

ACHILLES TENDONOPATHY AS A RARE ADVERSE EFFECT OF ORAL ISOTRETINOIN TREATMENT: TWO CASES

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ABSTRACT

Our aim is to report two cases of Achilles tendonopathy during oral isotretinoin therapy for acne vulgaris. Oral isotretinoin has been in use for more than three decades and a variety of adverse effects are ascribed to it; skin and mucus membranes being commonly involved. It's teratogenicity is well known. Achilles tendonopathy as an adverse effect of isotretinoin is very rarely reported. Here we discuss two patients who developed Achilles tendonopathy following administration of isotretinoin for acne.

KEYWORDS: Achilles Tendonopathy, Acne, Isotretinoin

INTRODUCTION

Isotretinoin, an orally active synthetic retinoid, is the most effective therapy for recalcitrant and nodular acne vulgaris. It induces long term remission in majority of acne patients. The drug has multimodal action; it causes apoptosis in sebaceous gland cells with decreased sebum production, inhibits inflammation, reduces Propionibacterium acne, normalizes keratinization and expression of tissue matrix metalloproteinases

Cheilitis and dry skin are the most common adverse effects of isotretinoin. Moreover, its cautious use in females at risk of pregnancy is well understood. Elevated liver enzymes and musculoskeletal adverse effects like myalgia, arthralgia, arthritis and muscle damage are also known to occur: however, Achilles tendonopathy is rarely documented. We report two cases of Achilles tendonopathy during treatment of acne vulgaris with isotretinoin.

Case 1

A 25 year-old unmarried female was started on 20 mg daily isotretinoin oral therapy for her severe acne on face. The drug was prescribed initially for ten days; she responded well and was advised to continue taking medicine for a period of six months. After two months, she started having pain around both Achilles tendons. The pain gradually increased in intensity during next two weeks. Ankle movements were painful and stiff particularly in the morning and during walking; her day-to-day life was interfered. On inspection there was no redness, deformity or swelling. Achilles tendons on both sides showed no heat, thickening, tenderness or crepitus on palpation. But patient experienced pain on hopping and when asked to raise heels off the ground. Erythrocyte sedimentation rate (ESR) and uric acid was within

normal limits; Rheumatoid Factor and C Reactive Protein (CRP) was negative. Imaging was not done. Achilles tendonopathy was suspected and isotretinoin was stopped. Patient was managed conservatively and recovered gradually over a period of few weeks. Rechallenge was not possible

Case 2

A 25 year-old unmarried female presented to with severe nodular acne of 6 months duration. After sending baseline investigations patient was started on isotretinoin 20 mg. The patient reported to the OPD after 10 days with improvement in her acne. However, she complained of a vague discomfort in her ankles; the treatment was continued. The patient telephoned after three days that she is not able to move her ankles without experiencing pain and discomfort. On reporting to the OPD the patient localized the pain to the region of Achilles tendon bilaterally. No signs of active inflammation of the tendon or joint were elicited. The patient's ESR was normal, Rheumatoid Factor negative; CRP negative, serum uric acid 4.6. A diagnosis of Achilles tendonopathy following isotretinoin was made. The Patient refused further treatment with isotretinoin and hence rechallenge was not possible. She recovered gradually in about a week.

DISCUSSIONS

Acne vulgaris, most prevalent dermatologic disorder, is a chronic inflammatory condition of pilosebaceous follicles commonly affecting young people. It is associated with considerable financial and psychological burden on affected individuals. Severe acne may cause scarring leading to disfiguring and distress. Isotretinoin has revolutionized the treatment of acne since its approval by U.S. Food and Drug Administration (FDA) in 1982. This prodrug, undergoes all-trans-isomerization to all-trans-retinoic acid (ATRA) which then binds to retinoic acid receptor (RAR)¹; but its exact molecular mechanism is not well described.

Isotretinoin causes numerous side effects; although most of them are predictable, dose dependent, and well described. Known adverse effects include dryness of skin and mucous membranes, teratogenicity, alopecia, eczema, photosensitivity, photophobia, keratitis, myalgia, arthralgia, abnormalities of liver function, elevation of triglyceride and cholesterol levels, acne flare, benign intracranial hypertension, mood change.

Achilles tendonopathy (even tendon rupture) is well documented with the use of oral and parental fluoroquinolones. Concomitant steroid therapy and renal insufficiency being risk factors². Ischemic, toxic and matrix-degrading processes have been implicated. But Achilles tendonopathy with isotretinoin is very rarely reported. Till the last search made, PubMed reveals just two scientific papers reporting Achilles tendonitis with isotretinoin in a few patients^{3,4}.

The relationship between isotretinoin intake and Achilles tendonopathy in both of our patients is "probable" according to the World Health Organization classification for causality of drug related reactions probability scale. Both these cases were reported to Adverse Drug Reactions Monitoring Centre (AMC) of Sher-e-Kashmir Institute of Medical Sciences (SKIMS) Srinagar.

CONCLUSIONS

Acne is common and isotretinoin is effective treatment for severe and treatment resistant acne. However, it is important for prescribers to be aware of its serious adverse effects. Women taking isotretinoin are advised to follow pregnancy prevention program as it is known to cause teratogenicity; but Achilles tendonopathy is very rarely reported in

literature. Here we have presented two young unmarried females who developed Achilles tendonopathy as an adverse effect of isotretinoin therapy. Keeping in view its widespread use we aim to make clinicians aware of this adverse effect of isotretinoin for timely recognition and appropriate action.

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