



## Case report

# Isotretinoin-induced arthritis: A rare but feasible diagnosis. Case report



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### ABSTRACT

Many medications and vaccines have had implications in the development of musculoskeletal and joint symptoms, and among them the use of retinoids has been associated with the development of musculoskeletal symptoms, as well as axial symptoms suggestive of spondyloarthritis, with sacroiliitis, and to a lesser extent the development of peripheral symptoms. We describe the debut of peripheral inflammatory symptoms with the use of isotretinoin, in a previously healthy patient.

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### Artritis inducida por isotretinoína: un diagnóstico infrecuente pero factible. Reporte de caso

#### RESUMEN

Muchos medicamentos y vacunas han tenido implicaciones en el desarrollo de síntomas osteomusculares y articulares. Entre ellos, el uso de retinoides se ha asociado con el desarrollo de síntomas musculoesqueléticos, así como síntomas axiales sugestivos de espondiloartritis, con sacroiliitis, y en menor proporción el desarrollo de síntomas periféricos. Describimos el debut de síntomas inflamatorios periféricos con el uso de isotretinoína, en una paciente previamente sana.

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## Introduction

When we face the scenario of a patient who presents a symptomatic articular clinical picture of inflammatory nature, we have in mind certain baseline conditions that predispose to its development, such as genetic susceptibility, which occurs in 50–70% of cases.<sup>1</sup> However, most of the time it requires an external trigger (epigenetic) that conditions the loss of immunological tolerance such as environmental situations,<sup>2,3</sup> smoking,<sup>4</sup> obesity<sup>5</sup> or infections,<sup>6</sup> as well as the exposure to certain substances such as the drugs<sup>7</sup> which have been described as causes of inflammatory and autoimmune exacerbations. Among these substances, the use of retinoids has been reported as a causal factor, usually associated with the development of musculoskeletal symptoms<sup>8,9</sup> and symptoms suggestive of spondyloarthritis, predominantly with sacroiliitis.<sup>10–12</sup>

There are few descriptions of cases with development of peripheral arthritis associated with the use of isotretinoin.<sup>13–16</sup> Therefore, the interest of our report lies in describing the onset of peripheral inflammatory symptoms with the use of isotretinoin in a previously healthy patient.

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## Case

A 43-year-old female patient with a history of acne conglobata at the age of 18 years, managed with topical treatment for approximately 18 months, with complete improvement of her underlying disease (at that time). The patient has a family history of rheumatoid arthritis in first maternal line. Previously, she was in a healthy joint and musculoskeletal condition. Due to reappearance of acne conglobata on the cheeks and chin, dermatology started management with isotretinoin 40 mg/day. Approximately 2 months after starting treatment, she began to present arthralgia in the right shoulder, exacerbated by exposure to cold. In her first assessment, she had a right lateral epicondylitis, without synovitis, and it was decided to start management with calcitriol 0.25 µg/day and hydrolyzed collagen 10 g/day. However, the condition evolved with painful symptomatic addition to the elbows, right knee and heels, with a tendinopathic nature that worsened at rest, without clinical synovitis, but with evident morning stiffness lasting a few minutes, while she continued taking the isotretinoin.

The paraclinical studies are: ESR 69 mm/h (0–20), CRP 14.6 mg/l (0–6). Otherwise, the entire immune profile was negative. Bearing in mind the symptomatic change, now with more noticeable inflammatory manifestations, a possible undifferentiated arthritis facilitated by the use of retinoid was considered. It was decided to add hydroxychloroquine 200 mg/day, and it was agreed with dermatology to discontinue treatment with isotretinoin.

2 months later, the patient refers improvement in the symptoms after suspending the isotretinoin, she never took the hydroxychloroquine, and brought a new set of paraclinical tests, with normalization of acute phase reactants (ESR 17 mm/h [0–20], CRP 5.5 mg/l [0–6]), therefore, it is considered an isotretinoin-induced arthritis, with an intermediate

probability according to the Naranjo scale (6 points)<sup>17</sup> and spontaneous resolution, in a patient with a history of risk due to a maternal history of rheumatoid arthritis. Currently, the patient remains asymptomatic after 2 years of discontinuation of the retinoid treatment.

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## Conclusion

Isotretinoin is the most widely used retinoid for severe acne due to its high efficacy. However, multiple side effects derived from its consumption have been described, among which is the appearance of musculoskeletal manifestations that can often occur even with low doses of the medication.<sup>16,18,19</sup> Cytopathic destruction of the synovial membrane has been suggested as a hypothesis of causality due to its detergent action.<sup>16,18</sup>

Musculoskeletal effects are common with the use of isotretinoin, having been reported in approximately 25% of patients.<sup>9,18</sup> At this point, very few cases of acute aseptic arthritis due to the use of retinoids have been described in the literature, beginning between 2–10 weeks after the start of the retinoid, usually in a monoarticular pattern with predominance in knees or ankles (some cases of polyarticular appearance with involvement of elbows, hips or toes), with joint effusion, and the study of the synovial fluid with findings of non-inflammatory type. In general, these symptoms resolve with non-steroidal anti-inflammatory drugs (NSAIDs), but above all the greatest impact is obtained by discontinuing the retinoid treatment. It is necessary to take into account that isotretinoin generates great benefits in patients with dermatoses, so many people prefer to endure pain or musculoskeletal limitations, as long as this avoids a recurrence of their skin condition.<sup>9,20</sup>

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## Ethical Considerations

The consent of the patient for the publication of the case was previously requested and it was approved by the ethics committee of the Medilaser clinic.

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## Conflict of interest

The authors declare that they have no conflict of interest.

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