OBSERVATION

Safe Use of Therapeutic-Dose Oral Isotretinoin in Patients With a History of Pseudotumor Cerebri

Drugs common in the treatment of acne vulgaris, such as minocycline and isotretinoin, have been reported in association with pseudotumor cerebri (PTC), which can lead to severe, irreversible symptoms, including vision loss. There is a paucity of data on isotretinoin use in patients with prior PTC.

Report of Cases | Case 1. A female patient in her teens presented with a 2-year history of severe, nodular, cystic acne of her face (Figure 1A), chest, and back with significant scarring. Her hormonal workup was unrevealing. Two years earlier, she had received minocycline for acne and had developed an unusually severe headache; lumbar puncture confirmed PTC. Prompt discontinuation of minocycline treatment led to long-term PTC symptom resolution. However, her acne was recalcitrant to treatment for several months with oral contraceptives, spironolactone (200 mg/d), topical antibiotics, and topical retinoids; she also required frequent intralesional triamcinolone for persistent painful cysts.

Isotretinoin therapy was initiated at 10 mg/d for 7 days, and the dose was increased slowly over 4 months to 40 mg/d; the patient noted skin dryness and facial erythema but developed no signs or symptoms concerning for PTC. After 9 months of isotretinoin therapy (cumulative dose, 120 mg/kg), her acne had markedly improved (Figure 1B).

Case 2. A woman in her late 20s presented with polycystic ovarian syndrome, severe inflammatory nodular acne with scarring (Figure 2A), and a history of minocycline-associated PTC (diagnosed at age 16 years via lumbar puncture). Her acne had not responded adequately to several topical retinoids at maximum concentrations, concomitant benzoyl peroxide, topical and oral antibiotics, spironolactone, and oral contraceptives. Multiple clinicians had avoided isotretinoin use given her history of PTC.

Owing to the recalcitrance of her acne to combination therapy with several agents, low-dose isotretinoin therapy was begun (initiated at 10 mg/d), and the dose gradually increased to therapeutic levels (cumulative dose, 140 mg/kg over 7 months of treatment). She experienced dramatic acne improvement with only mild residual scarring (Figure 2B). The only adverse effects were skin dryness and hypertriglyceridemia, both of which resolved after isotretinoin therapy was completed.

Case 3. A female patient in her teens presented with severe scarring, nodular acne and a history of PTC (confirmed by ophthalmologic and neurologic evaluation) that had developed after she had started isotretinoin therapy 3 years earlier. Her PTC resolved at that time with discontinuation of isotretinoin therapy. As with patient 2, her acne did not respond adequately to several topical retinoids at maximum concentrations, concomitant benzoyl peroxide, topical and oral antibiotics, spironolactone, and oral contraceptives. And again, as with patient 2, multiple clinicians had avoided isotretinoin use given her history of PTC.

Figure 1. Patient 1 Before and After Isotretinoin Treatment

A, Prior to isotretinoin treatment, severe nodular cystic acne, and a large linear scar on the cheek from prior cyst excision are visible. B, After 9 months of isotretinoin treatment (cumulative dose, 120 mg/kg), despite a thin layer of makeup, marked improvement of acne can be appreciated.
Low-dose isotretinoin therapy was begun (initiated at 30 mg/d), and the dose increased gradually to therapeutic levels (cumulative dose, 120 mg/kg over 9 months of treatment). Owing to her history of isotretinoin-associated PTC, an initial neurology consultation and monthly ophthalmology examinations were performed throughout the isotretinoin treatment period. She experienced dramatic acne improvement with only mild residual scarring. The only adverse effect was skin dryness, which resolved after isotretinoin therapy was completed.

Discussion | Pseudotumor cerebri is characterized by symptoms of increased intracranial pressure: headache, visual disturbances (blurry vision, diplopia), nausea and vomiting, and stiff neck. It is commonly idiopathic, primarily affecting women of childbearing age who are overweight. Less frequently, it can occur in association with other disease conditions (usually endocrinologic abnormalities such as polycystic ovarian syndrome). Despite many anecdotal reports of drug-associated PTC, there are 4 primary drug classes that are considered by experts to have a true association with PTC: (1) tetracyclines, including doxycycline and minocycline; (2) oral retinoids; (3) recombinant growth hormone; and (4) corticosteroids (following withdrawal). Cross-reactivity between these drug classes in patients with drug-associated PTC has not been reported. Symptoms usually regress completely after discontinuation of the drug therapy.

The pathophysiological mechanisms of drug-associated PTC are not fully understood. It has been postulated that tetracyclines may reduce cerebrospinal fluid outflow at the arachnoid villi, while oral retinoids (through excess retinols and retinol-binding protein) may be directly toxic to arachnoid villi function. We report safe use of isotretinoin in 3 patients with histories of drug-associated PTC. When acne warrants isotretinoin treatment, a patient history of PTC should not preclude its use if careful surveillance for PTC recurrence can be conducted. Baseline evaluation by ophthalmology and/or neurology services should be considered.

Suzanne J. Tintle, MD, MPH
Julie C. Harper, MD
Guy F. Webster, MD, PhD
Grace K. Kim, DO
Diane M. Thiboutot, MD

Author Affiliations: Department of Dermatology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania (Tintle, Thiboutot); Department of Dermatology, University of Alabama, Birmingham (Harper), Department of Dermatology, Jefferson Medical College, Philadelphia, Pennsylvania (Webster); Couture Dermatology and Plastic Surgery, Las Vegas, Nevada (Kim).

Corresponding Author: Suzanne J. Tintle, MD, MPH, Department of Dermatology, Penn State Milton S. Hershey Medical Center, 500 University Dr, Hershey, PA 17033 (stintle@hmc.psu.edu).

Published Online: November 18, 2015. doi:10.1001/jamadermatol.2015.3447.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the patients for granting permission to publish this information. We also thank James Q. Del Rosso, DO, and the American Acne and Rosacea Society (AARS) for review of this article. Dr Del Rosso received no compensation for his contributions.

Additional Information: This article underwent internal review by the AARS and passed the review process. Although the AARS does not endorse or recommend any specific patient management approach related to the subject of this article, the AARS does acknowledge that this article contributes information of important educational value to a challenging clinical scenario.


