

## Bilateral Sacroiliitis Due to Isotretinoin: Two Cases

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#### Abstract

Isotretinoin is an effective retinoid used for severe and persistent acne lesions but has various adverse effects that affects many systems in the body. Sacroiliitis is one of the musculoskeletal side effect of the drug that is discussed in the literature but is much rare. In this article, we present two cases with acute bilateral sacroiliitis using isotretinoin for acne vulgaris. Based on the onset of the symptoms and improvement of sacroiliitis after suspension of isotretinoin treatment, in the described cases, sacroiliitis were associated with the retinoid. **Key words:** Acne vulgaris, Sacroiliitis, Isotretinoin,

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### Introduction

Isotretinoin is a vitamin A derivative that is used for severe, nodulocystic acne lesions resistant to standart therapies, including systemic antibacterials (1, 2). Several studies have shown that isotretinoin induces apoptosis in various cells in the body, including sebaceous gland cells; thus, reduces sebum production and inflammation; also causes an antimicrobial effect on Propionibacterium acnes (3,4). Isotretinoin is the only disease modifying and the most effective drug in the management of acne lesions but may have serious mucocutaneous, musculoskeletal, neurological, and ocular side effects. The most frequent musculoskeletal side effects are myalgia and arthralgia. Rarely tendon calcifications. arthritis. osteopenia, vasculitis, skeletal hyperosteosis, transient pain in the chest can be seen (1, 5, 6). Ther are also case-reports in the literature about isotretinoin induced sacroiliitis. With increasing usage of isotretinoin, more frequent adverse effects are seen.



Therefore, we present two cases with sacroiliitis after isotretinoin therapy and we want to call attention again to this very rare side effect.

## CASE 1

A 36-year-old woman presented to our outpatient clinic with complaints of severe pain on lumbar region and hips for three days. She had difficulty to walk and also had morning stiffnes lasting an hour. She experienced pain especially after rest and the pain did not radiate to the legs. Her history was non-specific, she was a house wife, she had not had any trauma or any mechanical stress. But she had started 30 mg daily isotretinoin therapy for acne vulgaris on her face 5 months ago. In the last week, the dose had been increased to 120 mg/day. All of the routine health controls were normal before starting the therapy and any health problem had not been observed before. On physical examination, lumbar paravertebral muscles and sacroiliac joints were painful, the lumbar movements were restricted in all directions, modified schober test was measured as 4.2 cm. Sacroiliac stress tests (mennel and gaenslen) and straight leg tests were bilaterally positive. The chest expansion was 4.6 cm. Neurological examination was normal. The pain characteristics physical and the examination was considered to be inflammatory pathology. In laboratory examination, erythrocyte sedimentation rate (ESR) was 27, CRP was 2.8 (0-6). Complete blood count, routine biochemical tests and urinary analysis were normal. Brucella Wright test, rheumatoid factor (RF), anti-nuclear antibody (ANA) and HLA-B 27 were negative. The lumbar MRI showed no abnormality but in MRI examination of sacroiliac joints, symmetrical periartricular inflammatory edema signals were detected (figure 1). We stopped the isotretinoin therapy after consultation with the dermatologist and we started naproxen sodium 2X550 mg orally. We also recommended her resting, thermotherapy (3 times a day for 20 minutes) and pelvic tilt exercises.





Fig 1

# CASE 2

A 21-year-old male patient presented to our outpatient clinic with complaints of lumbar, bilateral gluteal and inguinal pain for a week. He had morning stiffness lasting for 2-3 hours and the pain aggravated by prolonged standing and by stair climbing. He was a student and he had not had any mechanical trauma. He had not any problem in his history except for isotretinoin treatment for 2.5 months. The treatment was started with 30 mg/day and had been increased to 60 mg/day ten days ago. On physical examination, he had a trendelenburg walking. Palpation of lumbar paravertebral muscles, sacroiliac and hip joints were painful. Lumbar and bilateral hip joints' range of motions were

also painful and restricted. Modified schober was 4 cm. Sacroiliac stress tests, FABER and straight leg tests were bilaterally positive. The chest expansion was 5.6 cm. Neurological examination was normal. On the analysis of labaratory findings, complete blood count, routine biochemical tests and urinary analysis were normal. ESR was 19, CRP was 3.1 (0-6). Brucella Wright test, RF, ANA and HLA-B 27 were negative.

We decided lumbar and pelvis MRI. Lumbar MRI showed a central small disc protrusion at L4-5. In the pelvic MRI, there were periarticular inflammatory edema signals on both of the distal sacroiliac joints (figure 2).





# Fig 2

As there were no pathological findings about the diseases that make sacroiliitis, we stopped the isotretinoin treatment and recommended him diclofenac sodium 2X75 mg orally, resting, local heat and pelvic tilt exercises.

At the 1st week evaluation, while the pain and lumbar restrictions were decreased, we started lumbar flexibility and strengthening core stability exercises to both of the patients. The complaints of the first patient were completely resolved at the 6th week, while the other patient had no symptoms at the 8th week evaluation. The control MRIs performed 12 weeks later showed no evidence of sacroiliitis.

### Discussion

Sacroiliitis, inflammation of sacroiliac joints, can be a manifestation of a wide

of diseases such range as spondyloarthropaties (ankylosing spondylitis(AS), psoriatic arthritis, reactive arthritis .arthritis related to inflammatory diseases and undifferantiated bowel spondyloarthropathy), infectious diseases ( brucellosis, tuberculosis), degenerative, metabolic and neoplastic pathologies (7). The MRI is the best imaging technique for detecting early inflammatory changes and for making differential diagnosis (8). The MRI findings of both of our patients were bilateral and symmetrical which is usually seen at AS, but their history, examination and labaratory findings did not fulfill the criteria of AS or the other diseases above. Therefore, we thought it might be associated with isotretinoin therapy while



the association had been reported in the literature, before.

The exact mechanism about isotretinoin induced sacroiliitis is not well understood but in the literature, it is suggessted that arthritis may be related to cell-mediated autoimmunity due to hypersensitivity reaction which induces damage at the lysosomal membranes of the synovial cells (9,10).

Another idea is that, isotretinoin treatment may make cells vulnerable to mild traumas (11). In the case-report of Dincer et. al, one patient was an amateur basketball player and another patient's complaints appeared during a football match (1). In addition, Rozin (10) and Eksioğlu (12) suggested that HLA-B27 positivity might make the patients using isotretinoin susceptible to the development of sacroiliitis. However, both of our patients were HLA-B27 negative and there were not any mechanical stresses in their histories.

The dose of isotretinoin is dependent on weight and the severity of the lesions. According to the guidelines, the treatment is started with 0.5-1.0 mg/kg/day and is continued until a cumulative dose of 120-150 mg/kg is achieved (13). It has been reported that lower dosage treatments can also be effective with diminished side effects but may be associated with higher relapse rates, requiring additional courses (14-16).

It is suggested that the condition does not leave any sequel (17). Similar with the previously mentioned cases in the literature, our patients' symptoms resolved after withdrawal of the drug and there were no signs of sacroiliitis at the third month which supported the role of isotretinoin in these cases we presented here. Both of our patients had acne vulgaris; however, acne fulminans, the more severe form of acne is more related with sacroiliitis, they may together be a part of SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis). Isotretinoin treatment may also induce sacroiliitis in the patients with acne fulminans (18,19). Furthermore, according to Pehlivan et al.,sacroiliitis is a rare sideeffect but inflammatory back pain without sacroiliitis due to isotretinoin can be seen widely (5)

In conclusion, the clinicians might be aware of the musculoskeletal side effects of isotretinoin and in patients receiving isotretinoin with inflammatory back pain without typical signs of spondyloartropathy, isotretinoin must be considered as an aetiological factor.

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