Long Term Skeletal Changes in a Young Woman Treated with Isotretinoin

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Introduction

Isotretinoin is an oral synthetic vitamin A medication used as a treatment for acne since 1982. Although isotretinoin use is very common in daily practice, there are still controversies involving isotretinoin and its long-term effects on the skeletal system: musculoskeletal pain, periosteal thickening, “retinoid hyperostosis”, premature epiphyseal closure in children, osteoporosis, extraspinal tendon and ligament calcification, ossification of the posterior longitudinal ligament or effects on vitamin D metabolism¹-¹⁵.

In this article we would like to focus in one of them: “retinoid hyperostosis”. It was described in 1983 by Pittsley and Yoder¹ and interestingly, appears at younger ages than patients with diffuse idiopathic skeletal hyperostosis (DISH) and mainly in the cervical spine and feet⁵-⁷.

Case report

Previously, we have described the case of a 36 years old woman with severe acne treated with isotretinoin since she was 25 years old¹⁶. Although she referred cervical pain, the presence of DISH at cervical spine, made us look for the presence of findings in other typical DISH locations, such as the dorsal spine, calcaneus or pelvis (figures 1 to 3).

Figure 1: Dorsal Spine: lateral view of the dorsal spine showing ossification in the anterior longitudinal ligament (arrows shows abnormal density along the anterior aspect of vertebral bodies).
Unfortunately, we can’t confirm the cumulative dose because the patient was visited in our hospital for the third course of isotretinoin.

Due to chronic cervical pain, a cervical spine X-ray was done 6 years later, with no regression of the ossification of the anterior longitudinal ligament. X-rays of the other locations were not performed because she didn’t refer pain or restriction of movement.

Discussion

DISH or senile ankylosing hyperostosis was described by Forestier and Rotes-Querol in 1950. It is characterized by calcifications and ossifications of the entheses, affecting mainly the spine and peripheral sites. It is commonly seen in people older than 50 years old, preferentially in men with cardiovascular risk factors. Most of them are asymptomatic.

Spinal DISH, with calcification of the anterior longitudinal ligament, is predominantly observed at the dorsal spine, although the cervical and lumbar spine can also be affected with progression of the disease. DISH at the cervical spine can cause dysphagia and it is important to prevent complications in patients undergoing endotracheal intubation or upper gastrointestinal endoscopy.

Peripheral involvement includes proliferation at enthesal sites specially in the pelvis (iliac crests, ischial tuberosities, pubis, lateral acetabulum and greater and lesser trochanters) and feet (insertion of the fascia plantar or the Achilles tendon).

In patients under treatment with isotretinoin, the standard regimen consists of achieving a cumulative dose of 120-150 mg /kg. The current trend is to indicate low doses (20-30 mg per day) for longer periods of time, with the aim of minimizing mucocutaneous adverse effects and long-term side effects on the bone, as well as increasing patient compliance. However, at recommended doses, more than 20% of patients experience a relapse within two years that requires retrial.

The most common adverse effects are dryness of lips, skin and eyes, followed by headaches, joint and muscle aches, hypertriglyceridemia and transaminase elevation.

This case report has several limitations: we don’t have pretherapy X‐rays, and we can’t confirm the cumulative dose.

The question suggested by other authors, like Ling TC in 2001, for the need of radiological monitoring at baseline or during therapy, especially in patients taking high doses of isotretinoin for long periods, is still debated 20 years later.

Conclusions

In patients receiving isotretinoin, arthralgias are common and normally transitory. However, long-term effects on the skeletal system still remain controversial.

Informed consent was obtained from the patient for the publication of this report.

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