Systemic Retinoids and Thyrotoxicosis in (Multi) Nodular Goiter: Side Effect or Coincidence?

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Sir,

Systemic retinoids such as isotretinoin and acitretin are valuable and indispensable pharmacological therapy in dermatology but with various side effects. A 23-year-old female patient attended for the treatment of facial acne lesions present for 6 years. She stated that her thyroid function tests were normal and she was not using any other drugs. She was given oral isotretinoin for 7 months with a total cumulative dose of 150 mg/kg. During the last 2 months of therapy, she experienced intermittent tremor, nervousness, contractions, and cramps in her fingers and toes. The laboratory examinations revealed that free triiodothyronine (T3) was 3.98 pg/mL (1.8–3.9 pg/mL), free thyroxine (T4) was 1.23 ng/dL (0.61–1.12 ng/dL), thyroid-stimulating hormone (TSH) was 0.38 uIU/mL (0.4–4 uIU/mL), and...
thyroid autoantibodies were negative. She was diagnosed to have silent thyrotoxicosis with nodular goiter ultrasonographically [Figure 1].

A 63-year-old female patient attended for the treatment of palmoplantar psoriasis present for 2 years. She had hypertension, diabetes, and bronchial asthma without any known thyroid disorder. She stated that her thyroid function tests were previously normal. She was using oral metformin and enalapril but she was not using amiodarone. She was put on oral acitretin 35 mg/day. After 4 months of therapy, she complained of hair loss. The laboratory examinations revealed that free T3 was 4.21 pg/mL, free T4 was 1.25 ng/dL, TSH was 0.011 uIU/mL, and thyroid autoantibodies were negative. She was diagnosed to have multinodular goiter with thyrotoxicosis following ultrasonographic examination and fine needle aspiration cytology. She was prescribed oral methimazole 10 mg per day. The patient stopped both acitretin and methimazole by herself following 7 months of acitretin usage. One month following cessation of acitretin, her free T3 was 3.78 pg/mL, free T4 was 1.03 ng/dL, and TSH level was 1.12 IU/mL [Figure 1].

Minuk and Jackson reported development of transient silent thyrotoxicosis during isotretinoin treatment. They proposed that follicular disruption and leakage of thyroid hormones into the circulation are the probable underlying mechanisms. Yıldırım et al. evaluated thyroid function tests in 51 patients treated with 0.5–1 mg/kg/day oral isotretinoin. They reported a patient whose TSH level got lower than normal limits at 3rd month and returned to normal levels at 6th month. They also reported three patients with slightly elevated levels of free T3 during the treatment.

Retinoic acid and thyroid hormone receptors interact with each other and form heterodimers that function together in the induction of gene synthesis. Retinoic acid is used to redifferentiate undifferentiated thyroid cancers. Retinoic acid treatment increases radioactive iodine uptake by malignant thyroid cells.

The development of thyrotoxicosis in our patients might not have been a coincidence as this was a transient event. Retinoids might have led to increased iodine uptake and consequent release of thyroid hormones by benign thyroid cells in our (multi) nodular goiter patients with iodine insufficiency, and this might have resulted in transient hyperthyroidism. This proposal needs further investigation.

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Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

References
1. Minuk E, Jackson R. Thyrotoxicosis developing while on isotretinoin. J Am Acad Dermatol 1986;15:120.
2. Yıldırım N, Dogan S, Atakan N. Evaluation of thyroid function tests of acne vulgaris patients treated with systemic isotretinoin. J Dermatolog Treat 2017;28:141-4.
3. Li H, Bai B, Zhang Q, Bao Y, Guo J, Chen S, et al. Ectopic cross-talk between thyroid and retinoic acid signaling: A possible etiology for spinal neural tube defects. Gene 2015;573:254-60.
4. Fernández CA, Puig-Domingo M, Lomeña F, Estorch M, Camacho Martí V, Bittini AL, et al. Effectiveness of retinoic
acid treatment for redifferentiation of thyroid cancer in relation to recovery of radioiodine uptake. J Endocrinol Invest 2009;32:228-33.

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