Successful Use of Oral Acitretin in Oral Lichen Planus

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Abstract

Lichen planus is a common inflammatory disorder affecting skin, mucous membranes, nails, and hair. At least two-thirds of cases occur between 30 and 60 years of age. Lichen planus can affect the mucosal surfaces of mouth, genitalia, conjunctiva, esophagus, anus, and urethra. Oral lichen planus is relatively common than lichen planus of other mucosal areas. Oral lichen planus is very refractory to treatment. Oral and topical steroids, topical tacrolimus, azathioprine, cyclosporine, and dapsone are the drugs used to treat oral lichen along with acitretin. We hereby report the successful treatment of oral lichen planus with acitretin in three patients.

Keywords: Acitretin, mucosal, oral lichen planus

INTRODUCTION

Lichen planus is a unique, common inflammatory disorder that affects skin, mucous membranes, nails, and hair. The 5 P’s – purple, polygonal, pruritic, plane and papule characterizes lichen planus.[3] Lichen planus can affect the mucosal surfaces of mouth, vagina, esophagus, conjunctiva, urethra, anus, nose, and larynx. Its prevalence is estimated at approximately 1% of adult population. Oral involvement occurs in approximately 60%–70% of patients.[2] Here, we report clinically diagnosed cases of oral lichen planus successfully treated with systemic acitretin.

CASE REPORTS

Case 1

A 60-year-old non-diabetic, normotensive male patient presented with chief complaints of painful whitish lesion involving both right and left buccal mucosae of more than one month duration duration. On clinical examination, there was classic lacy white linear hyperkeratosis on an erythematous base involving both buccal mucosae. There were no skin lesions. Systemic examination was within normal limits. He had received treatment in the past in the form of topical tacrolimus 0.03% ointment, intralesional injections of triamcinolone acetonide twice, and systemic thalidomide 100 mg once a day for 3 months with little improvement. He was put on tablet acitretin 25 mg once a day after doing baseline lipid profile, hemogram, and liver function test which were within normal limits. After 3 weeks, lipid profile and liver enzymes were repeated which showed elevated triglyceride levels. Clinically, perilesional erythema and size of the lesion showed reduction. Furthermore, there was a marked improvement in pain. Tablet atorvastatin 20 mg once a day was added to the treatment to control hypertriglyceridemia. Acitretin was continued for further 9 weeks with close monitoring of lipid profile and liver enzymes which remained in normal range. The patient received treatment for a total period of 12 weeks with satisfactory improvement in pain, erythema, and size of the lesion [Figures 1 and 2]. The patient tolerated the treatment well except for dryness of lips which was taken care by frequent topical application of emollient. The patient was followed up monthly for subsequent 3 months with no recurrence. His triglyceride level also returned to normal, six weeks after discontinuing acitretin.

Case 2

A 45-year-old non-diabetic, normotensive male came with the complaint of whitish lesion over lower lip since two months. The lesion was asymptomatic. Clinical examination revealed classic lacy white lesion involving lower lip. There were no...
skin lesions and systemic examination was within normal limit. He had received treatment in the past in the form of topical tacrolimus 0.03% ointment, intralesional injections of triamcinolone acetonide, and systemic weekend pulse therapy with 32 mg of methylprednisolone for 3 months with little improvement. Tablet acitretin 25 mg once a day was started after doing baseline lipid profile, hemogram, and liver function test which were within normal limits. After 3 weeks, lipid profile and liver enzymes were repeated which showed elevated triglyceride level. Clinically, the lesion reduced in size. Tablet atorvastatin 20 mg once a day was added to the treatment to control hypertriglyceridemia. Acitretin was continued for further 9 weeks with close monitoring of lipid profile and liver enzymes which remained in normal range. After 12 weeks of treatment, lesions completely healed without scarring or pigmentary changes. Hence, acitretin was discontinued and the patient was followed up. The patient tolerated treatment well except for dryness of lips which was taken care by frequent topical application of emollient. The patient was followed up monthly for subsequent 3 months with no recurrence. His triglyceride level also returned to normal, six weeks after discontinuing acitretin.

Case 3
A 72-year-old male non-diabetic, normotensive came with the complaint of pigmented painful lesion involving hard palate of four months duration. On clinical examination, there was hyperpigmented lesion over hard palate [Figure 4]. There were no skin lesions and systemic examination was within normal limit. He had received treatment in the past in the form of topical tacrolimus 0.03% ointment, intralesional injections of triamcinolone acetonide twice, and systemic prednisolone 20 mg once a day for 3 weeks which was tapered off over a period of 8 weeks to 5 mg daily with little improvement. Tablet acitretin 25 mg was started once a day after doing baseline lipid profile, hemogram, and liver function test which were within normal limits. After 3 weeks, lipid profile and liver enzymes were repeated which showed elevated triglyceride level. Clinically, there is a marked reduction in pain. Tablet atorvastatin 20 mg once a day was added to the treatment to control hypertriglyceridemia. Acitretin was continued for further 9 weeks with close monitoring of lipid profile and liver enzymes which remained in normal range. The patient received treatment for total period of 12 weeks with satisfactory improvement in pain, and a marked reduction in hyperpigmentation of hard palate is seen [Figure 5]. The patient tolerated the treatment well except for dryness of lips which was taken care by frequent topical application of emollient. The patient was followed up monthly for subsequent 3 months with no recurrence. His triglyceride level also returned to normal, six weeks after discontinuing acitretin.

**Discussion**

Several treatment approaches are useful in the management of oral lichen planus. Replacement of amalgam or gold dental restorations was also advisable.[3] In our patients, there was no such history. Topical and systemic steroids are the mainstay of treatment in oral lichen planus while retinoids, cyclosporine, thalidomide and dapsone are the second line of drugs used in the management of oral lichen planus.[4]

Silverman and Bahl[5] in their study revealed shorter remission period with oral and intralesional steroid injections as compared to systemic retinoids. We also found similar results in our two patients. Furthermore, in their study, they also found that thalidomide is more useful in erosive lichen planus. In our patients, as there were no erosions; thalidomide was found to be ineffective.

Acitretin, which is the pharmacologically active metabolite of etretinate, has been shown to act all three retinoic acid
their effect through different pathways. Retinoid receptors’ involvement in the control of inflammation is largely mediated through their ability to downregulate (transrepress) expression of proinflammatory transcription factors, especially activator protein-1. Furthermore, acitretin suppresses the appearance of mucosal lesions by inducing apoptosis and perhaps regulation of cytokine expression.

The remission period with steroid was very short and steroid-sparing immunosuppressive drug was warranted in all cases and hence we tried acitretin; with satisfactory response and longer remission was achieved. Malignant transformation of persistent erosive mucosal lichen planus is very remote but cannot be completely ruled out. Retinoid molecules mediate their chemopreventive and chemotherapeutic effects through two families of receptors: RARs (alpha, beta, and gamma) and retinoid X receptors (alpha, beta, and gamma). Through binding to these retinoid receptors, retinoids mediate their effects on cellular differentiation and on programmed cell death through the regulation of gene transcription and interaction with transcription factors. In most patients with retinoid hyperlipidemia, simple measures, such as weight reduction, appropriate dietary modifications, physical activity, and dose reduction are sufficient to reverse the triglyceride levels despite continued therapy. Statins and resins are probably more effective than gemfibrozil against retinoid-induced hyperlipidemia.

There are multiple reports of successful use of acitretin for the treatment of cutaneous lichen planus; however, there are few reports on the use of acitretin monotherapy in mucosal lichen planus. Kolios et al. reported good response with oral alitretinoin 30 mg/day in cutaneous, oral, and esophageal lichen planus after 4 weeks of therapy. Placebo-controlled or randomized controlled studies of the use of acitretin in lichen planus are lacking. A meta-analysis of sixteen studies on the treatment of cutaneous lichen planus showed increased overall response rates with acitretin. Thus, there is a definite evidence for the use of acitretin in lichen planus. The same is illustrated by our case series where significant improvement was seen in our three patients of oral lichen planus. Further controlled studies are required to assess safety and efficacy of oral acitretin in patients of mucosal lichen planus.

**Conclusion**

Lichen planus is chronic inflammatory disorder. Oral lichen planus is more refractory to treatment. Systemic steroids are the first line of treatment along with topical tacrolimus. Acitretin as a steroid sparing agent is equally effective in treating oral lichen planus.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.
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