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# ISOTRETINOIN INDUCED PROXIMAL MYOPATHY: CASE REPORT AND REVIEW OF LITERATURE

**Omer Sawsan A.[1], Alkadhem, Sajjad M.[2], Alamer, Norah J. [2], Albesher Mohammed A. [3], Salim I Ibtihal [4]**

[1] Medical Consultant at KFHH; Associate Professor of Medicine; University ofGezira, Sudan.
[2] Medical Interns, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia
[3]Saudi Board Internal Medicine Resident R4 .College of Medicine, KFU Alhassa
[4]MBBS, University of Kordofan; Sudan; MD Dermatology; SMSB; Sudan, Dermatological Specialist, PSBJH

**Abstract:**
*Acne vulgaris is a disorder of the pilosebaceous follicles commonly occurs in the adolescent. Isotretinoin is used for the treatment of severe acne vulgaris either topically or orally. Most of the effects of isotretinoin are predictable and well described such as dryness of eyes, lips and nasal mucosa. Musculoskeletal side effects such as myalgia, arthralgia, arthritis, and muscle damage are usually mild and myopathy involving pelvic girdle muscles is rarely reported. The following is a case report for one patient presented to our hospital (King Fahad hospital- Alhfuof); with severe myopathy affecting pelvic girdle muscles, after treatment with oral isotretinoin.*

**Keywords:** *acne vulgaris; isotretinoin; myopathy; adult; Pharmacology.*

**Corresponding author:**
**Dr. Sajjad Mohammed alkadhem,**
*Medical Intern, College of Medicine,*
*Imam Abdulrahman Bin Faisal University,*
*Dammam, Saudi Arabia*
*E-mail:sadaoy.15@gmail.com,*
*Mobile no.: +966507764608*
*P.O. BOX alumran 4788, Saudi Arabia 36355*

QR code

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## INTRODUCTION :

Acne vulgaris has a significant psychological impact on affected individuals. Isotretinoin (vitamin A analog) is used for the treatment of severe acne vulgaris (topically or orally), and many of its side effects are similar to those caused by hypervitaminosis A syndrome (1). It is associated with myalgia and muscle stiffness in 16-51% as reported in one study and elevated serum creatinine kinase in 41%of cases especially in those who exposed to vigorous exercise. (2).Severe acute myopathy is reported in some cases. (3).

## CASE PRESENTATION:

This is a case of A 17-year-old male; secondary school student; presented to our hospital with severe lower limbs cramps and generalized feeling of ill health and inability to walk for one week, on a background history of recurrent episodes of severe acne vulgaris in the face and chest for the past ten months; apart from this his past medical was not significant. Two months before the presentation he was started on oral isotretinoin 40 mg daily, in addition to topical antibacterial washes. The patient responded well to the isotretinoin described by a dermatologist, but after one month of treatment, the patient started to have thigh and back pain dull aching relieved by analgesics, and skin eruption in the chest, face, and back. In the emergency room, the patient was ill-looking, unable to walk and afebrile, the blood pressure was (125/70), pulse was (106/ min.), and his weight was 70 kg. He was not pale or jaundiced. The mucous membrane of the mouth was normal. No cervical lymphadenopathy was detected. Examination of the cardiopulmonary systems and the abdomen was normal. Musculoskeletal and skin examination, showed maculopapular erythematous rash over the face, chest, and upper back. Restriction of movement in the lower limbs due to pain, mainly in the proximal region, also the Grove's sign was positive. There was tenderness over the muscles, but no erythema or peeling. Upper limbs examination was unremarkable.Investigations were within normal range for Complete blood count, liver function, renal function test, and serum electrolytes. Level of creatinine kinase (CK) was 48 IU/L and lactate dehydrogenase (LDH) of 120. MRI for thigh muscles showed no evidence of myositis. Muscle biopsy was not done. A provisional diagnosis of isotretinoin-induced myopathy was made. isotretinoin was discontinued. The patient responded to bed rest and prednisone 20 mg, local clindamycin which was given after dermatologist consultation.

## DISCUSSION:

Isotretinoin, 13-cis-retinoic acid, is a retinoid effective in the treatment of severe acne vulgaris. Myalgia occurs in up to 15% of patients who are treated with isotretinoin (4).Drug-induced myopathies requires awareness and attention from clinician: they might cause significant morbidity; so early recognition is important to help in full recovery; patients on myotoxic drugs need follow-up for neuromuscular adverse effects and CPK levels; high dose or overdose may increase the of toxicity; pharmacogenomics has an immense role in this regard .(5)Drug-induced myopathies can manifest as muscle weakness, increased CPK levels, myalgia, myoglobinuria, and EMG and histologic changes. Clinical picture can range from mild muscle pain and cramps to severe weakness with rhabdomyolysis, renal failure, and death. Statins, steroids, antiviral therapy, colchicine, and chloroquine are examples of drugs which may be myotoxic. Mechanism of drug-induced myotoxicity is multifactorial: brunt may be on muscle organelles, for example, mitochondria, lysosomes, and myofibrillar proteins; muscle antigens can get altered leading to inflammation or immunologic reaction; nutritional and electrolyte imbalances may occur resulting in muscle dysfunction.[5] Muscle constitutes 45% of total body mass and it is well perfused and display dynamic metabolic machinery. Skeletal muscles are responsible for 80% of total glucose uptake and >30% of resting metabolic rate. These inherent properties make muscles vulnerable to toxic effects of circulating drugs.

Arthralgia and myalgia have been reported in 2–5% of patients receiving oral isotretinoin >0.5 mg/kg/day. Malaise, fever, and an increase in CPK may be associated in some patients. CPK may be raised in a variable percentage of patients receiving isotretinoin; it may or may not be associated with muscular signs and symptoms and is more common in patients who are involved in the vigorous physical exercise. (5) Isotretinoin is a prodrug; it gets isomerized to all-trans-retinoic acid in the body. Substantial evidence favors the role of forkhead box class O (FoxO) transcription factors in therapeutic, adverse, teratogenic, and chemopreventive effects of the drug. Isotretinoin causes hyperactivation of FoxO1 which mediates upregulation of atrogin 1 and muscle-specific ring finger protein 1, the two ubiquitin ligases involved in skeletal muscle atrophy. Thus, isotretinoin causes FoxO-induced catabolic events in muscle cells that may manifest as muscular

signs and symptoms as well as the release of CPK. (5). Differential diagnosis of muscle disorders can be broad. In our patient, drug-induced myopathy was diagnosed by exclusion putting in mind the young age of the patient; in addition to the following criteria: first, the temporal relationship between drug intake and appearance of symptoms muscle weakness; drug-induced myopathy appears weeks or months after use of the offending drug. In our patient, several weeks existed between the commencement of treatment with isotretinoin and appearance of features of myopathy. Second, our patient had never experienced muscular symptoms in the past. Third, the absence of any other apparent cause of myopathy. Fourth, complete resolution of signs and symptoms following discontinuation of isotretinoin.

## CONCLUSION:

It is essential that the clinicians should be aware of the toxic effects of isotretinoin on muscles and not to exceed the maximum dose to avoid myopathy as much as possible. Early recognition of isotretinoin toxicity will prevent permanent damage to muscles.

## CONFLICT OF INTEREST:

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript for publication.

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