A case of sensitization to Alitretinoin

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Abstract

Alitretinoin is a unique retinoid authorised for the treatment of adults with severe chronic hand eczema (CHE) refractory to potent topical steroids. The most common adverse events (AEs) were typical class effects of oral retinoids including headache, flushing and skin disorders. To our knowledge, there are no cases of sensitization to alitretinoin reported in literature. We present a case of sensitization to alitretinoin.


Key words: alitretinoin, chronic hand eczema, patch test

Introduction

Alitretinoin (9-cis-retinoic acid) is a unique panagonist retinoid, capable of binding to all six known retinoid receptors (RAR-alpha, -beta, -gamma, and RXR-alpha, -beta, -gamma), with immunomodulatory and anti-inflammatory activity that is authorised for the treatment of adults with severe chronic hand eczema (CHE) refractory to potent topical steroids (1).

Currently, the most common adverse events (AEs) and abnormal laboratory test results, such as diagnostic protocols applied to patients, are the same as those previously referred with other oral retinoids and RXR agonists use (2).

From our literature review, there are no cases of sensitization to alitretinoin reported.

So we present a case of sensitization to alitretinoin in a woman who has been suffering from CHE for several years, unresponsive to potent topical corticosteroids, then the first case of sensitization.

Case report

In November 2011 we studied a 42-year-old female nurse, who has been affected by chronic hand eczematous dermatitis (Fig. 1) since 2008 being resistant to conventional therapies. In fact the patient had received earlier treatment with topical corticosteroids, such as methylprednisolone aceponate and clobetasol propionate for several years, with no improvement in the condition. This had a negative impact on the quality of her life so, the patient came to our specialist hand surgery at “Sapienza” University of Rome (Italy).

After the first assessment, the patient was considered to have a “very severe disease” both in the PGA and in MtIcss score (3). An allergological study was then carried out on
The investigations serum chemistry, such as liver and thyroid function, lipid profile and $\beta$-HCG was required in order to start systemic therapy with Alitretinoin, this was in the range of normality. So the patient was eligible and then she started the treatment with oral alitretinoin 30 mg once daily. 15 days later, we observed worsening skin lesions in our patient (Fig. 2 a-b). Then we stopped the drug for 2 weeks and we only treated the patient with systemic (metilprednisolone 16 mg/die for 1 week, 8 mg /die 7 days next) and topical corticosteroids (hydrate calcipotriol / betamethasone dipropionate, repairing emulsion, resulting in an improvement in the hand dermatitis. We subsequently restarted the oral alitretinoin at a dose of 10 mg once daily and this therapy resulted in a significant worsening of skin lesions, such as positive oral challenge test. In case of a possible active sensitization, we patch tested the patient with specific molecules used during therapy.

So, a patch by patch these above cited molecules was performed and after 48 and 96 hours (D2 and D4) and one week-(D7) reading gave an alitretinoin positivity ++.

For this reason it was decided to completely stop taking alitretinoin and the woman undertook cyclosporin therapy at the dose of 5 mg/Kg/die resulting in disease resolution.

The case has been referred to the Italian Agency for Drug Adverse Reactions.

Discussion

CHE is a significant cause of morbidity both in the general population and in many categories of worker (4, 5). A number of treatments are traditionally used, and are often effective, but in spite of this, a sizeable group of patients develop chronic recalcitrant hand eczema (6). Retinoids are known to influence keratinization and inflammation, and acitretin has shown some effect in the treatment of chronic hand eczema. Alitretinoin (9-cis-retinoic acid) is a panagonist retinoid binding to all six known retinoid receptors (RAR-\(\alpha\), -\(\beta\), -\(\gamma\) and RXR-\(\alpha\), -\(\beta\), -\(\gamma\)). Several studies have been carried out with this new drug, and it has been shown to be effective in 28% to 89% of patients with previously intractable hand eczema (7). Alitretinoin 30 mg taken once daily was well tolerated when taken for up to 24 weeks and the AEs were typical class effects of oral retinoids including headache, flushing and skin disorders. For example, Dirschka et al. (8) report the following AEs: headache, mucocutaneous dryness, and three serious AEs: vertigo, furuncle and angioneurotic oedema after pharynx infection. The most common laboratory abnormalities were increased serum cholesterol and triglycerides, with corresponding changes in high-density and low-density lipoprotein, and lowered levels of thyroid-stimulating hormone. TOCCATA Diepgen et al. study (9) states headache as the most frequent AE, followed by increased blood triglycerides and increased blood cholesterol. Serious adverse drug reactions were documented in only four patients: lymphatic oedema, paranoia, recto-sigmoiditis and soft-tissue swelling.

From what is seen in the literature no author has ever reported cases of sensitization to alitretinoin. However, we present this as the first case of sensitization. In fact our patient showed the following features:

- worsening of skin lesions after 30 mg once daily drug ingestion
- an improvement of the disease after 2 weeks of alitretinoin discontinuation
- a worsening after drug re-administration such as positive oral challenge test
- positive patch test with alitretinoin 100% 48 and 96 hours reading
- negative results of all other allergological tests.
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References

2. Ruzicka T. Alitretinoin induces complete response and can re-induce response in patients with severe CHE [oral presentation]. 17th Annual Congress of the European Academy of Dermatology and Venereology 2008; Sep 17-20; Paris
5. Usatine RP, Riojas M. Diagnosis and management of contact dermatitis. Am Fam Physician 2010; 82(3):249-55