

Inflammatory Back Pain in Patients Treated with Isotretinoin

To the Editor:

Despite the positive effects of isotretinoin on a number of cancers and severe skin conditions, several disorders of the musculoskeletal system have been reported in patients who are treated with it. Reactive seronegative arthritis and sacroiliitis are very rare side effects^{1,2,3}. We describe 4 cases of inflammatory back pain without sacroiliitis after a month of isotretinoin therapy. We observed that after termination of the isotretinoin therapy, patients' complaints completely resolved.

Musculoskeletal system side effects reported from isotretinoin treatment include skeletal hyperostosis, calcification of tendons and ligaments, premature epiphyseal closure, decreases in bone mineral density, back pain, myalgia and arthralgia, transient pain in the chest, arthritis, tendonitis, other types of bone abnormalities, elevations of creatine phosphokinase, and rare reports of rhabdomyolysis. Musculoskeletal symptoms are common with isotretinoin therapy, but sacroiliitis is a very rare adverse event considering the number of patients treated with these drugs.

Case 1. A 32-year-old woman started isotretinoin for treatment of acne vulgaris. On the 15th day of treatment, severe backache, hip joint pain, and morning stiffness lasting 1–2 h occurred. Seronegative arthritis was suspected. Sacroiliac magnetic resonance imaging (MRI) was normal and HLA-B27 test was negative. Her erythrocyte sedimentation rate (ESR) was 16 mm/h and C-reactive protein (CRP) was 2 mg/l. Her complaints diminished with indomethacin and ibuprofen treatment. However, morning stiffness lasting half an hour and pains at night resumed. She discontinued the isotretinoin medication in the fifth month. After 20 days her complaints were resolved and never recurred.

Case 2. A 22-year-old man took 15 mg/day isotretinoin for treatment of acne vulgaris. On the 20th day, he complained about backache and hip joint pain that led to disrupted sleep. His complaints continued during the day. He had morning stiffness for 2 h. He was evaluated for seronegative arthritis. Sacroiliac MRI was normal and HLA-B27 test was negative. The ESR was 24 mm/h and CRP 3.4 mg/l. His complaints lessened with nonsteroidal antiinflammatory drug (NSAID) treatment. He discontinued isotretinoin before completing the 6-month treatment period. After 1 month his complaints resolved.

Case 3. A 19-year-old man presented to the rheumatology outpatient service with complaints of backache, hip joint pain, and morning stiffness. He had started isotretinoin for treatment of acne vulgaris 4 months before. His complaints began in the first month of treatment. His backache increased. A sacroiliac MRI was normal and despite some unrelated disorders revealed in laboratory tests, HLA-B27 test was negative. The ESR was 13 mm/h and CRP 5.5 mg/l. The isotretinoin therapy ended in the fourth month. He switched to NSAID, which helped, and the complaints resolved completely by the 15th day of the discontinuation.

Case 4. A 35-year-old woman had severe backache and gluteal pain in the morning and at night after isotretinoin treatment for acne vulgaris. Seronegative arthritis was suspected. A sacroiliac MRI was normal and HLA-B27 test negative. The ESR was 27 mm/h and CRP 3.41 mg/l.

Although 3 NSAID were administered, her complaints did not improve. She discontinued isotretinoin in the third month. Over 20 days her complaints gradually resolved.

In the literature, there are reports of different mechanisms and pathways indicating that isotretinoin causes immune dysfunction and leads to arthritis and vasculitis. Because of its detergent-like effects, isotretinoin induces some alterations in the lysosomal membrane structure of the cells, and this predisposes to a degeneration process in the synovial cells. It is thought that isotretinoin treatment may render cells vulnerable to mild traumas that normally would not cause injury⁴.

Activation of an infection trigger by isotretinoin therapy is complicated⁵. According to the Naranjo Probability Scale, there is a potential relationship between isotretinoin therapy and bilateral sacroiliitis⁶. It is thought that patients who are HLA-B27-positive could be more prone to developing sacroiliitis and back pain after treatment with isotretinoin, or that sacroiliitis might have been triggered by isotretinoin in such patients. However, our patients were HLA-B27-negative.

Although sacroiliitis is an uncommon side effect for isotretinoin treatment, inflammatory back pain without sacroiliitis can be seen widely. Isotretinoin used for the treatment of acne vulgaris could cause or trigger inflammatory back pain without sacroiliitis in healthy individuals. We recommend that patients with back pain be questioned about their use of isotretinoin, and rheumatologists need to be aware about complaints that may result from its use.

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