ORIGINAL ARTICLE

A retrospective descriptive study of oral azole antifungal agents in patients with patch test–negative head and neck predominant atopic dermatitis

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Background: Head and neck dermatitis is a subtype of atopic dermatitis driven by *Malassezia* yeast.

Objective: We sought to evaluate the response of these patients to systemic azole antifungals.

Methods: We queried the electronic medical records from our institution for patients that were referred for allergy patch testing, were ultimately given the diagnosis of head and neck dermatitis, and were treated with oral azole antifungals over a 2-year period.

Results: Twenty-four patients met inclusion criteria and were analyzed. Most patients noted their characteristic flare beginning during their teenage, young adult, or adult years. All were noted to have some involvement of the head and neck, and 17 responded to treatment. The mean time taking an azole antifungal medication was 8 months, with a mean overall follow-up of 10 months.

Limitations: This was a retrospective descriptive study, from a single institution, of a limited number of patients, and did not use a validated scoring system.

Conclusion: Itraconazole and other azole antifungals were an effective treatment for more than two-thirds of adult patients with head and neck predominant atopic dermatitis. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2014.04.045.)

Key words: atopic dermatitis; contact dermatitis; eczema; fluconazole; head and neck dermatitis; itraconazole; ketoconazole; *Malassezia*; occupational dermatitis; seborrheic dermatitis.

Malassezia is a lipophilic yeast that proliferates after puberty over the upper body, head, and neck.[1,2] It may trigger a difficult to treat form of atopic dermatitis (AD) descriptively called head and neck dermatitis (HND). Patients with this condition, when compared to AD without cephalic involvement, have much higher levels of immunoglobulin E–mediated sensitivity to the commensurate *Malassezia* species.[3] Although it may appear similar to seborrheic dermatitis (SD), it is typically more pronounced and inflammatory, with involvement beyond the characteristic locations of SD. Specific immunoglobulin E testing, skin-prick testing (SPT), and atopy patch testing (APT) often show a reactivity to *Malassezia* in patients with HND but not those with SD.[4,5] In vitro data shows that the predominant species, *Malassezia globosa* and

Abbreviations used:

AD:	atopic dermatitis
APT:	atopy patch test
HND:	head and neck dermatitis
SD:	seborrheic dermatitis
SPT:	skin-prick testing

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Funding sources: None.
Conflicts of interest: None declared.
Accepted for publication April 7, 2014.

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Published online June 9, 2014.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2014.04.045

Malassezia restricta,[2] cause a T_H2 cytokine release in human keratinocytes that is consistent with AD.[6,7] Multiple studies have noted some success in treating HND with oral antifungal medications.[8] We review the effectiveness of oral azole antifungals in patients with persistent cephalic dermatoses that were referred for patch testing by a dermatologist, had negative or irrelevant patch testing, and who were ultimately diagnosed with HND.

CAPSULE SUMMARY

- Cephalic atopic dermatitis that flares after puberty may be driven by a reaction to cutaneous *Malassezia* yeast.
- Seventeen of 24 patients with head and neck dermatitis responded to a 2-month course of an oral azole antifungal medication after negative patch testing.
- Dermatologists may consider oral azole antifungal agents as a treatment option for adult patients with resistant head and neck dermatitis that is not suspected to be contact dermatitis.

METHODS

After institutional review board approval, the Ohio State University Medical Center information warehouse containing diagnoses, prescriptions, and encounters was queried for patients that had been referred to the investigator, had an *International Classification of Diseases, 9th revision* code for AD and related diseases (691.8), and were given at least 1 prescription for systemic itraconazole, fluconazole, or ketoconazole between January 2011 and January 2013. Success was defined as documented clearance, near clearance, or marked improvement noted in their chart at a 2-month follow-up visit. Patients that had been treated with itraconazole before the initial referral and those that did not follow-up were excluded.

Statistics

Descriptive statistics, odds ratios, and plots were computed using Excel (Microsoft, Redmond, WA) and JMP software (v 10.0.2; SAS Institute Inc, Cary, NC).

RESULTS

Inclusion and exclusion

Thirty-five patients met the initial criteria. Eleven patients were excluded. Pityrosporum folliculitis and tinea nigra were incidental diagnoses on 5 patients who were patch tested. Four patients did not return for scheduled follow-up visits. Two patients were excluded for previous treatment with itraconazole by the referring dermatologist.

Descriptive data

The average age of the 24 patients was 44 years, and the majority of patients were white and female. The age at which these patients developed any skin disease was evenly distributed, although only 2 (8%) ascribed to typical infantile eczema. Twenty-two of 24 (92%) patients noted head and neck involvement beginning during their teenage, young adult, or adult years. Six (25%) patients had concomitant asthma and 13 (54%) patients had seasonal rhinitis. Most patients had previously been treated with systemic corticosteroids (67%), and all patients had been prescribed topical corticosteroids. No patient had previously been treated with other systemic immunosuppressive medications. Intramuscular triamcinolone was administered to 3 patients (13%) at the time of initiation of a systemic azole. All patients were initially prescribed itraconazole 200 mg daily, but because of cost or insurance plan, 3 (13%) were switched to fluconazole 200 mg daily, and 3 (13%) were switched to ketoconazole 200 mg daily.

Clinical success

Seventeen of the 24 (71%) patients were found to have dramatic improvement at the 2-month follow-up appointment. Nine of 17 (53%) patients were switched to pulse dosing after the 2-month appointment of 200 mg of the azole twice weekly. Two of 17 (12%) were able to discontinue the medication on the first visit and did not return for future visits. Of all 17 patients, the mean duration on medication was 8.4 months, with a mean follow-up of 10.4 months. However, a progressive discontinuance rate was noted (Fig 1). Table I reviews the odds ratios for success with antifungal therapy.

Side effects

Few side effects were noted. Discontinuation because of side effects occurred in only 1 patient (4%), who discontinued the medication because of flushing and headaches. However, she was successfully rechallenged, and her disease was well controlled. One other patient had mild transaminitis and temporarily stopped but was able to successfully restart itraconazole.

DISCUSSION

Most of these patients had previously been treated with immunosuppressive medications in the form of systemic corticosteroids, and after negative patch