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Secondary Intracranial Hypertension Associated with Alitretinoin Treatment for Twenty-Nail Dystrophy

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Dear Editor:

Intracranial hypertension (ICH) is a condition with increased intracranial pressure without structural cause. It is characterized by severe headaches, nausea, vomiting, and visual disturbances[1]. Prompt diagnosis and treatment are necessary to prevent permanent visual impairment. Medications may sometimes trigger ICH. ICH related to alitretinoin is rarely reported. Herein, we present a case of a female who developed iatrogenic ICH under alitretinoin treatment for twenty-nail dystrophy.

A 37-year-old Korean female visited the emergency department for persistent and pulsatile headaches, blurred vision, diplopia, nausea, and vomiting for one week. She complained of tenderness in the temporal and ocular areas. On physical examination, both eyes showed papilledema, but there were no signs of meningeal irritation. Cerebrospinal fluid (CSF) studies showed elevated pressure (>40 cmH_2O) with normal composition. There were no significant findings on brain computed tomography and magnetic Resonance Imaging with venography. Other laboratory findings were unremarkable except mild proteinuria and hematuria. She had been treated with alitretinoin for four months for twenty-nail dystrophy, and mesoglycan and valsartan for six months for immunoglobulin (Ig) A nephropathy. The patient was admitted for secondary ICH. The patient had started on 30 mg/day oral alitretinoin. She made a dose adjustment to 20 mg at 17 weeks of treatment due to severe headaches. However, we discovered that the patient's self-oral multivitamin supplement contained vitamin A. Although serum vitamin A level was unavailable, alitretinoin treatment combined with an oral vitamin A supplement was suspected as the cause of ICH. She was told to stop taking alitretinoin and the multivitamin. She was treated with CSF drainage with tapping and intravenous mannitol. She was discharged after six days and showed no sequelae at her six-month follow-up.

ICH is confirmed through the presence of papilledema and an increased CSF pressure[2]. Medications associated with ICH include retinoids, tetracyclines, lithium, mesalamine, and leuprorelin[1]. According to a safety analysis of the phase III trials and post-marketing surveillance, there were eight cases of ICH related to alitretinoin[3]. Additionally, Onnis et al.[4] reported a case of ICH in a retrospective study that analyzed patients with inherited ichthyosis treated with alitretinoin.

Medical conditions that require caution for ICH when prescribing retinoids include thyroid dysfunction, Cushing's disease, systemic lupus erythematosus, obesity, prolonged corticosteroid therapy, and corticosteroid withdrawal[2]. Our patient had no associated factors listed above. Our patient maintained normal renal function throughout the admission period. Furthermore, her symptoms related to ICH were alleviated while she was still taking mesoglycan and valsartan. Therefore, IgA nephropathy and its medications would have limited associa-

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tion with ICH in this case.

A probable explanation for our case might be the synergistic effect of alitretinoin and a multivitamin supplement containing vitamin A, resulting in hypervitaminosis A. The underlying mechanism is unkown, but an effect of retinal on CSF absorption is presumed[1]. Medications to avoid while taking alitretinoin include tetracycline antibiotics, other retinoids and vitamin A supplements[5].

To the best of our knowledge, this is the first case reporting iatrogenic ICH related to alitretinoin in a patient with twenty-nail dystrophy. Implementation of Drug Utilization Review has reduced drug-related adverse events, but over-the-counter drugs are still in blind spot. This rare case highlights the importance of properly educating patients about factors related to ICH, and to avoid not only tetracycline or other retinoids, but also vitamin A supplements while taking alitretinoin.

CONFLICTS OF INTEREST

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