

Radiographic Bone Surveys after Isotretinoin Therapy for Cystic Acne

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Ellis CN, Pennes DR, Martel W, Voorhees JJ. Radiographic bone surveys after isotretinoin therapy. *Acta Derm Venereol* (Stockh) 1985; 65: 83-85.

Seven patients underwent retrospective radiographic examination 10 to 16 months after high dose isotretinoin therapy for severe cystic acne. One patient, who received the highest isotretinoin dose (approximately twice the average dose taken by the remaining patients), had multiple small hyperostoses of the thoracic spine and tarsi navicular. These findings were identical to the skeletal changes known to occur during retinoid administration. Prospective studies are needed to ascertain the risk of developing hyperostoses during isotretinoin therapy for acne at the lower doses currently employed. In this preliminary study, clinically significant hyperostoses were not a late sequela of high dose isotretinoin treatment for acne. *Key words: Retinoids; 13-Cis-retinoic acid; Hyperostosis.* (Received August 31, 1984.)

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The development of hyperostoses during isotretinoin therapy for ichthyosis was first described by Pittsley & Yoder (1) and investigated prospectively by us (2, 3). We have determined that as few as six months of isotretinoin administration at doses required for the treatment of disorders of keratinization may cause hyperostoses, particularly in the spine. These findings have generated concern among clinicians that patients taking isotretinoin for severe acne may develop hyperostoses, although at the time of this writing, no such cases have been reported.

To determine if isotretinoin, at doses used to treat severe cystic acne, causes the

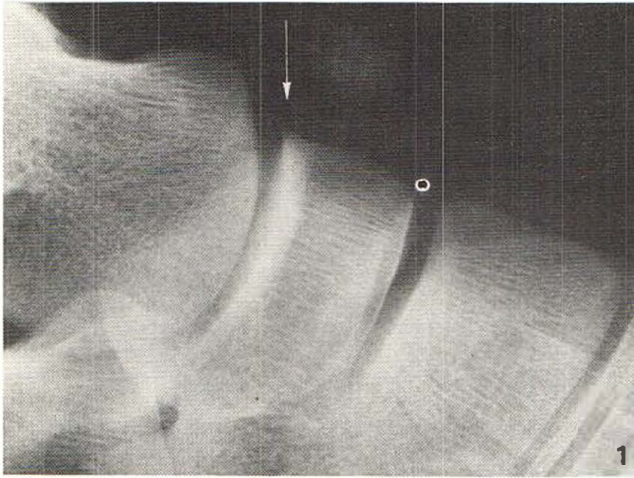


Fig. 1. Detail from lateral view of the left foot shows a hyperostosis arising from the dorsal surface of the navicular articulation (arrow).

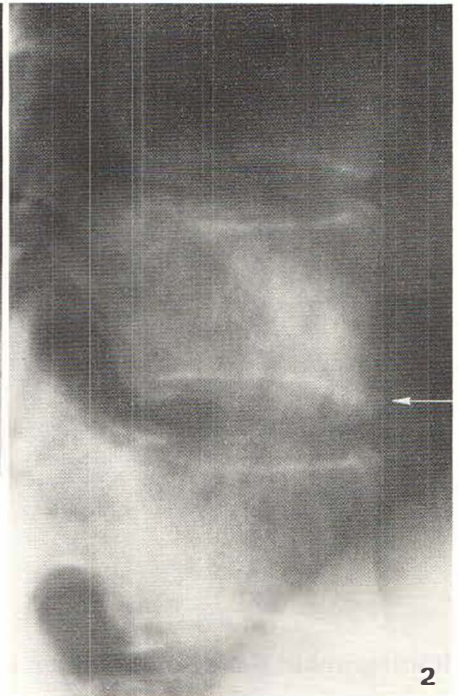


Fig. 2. A hyperostosis arises from the anteroinferior margin of a lower thoracic vertebral body (arrow).

development of hyperostoses, we retrospectively obtained bone radiographs in a small group of such patients. We sought to determine if hyperostoses had developed as a late sequela of the isotretinoin treatment. We thought it worthy for the same radiologists who had studied the radiographs of our patients with disorders of keratinization (2, 3) to examine the same views from a small number of isotretinoin-treated acne patients.

MATERIALS AND METHODS

Ten patients participated in our open study of isotretinoin for severe cystic acne, which had the approval of our Institutional Review Board. Informed consent was obtained from all patients, and, for minor patients, from their parents as well. Isotretinoin was administered twice daily. Our protocol required that the dosage not exceed 3.0 mg/kg/day; otherwise, we adjusted the doses as needed to achieve maximum clinical benefit. Isotretinoin was the only medication used by our patients during the study.

Our radiographic series was as follows: cervical, thoracic, and lumbosacral spine, frontal and lateral views; sacroiliac joints, frontal angled view; knees and elbows, anteroposterior views; feet, anteroposterior and lateral views; hands and wrists, posteroanterior view.

Three of our ten patients are not reported herein. Two could not return for radiographs. One patient had had radiographs taken prior to retinoid therapy which demonstrated severe skeletal abnormalities. The effect of isotretinoin, if any, on the skeleton of this patient could not be determined, and he is not included in our results.

RESULTS

We report seven patients (two women and five men). At the initiation of isotretinoin therapy, the women were 14 and 16 years of age; the men's ages ranged from 12 to 20 with a mean of 18 years. Radiographic evaluation was performed 10 to 16 months after each patient stopped isotretinoin treatment.

One of the seven patients had small hyperostoses arising from the thoracic spine at multiple levels and from the dorsal surface of the tarsal navicular bilaterally (Figs. 1 and 2). He was a man, 20 years of age, who had taken 1.8 mg/kg/day of isotretinoin for two courses of 16 and 16.5 weeks, separated by one month without therapy. He had received the largest total dose (27.4 g) and total dose per body weight (408 mg/kg) among the seven patients. His doses are two times the average of that received by the remaining 6 patients.

Skeletal surveys in the remaining patients demonstrated no significant abnormalities, although tiny bony protuberances were seen in the cervical spine in one patient and in the thoracic spine in another. The findings were subtle, and probably represented developmental variants.

For all patients, the mean duration of isotretinoin therapy was 24 weeks ± 3 SE. The mean dosage of isotretinoin taken by the patients was 15.8 g (± 2.5) or 239 mg/kg (± 33). Daily doses ranged from 0.6 to 2.4 mg/kg/day and the mean daily dose for the 7 patients was 1.4 mg/kg/day.

None of the patients reported symptoms referable to the skeletal system during or after isotretinoin therapy. None had previously taken vitamin A therapy.

DISCUSSION

Our patients participated in an early, open trial of isotretinoin for severe recalcitrant nodulocystic acne from January to November 1982. At that time, we employed higher doses of isotretinoin than are currently recommended (4). Only one patient received less than 0.8 mg/kg/day at any time during the study. Five of our patients with cystic acne received dosages of isotretinoin comparable to those taken by our patients with ichthyosis who developed hyperostoses (2, 3). Therefore, our patients should reflect the present potential for acne patients to develop hyperostoses after isotretinoin therapy.

However, only one of our seven acne patients had hyperostoses that were likely to have been caused by the treatment. The radiographic changes in this patient were similar to, although less dramatic than, those that we noted in our previous work (2, 3). Indeed, the hyperostoses in our patient were so small that they would not likely have been detected unless specifically sought. Our patient was asymptomatic during and after isotretinoin treatment. The other six patients also had no symptoms throughout the study and had no skeletal hyperostoses 10 to 16 months after completing their isotretinoin therapy.

In this preliminary study employing thorough radiographic evaluations in 7 patients, hyperostoses developed in one patient as a late sequela of high-dose isotretinoin treatment for acne. The hyperostoses detected were small and of no clinical significance. Therefore, in the lower dosages now advised (4), it appears most unlikely that isotretinoin therapy for acne will cause substantive skeletal toxicity.

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