CASE REPORT

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Isotretinoin Treatment-Induced Sacroiliitis

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ABSTRACT Isotretinoin, which is commonly used for the treatment of severe and treatment-resistant acne vulgaris, is associated with many adverse effects including musculoskeletal pain and arthralgia, and rarely sacroiliitis. Isotretinoin-induced sacroiliitis is typically limited with the discontinuation of isotretinoin and usually reduces with non-steroidal anti-inflammatory drugs. In this article, we present a patient using isotretinoin for her facial acne, lived inflammatory pain in her lower back and right hip region after 8 weeks of isotiretionin treatment and diagnosed sacroiliitis. As a result we want to draw attention to the fact that this drug can cause low back pain and sacroiliitis as a side effect.

Keywords: Sacroiliitis; low back pain; acne vulgaris

Isotretinoin, a vitamin A derivative, is approved by the Food and Drug Administration as a cure for severe recalcitrant acne vulgaris, and recommended for severe nodular acne and treatment resistant moderate acne.[1] Many adverse effects associated with the isotretinoin use have been reported. Among those, the most common adverse effects include mucocutaneous, musculoskeletal and ophthalmological systems. These adverse effects are temporary and reduce without sequelae following the discontinuation of the drug.[1]

Adverse effects in the musculoskeletal system are bone abnormalities and rheumatologic manifestations.[2] Seronegative spondyloarthropathy (SpA) like abnormalities including hyperosteosis, extraspinal calcifications, diffuse idiopathic skeletal hyperosteosis, bilateral and unilateral sacroiliitis, enthesopathy, costochondritis, and arthralgia, arthritis, myalgia, myopathy, vasculitis, and other complications have all been reported.[2] While arthralgia and myalgia are more common in case reports, sacroiliitis has been described as a rare side effect.[3-6] Herein, we report and describe the case of a 26-year-old female diagnosed with sacroiliitis after 8 weeks of isotretinoin treatment.

CASE REPORT

A 26-year-old female patient had used isotretinoin 30 mg daily for her facial acne for a period of 2 months, 2 years ago. After 8 weeks of isotretinoin treatment, she experienced inflammatory pain in her lower back and right hip region. Due to this pain, the isotretinoin treatment was ceased. While the lower back pain decreased, her right hip pain was persistent. She did not report any significant trauma and she had no histories of recent genitourinary or gastrointestinal infections. Her written inform consent was provided.

Regarding physical examination, the lumbar flexion of the patient was normal and the sacroiliac stress test was positive on the right side. There were no enthesopathy, peripheral arthiritis, ocular findings, cutaneous lesions. The other locomotor and neurologic system findings appeared to be normal.

Laboratory analysis showed that blood chemistry and complete blood count were in a normal range, while acute phase reactants including C-reactive protein and erythrocyte sedimentation levels were elevated [10.88 mg/dL (normal range: ≤0.5 mg/dL) and 87 mm/h (normal range: 0-20 mm/h), respectively]. These levels decreased to normal

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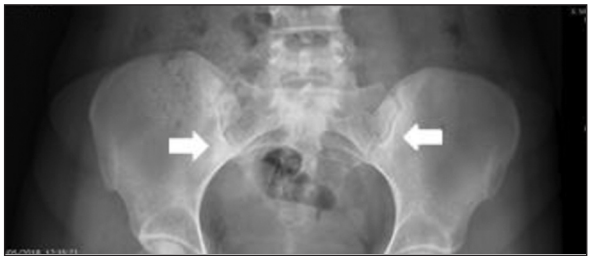

FIGURE 1: Sclerosis and irregularities at the bilateral iliac and sacral wings, particularly at the inferior articular parts on the right side (anterior-posterior pelvis radiography).

ranges (0.09 mg/dL and 10 mm/h, respectively) 2 weeks after the discontinuation of isotretinoin. The patient's human leukocyte antigen (HLA) B27 was negative.

The radiography of the sacroiliac joints showed signs of sclerosis and irregularities at the inferior articular parts bilaterally, especially on the right side (Figure 1). Magnetic resonance imaging (MRI) detected bone marrow edema in the inferior parts of sacral and iliac wings of both sacroiliac joints, consistent with active sacroiliitis (Figure 2).

The patient was treated with sulfasalazine (dose increasing up to 3 g/day) and non-steroidal anti-inflammatory drug (NSAID) for a three-month period. As a result of this treatment, the pain diminished significantly and in a 6 month period the patient had no symptoms. Control MRI was performed 11 months after our patient's pain stopped and there were no findings of active sacroiliitis, no effusion, no synovitis and no abnormal bone marrow signals detected (Figure 3).

DISCUSSION

Isotretinoin is commonly used as a systemic and effective medication for the treatment of severe and treatment-resistant acne vulgaris and sacroiliitis can rarely occur as an adverse effect.[3-6] The reported prevalence is between 2.38% to 8.20%.[7,8] Sacroiliitis, which can be defined as the inflammation of the sacroiliac joint, is a primary manifestation of axial SpA and may be seen in many other rheumatic and non-rheumatic disorders such as familial Mediterranean fever, Behçet's disease, hyperparathyroidism, and various pyogenic sources.[9] In the literature, there are reports of cases of unilateral or bilateral sacroiliitis after isotretinoin use.[3-8,10]

The mechanism of the sacroiliitis is not understood clearly. It is thought that isotretinoin shows detergent-like effects and induces changes in lysosomal membrane structures, causing degeneration in synovial cells, induces hypersensitivity reactions on these cells, and causes synovial cells to become sensitive to minor or mild traumas.[11,12] It is also thought to lead in the increase of matrix metalloproteinase-2 activity and the ravage of membrane in the joints.[12] Some authors noted that patients with a positive HLA-B27 can be more inclined to develop sacroiliitis with the isotretinoin use.[5,12] But the majority of such case reports declare that HLA-B27 is found negative.[3,6,7,10,12-14] In our case, the patient had a negative HLA-B27 as well. MRI was performed after 3 weeks of her initial pain and it showed increased signal intensity and bone marrow oedema of the sacroiliac joints.

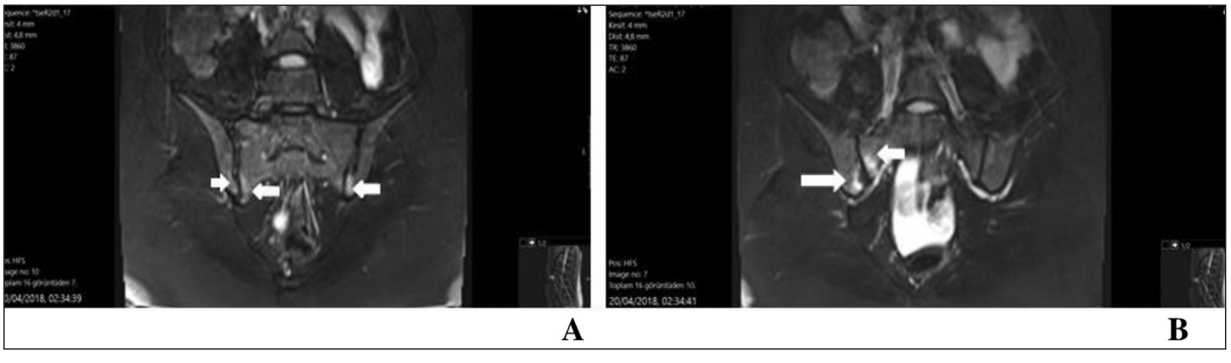

FIGURE 2: Increased signal intensity and bone marrow edema in the inferior portion of bilateral sacroiliac joint, prominent on the right side (water-only T2-weighted Dixon image, oblique-coronal planes).

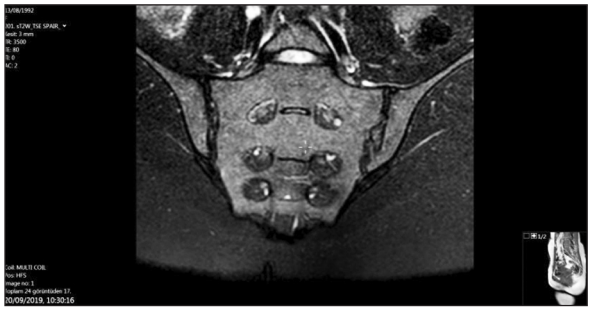

FIGURE 3: Normal findings on control magnetic resonance imaging of bilateral sacroiliac joint (T2-weighted spectral adiabatic inversion recovery image, oblique-coronal plane).

Pain in patients occurs days or months after isotretinoin is administered and the location of the pain may vary.[10,14] While patients commonly have lower back pain, they can also experience pain in one or both buttocks, hip pain or thigh pain.[15] In a prospective study examining rheumatological side effects, especially the manifestation of sacroiliitis in patients using isotretinoin for moderate and (or) severe acne vulgaris, Baykal et al. reported lethargy in 37 (50.7%), myalgia in 31 (42.5%) and lower back pain in 36 (49.3%) of 73 patients.[8] In 16 (21.9%) of these 36 patients, low back pain was reported as inflammatory nature, and sacroiliitis was diagnosed in 6 (8.2%) of these patients by MRI. In another prospective controlled study, follow-up results regarding the rheumatologic symptoms of patients who received systemic therapy (isotretinoin and tetracycline) for the treatment of acne vulgaris were presented.[7] There were 42 patients in the isotretinoin group and 32 patients in the tetracycline group. In the first month of the treatment, inflammatory lower back pain developed in 6 (14.28%) of the patients in the isotretinoin group, where in the tetracycline group none of the patients showed any symptoms. In addition, in the isotretinoin group, three patients were reported to have achilles enthesopathy, and one patient suffered from both achilles enthesopathy and unilateral sacroiliitis. In our case, the patient had no symptoms of pain before isotretinoin use. After 2 months of isotretinoin treatment, she experienced pain in the lower back and hip.

Isotretinoin-induced sacroiliitis is typically self-limited with the discontinuation of isotretinoin and usually reduces with NSAIDs and\or disease-modifying anti-rheumatic drugs within weeks or months of administration, but in the literature for some cases immunosuppressive agents' usage has also been reported.[13,14] After discontinuation of isotretinoin and 3 months of sulfasalazine and NSAID treatment, the pain of our patient ended.

In the literature, it is depicted that control MRI of the sacroiliac joints is performed at different times, between 2 months and 3 years after discontinuation of isotretinoin.[3,4,6,10,12] These MRI findings were reported as normal, fluctuated or in regression.[3,4,6,10,12] Control MRI of the sacroiliac joints which was performed 11 months after our patient's pain stopped, showed normal images. Our case report is valuable in terms of the fact that the patient was controlled both clinically and by MRI after 11 months, although her symptoms had completely disappeared.

In conclusion, with this case report we want to shed light on lower back and/or hip pain which may occur after administering isotretinoin. If there is any related pain in such patients, sacroiliitis has to be connoted as a diagnosis and this drug's administration should be terminated and other necessary treatments should be applied.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Erbil Dursun;* ***Design:*** *Erbil Dursun, Tuğba Gökbel;* ***Control/Supervision:*** *Erbil Dursun, Tuğba Gökbel;* ***Data Collection and/or Processing:*** *Güler Gözpınar, Tuğba Gökbel;* ***Analysis and/or Interpretation:*** *Tuğba Gökbel;* ***Literature Review:*** *Güler Gözpınar, Tuğba Gökbel;* ***Writing the Article:*** *Güler Gözpınar, Tuğba Gökbel;* ***Critical Review:*** *Erbil Dursun, Nigar Dursun.*

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