromycin; Rosacea

INTRODUCTION

Rosacea is a common skin disease characterized by transient or persistent central facial erythema, visible blood vessels, and frequently, papules and pustules. Treatment of rosacea is usually based on a combination of systemic and topical antibiotics. Since the 1950's, tetracycline and erythromycin are the most commonly used oral antibiotics (1-3). However, long-term treatment with antibiotics is not well tolerated because of side-effects including gastrointestinal intolerance, photosensitivity and candidiasis (3). Moreover, given the chronic nature of the disease, there is a possibility of developing bacterial resistance (1). Azithromycin is a newly developed macrolide which offers some advantages compared to previously used antibiotics (4). It has unique pharmacokinetics that maintains prolonged tissue levels and allows less frequent dosage. Fernandez-Obregon (5) reported that all of ten patients who were not tolerated or controlled by conventional treatment demonstrated a significant improvement with the oral use of azithromycin. After then, azithromycin has been found to be effective in the intractable rosacea in several clinical reports (1, 6, 7).

We report a case of a 52-yr-old rosacea patient who was refractory and complicated by reactions to conventional topical and oral medications. After 10 weeks of oral azithromycin, her lesions had mostly disappeared and the patient suffered no specific side-effects related to the medication. Our case showed that oral azithromycin could be a viable new treatment option for intractable rosacea cases.

CASE DESCRIPTION

A 52-yr-old postmenopausal woman complained of a 10-month history of multiple erythematous papules and some pustules on both cheeks on February 11, 2008 (Fig. 1). The lesions were characterized by progressive extension and continuous flushing. There was neither a familial history of similar lesions nor previous significant medical history. Physical examination revealed multiple pinhead to rice-sized erythematous papules and pustules on both cheeks. Laboratory studies including complete blood cell count (CBC), blood chemistry, and anti-nuclear antibody (ANA) were within normal limits. More than ten demodex mites were observed on the demodex study. On the standard patch test, only nickel sulfate showed a positive response.

On the basis of medical history and clinical findings, the patient was diagnosed as rosacea. However, her skin lesions were not controlled by topical application of benzoyl peroxide, metronidazole twice a day or crotamiton once a day, or oral administration of doxycycline 200 mg for a month, metronidazole 500 mg for two weeks or isotretinoin 10 mg for a month. Rather her rosacea was aggravated or complicated by these medications. After taking conventional treatment of rosacea, she complained of diffuse facial erythema, swelling and aggravated papules (Fig. 2). We then prescribed oral azithromycin, which has both anti-inflammatory effects and leads to a reduction in reactive oxygen species. Two weeks after oral administration of 500 mg per day of azithromycin, facial erythema and swelling was reduced. Since then, papular lesions which are presented on the cheek were begun to decrease. After 10 weeks of oral azithromycin, the

lesions had mostly disappeared, and no specific side-effects related to the medication were noted (Fig. 3). Also until 6 months after treatment, the patient had not experienced any recurrence or aggravation. This patient provided informed written consent prior to usage of her photographs.

DISCUSSION

Rosacea is a common cutaneous disorder which occurs most frequently in light-skinned middle aged women. There are variable cutaneous signs of rosacea such as flushing, erythema, telangiectasia, edema, papules and pustules (2).

While the pathogenesis of rosacea remains unknown, several



Fig. 1. Multiple pinhead to rice-sized erythematous papules, typical features of rosacea, were present on both cheeks.



Fig. 2. The patient's skin lesions were not controlled by conventional treatments for rosacea, but rather, were aggravated.



Fig. 3. Ten weeks after taking oral azithromycin, the patient's skin lesions had mostly disappeared.

factors have been implicated including inherent abnormalities in cutaneous vascular homeostasis and dysregulated thermal mechanisms. Recent reports suggest that the effects of reactive oxygen species can contribute to the development of rosacea (8).

Conventional treatment of rosacea is based on a combination of systemic and topical antibiotics. Since the 1950's, tetracycline and erythromycin are the most commonly used oral antibiotics (1-3). The therapeutic activity of commonly used antimicrobials including tetracycline, doxycycline has been mainly attributed to their anti-inflammatory activities (9, 10). These results indicate that antibiotics used in the treatment of rosacea affect various inflammatory processes such as the migration of neutrophils, production of pro-inflammatory cytokines including interleukin-1, 6, 8, 10, tumor necrosis factor- α , leukotriene B4, and oxidative burst in phagocytes (11-13). Topical metronidazole and oral tetracyclines effectively treat about 80%-90% of rosacea patients (6). However, long-term treatment with antibiotics is not well tolerated due to requiring frequent administration, poor compliances and side-effects including gastrointestinal intolerance, photosensitivity and candidiasis (5, 7). In addition, some patients do not respond to variable combination therapies and rather aggravated by their complications. Modi et al. (1) reported a rosacea patient who were developed tense bullae and hypopigmented scarring after taking oral doxycycline 100 mg.

Oral azithromycin is a newly developed macrolide which offers some advantages over previously used antibiotics. It has unique pharmacokinetics that allows it to penetrate into intracellular compartments rapidly and maintain prolonged tissue levels. This allows for less frequent application and shorter duration of treatment which may increase compliance. With its high affinity for inflammatory tissues, azithromycin can achieve steady state tissue levels in approximately 72-96 hr (14). Moreover, after administration of oral azithromycin, tissue reactive oxygen species, an etiologic factor in the development of rosacea, were greatly decreased in some cases (7).

The utility of oral azithromycin was confirmed by several clinical studies. Fernandez-Obregon (5) reported that all of ten patients who were not tolerated or controlled by conventional treatment of rosacea demonstrated a significant improvement with the oral use of azithromycin. In addition, Modi et al. (1) treated a 67-yr old man who had photosensitivity to the doxycycline and hyperpigmented dyschromia to the minocycline with an oral use of azithromycin in a dose of 250 mg 3 times weekly. Bakar et al. (4) reported that treatment with oral azithromycin led to 75% decreases in the total number of lesions and an 89% decrease in inflammatory lesions compared with basal status. Another open-label study showed that azithromycin is as effective as standard dose of doxycycline and has a positive impact on the quality of life of patients compared with conventional treatment regimens (15).

Azithromycin may also be an acceptable agent for those using

other medications, because it has no known major drug interactions. Additionally, azithromycin shows lower incidences of gastrointestinal discomfort compared with erythromycin (16). According to one clinical study, only two of 32 patients complained of mild gastric discomfort and no one withdrew from the study due to the side-effects of azithromycin (17). In our case, there were no specific side-effects related to the medication.

In summary, we report a case of a 52-yr-old woman who presented with intractable multiple, pinhead to rice-sized erythematous papules on her face, which were controlled by oral azithromycin. Our case shows that azithromycin could be a new treatment option for the treatment of intractable rosacea.

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