

LETTER TO THE EDITOR

Itraconazole as a continuous treatment for atopic dermatitis? A case report

Editor

Hypersensitivity to *Malassezia* species has been implicated in the aetiology of the so-called 'head and neck dermatitis' (HND) variant of atopic dermatitis (AD).¹ Improvement of HND with itraconazole as a single therapy was reported earlier.¹ We report a HND patient who showed an excellent response to itraconazole, but relapsed after stopping.

A 29-year-old Caucasian man presented a 2-year history of uncontrolled AD. He did not respond to treatment with topical and systemic corticosteroids, antihistamines, emollients, oral antibiotics and topical antifungal agents. His medical history was significant for AD, asthma and allergic rhinitis. A widespread erythematous and squamous skin eruption located on the head, the neck and the breast area was seen on physical examination (see Fig. 1). Serological test showed positive outcomes for *Malassezia sympodialis* (1.29 kU/L) and for the following allergens: house dust mite (>100 000 kU/L), cat (>100 000 kU/L), dog (44.40 kU/L), tree (>100 000 kU/L), grass (>100 000 kU/L), mugwort (3.27 kU/L), mould (1.18 kU/L), soy (0.37 kU/L) and peanut (0.41 kU/L). The total IgE level was 1962 kU/L. Systemic itraconazole (100 mg twice daily) was added to the regime of topical fluticasone, hydroxyzine, bathing restrictions and emollients. One month later the dermatitis was almost cleared. However, his skin condition deteriorated after stopping itraconazole. Treatment with itraconazole was resumed successfully at the same dose for 2 months. The dose was subsequently lowered to 100 mg once daily for a month followed by three times a week for another month during which his HND relapsed again. Liver function tests were done every 3 months. Although liver function test were not elevated, we decided to switch to azathioprine because of the potential side-effects of hepatotoxicity. After a few weeks, azathioprine therapy led to a stable remission on all the involved body parts of the patient.

Malassezia sympodialis plays an important role in the HND variant of AD through increasing the inflammatory response by damaging the epidermal barrier function, increasing the local immune response through local production of various interleukins and sensitization to cross-reactive allergens.¹ Other *Malassezia* species (e.g., *M. globosa*, *M. furfur*) were isolated less frequently.¹ All species are highly sensitive to itraconazole.¹ Short-term treatment with itraconazole was reported to be



Figure 1 Distribution of erythematous and squamous lesions on the head, the neck and the breast.

effective in HND, presumably due to the antifungal effects.² Our patient had a recurrence of dermatitis each time after stopping or decreasing the dose of itraconazole. Therefore, long-term use of this agent should be necessary. However, long-term treatment is hampered by its potential hepatotoxicity. Besides, there is a lack of experience in the use of long-term itraconazole.³ Other antifungal therapies (such as amphotericin B) are also dissuaded.³ In contrast, there is considerably more experience with long-term (off-label) use of azathioprine in AD.⁴

Hepatotoxicity is a known adverse drug reaction for both thiopurines (e.g. azathioprine) and itraconazole. Reported incidences of hepatotoxicity in the literature range from 3 to 15% for thiopurines and between 5 and 15% for itraconazole, and mostly involve elevated liver function tests.^{5–7} Although rare cases of severe hepatotoxicity have been described for both itraconazole and azathioprine, only for itraconazole long-term (i.e. uninterrupted or cumulative use for more than 6 months) use is dissuaded by the manufacturer, indicating lack of safety data on long-term clinical use.^{8,9} Evidence for safety is present for the use of azathioprine in dermatology, specifically in AD.¹⁰ Furthermore, extensive safety data are available for long-term (up to 10 years) use of thiopurines, specifically in inflammatory bowel disease.⁵ An important condition for the safe prescription of azathioprine is performing liver function tests.⁴

Comparing itraconazole with azathioprine with respect to mode of action itraconazole has direct effect on

M. sympodialis, which is an important triggering factor in the HND type of AD, thereby preventing dermatitis instead of suppressing dermatitis.

In view of their advantageous mode of action future research should be directed to the long-term treatment in the HND type of AD with itraconazole or other anti-fungal agents focussing on their side-effects such as toxicity and development of resistance.

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