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Case Report
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Ultrasound monitoring for minocycline-induced idiopathic intracranial hypertension

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Abstract

We report a rare case of idiopathic intracranial hypertension following oral minocycline therapy for the treatment of acne. A 29-year-old, non-obese female, with a history of minocycline use for 1 month for treatment of acne presented with headache and transient blurred vision for 3 weeks. She was found to have bilateral disc edema with normal visual acuity and color vision. Magnetic resonance imaging of the brain was normal with partially empty sella features and enlarged tortuous optic nerve in both eyes. Cerebrospinal fluid opening pressure was high. Ultrasound B-scan was done to serially monitor the optic nerve sheath diameter. She improved significantly after stopping the minocycline and following intracranial pressure lowering measures. Idiosyncratic reaction of intracranial hypertension with minocycline can be symptomatic as early as 1 week. Consultants should be aware of this as early consult with ophthalmologists/neurologists can prevent visual loss. A simple ultrasound B-scan can prove to be a vital non-invasive tool in monitoring these patients.

Keywords: *adverse drug reaction, idiopathic intracranial hypertension, minocycline, ultrasound B–scan*

Introduction

Idiopathic intracranial hypertension (IIH), defined by the modified Dandy criteria, is a disorder of unknown etiology characterized by raised intracranial pressure, which can cause severe visual loss if left untreated.[1,2] Certain drugs are implicated in IIH, such as vitamin A, tetracyclines and its derivatives, oral contraceptives, lithium, cyclosporin, etc.[3] The term "idiopathic intracranial hypertension" emphasizes our general lack of understanding of the pathophysiology of this disorder. Therefore, patients who develop a syndrome of raised intracranial pressure secondary to specific medications are still conventionally classified as IIH. Minocycline, the implicated drug in our case, is a tetracycline derivative used in the treatment of acne, malaria, urinary tract infections, etc. We describe a rare

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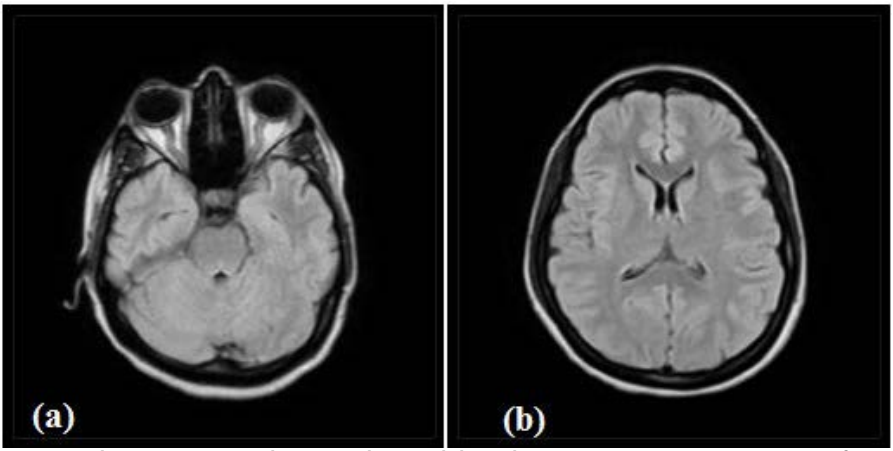

Fig. 1. (a) Flair sequence (axial section) showing bilateral tortuous optic nerves suggestive of raised intracranial tension. (b) Flair sequence (axial section) showing normal study.

case of minocycline-induced IIH and the role of non-invasive ultrasound B-scan in monitoring these patients.

Case presentation

A 29-year-old, non-obese female presented to the Department of Ophthalmology with a history of headache and transient blurred vision for 3 weeks. She also reported to be on treatment for acne with oral minocycline 50 mg once daily for a period of 1 month. There was no history of vomiting, diplopia, or history suggestive of any focal neurological weakness. Systemic examination was within normal limits. On examination, her best-corrected visual acuity was 20/20 with normal near vision (N6) and color vision in both eyes. Anterior segment examination and pupillary reaction were within normal limits. Extraocular movements were full and normal. Dilated fundus evaluation revealed bilateral disc edema suggestive of established papilledema. Disc edema evaluation with neuroimaging showed essentially normal magnetic resonance imaging of the brain with magnetic resonance venogram, bilateral tortuous optic nerves, and partially empty sella, suggesting raised intracranial tension (Fig. 1). The visual field analysis (30-2) showed an enlarged blind spot (Fig. 2). Full blood tests, including erythrocyte sedimentation rate and thyroid profile, were normal. Lumbar puncture for cerebrospinal fluid (CSF) analysis was normal except for a raised opening pressure of 34 cm H_20. Ultrasound B-scan (axial mode) was done to monitor the optic nerve sheath diameter (ONSD), which measured 5.2 mm in the right eye and 5.0 mm in the left eye (Fig. 3).

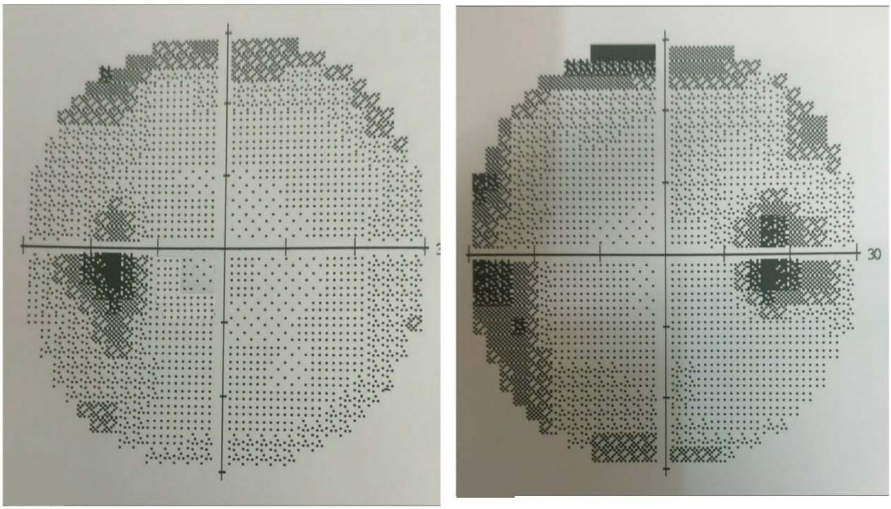

Fig. 2. Visual field analysis showing an enlarged blind spot in both eyes.

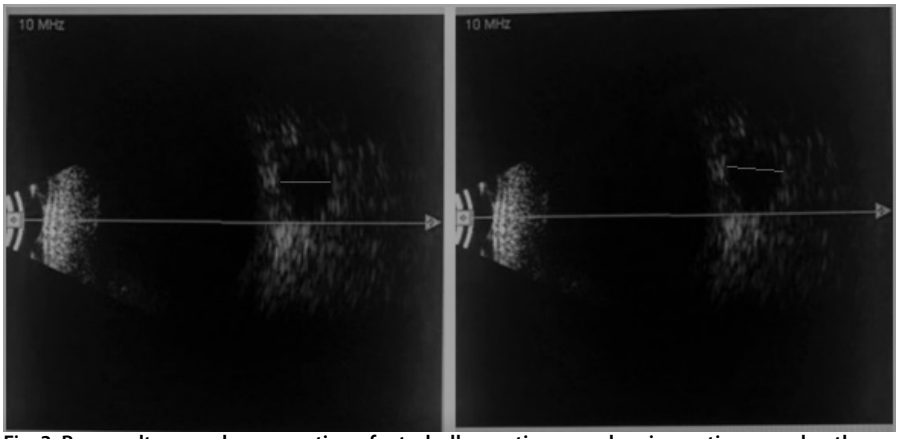

Fig. 3. B-scan ultrasound cross-section of retrobulbar optic nerve showing optic nerve sheath diameter at presentation (5.2 mm in the right eye and 5.1 mm in the left eye).

Diagnosed with IIH, the patient was treated with intravenous mannitol therapy (100 ml thrice daily for 3 days) and subsequently with oral acetazolamide (250 mg twice daily for a week, 250 mg thrice daily in the next week, 500 mg thrice daily for the next 3 weeks, and then tapered over 2 months). Minocycline was discontinued soon upon diagnosis. The patient tolerated oral acetazolamide well with minimal symptoms of gastritis and tingling sensation

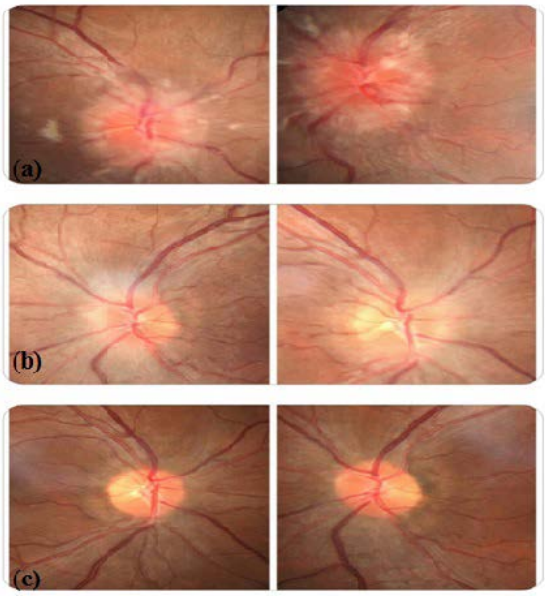

Fig. 4. Disc findings at presentation (a), treatment (b), and after treatment completion (c).

in the upper extremities, which were managed with oral antacid and potassium supplements, respectively. There was significant improvement in the patient's symptoms, with gradual resolution of disc edema over the next 3 weeks on clinical examination (Fig. 4).

Ultrasound B-scan was done serially in axial mode, showing reduction in the ONSD over the following weeks. Clinical resolution of disc edema was seen much later when compared to the ultrasound reduction in diameter. Lumbar puncture procedure was not repeated to measure opening pressure. ONSD was 3.4 mm in the right eye and 3.3 mm in the left eye at the end of 3 months and oral acetazolamide was stopped at that point. The ultrasound B-scan was repeated monthly for the next 3 months and showed no increase of fluid around the optic nerve.

Discussion

IThe term "idiopathic intracranial hypertension" emphasizes our general lack of understanding of the pathophysiology of this disorder.Therefore, patients who develop a syndrome of raised intracranial pressure secondary to specific medications are still conventionally classified as IIH. We applied the Naranjo adverse drug reaction score[4] to our case: the pre-existing case reports, the presence of a

temporal association between the administration of the drug and the onset of the adverse drug reaction (ADR), and the resolution of the pathology following dechallenge, puts this ADR under the "probable" category with a Naranjo score of seven. Rechallenge was not done in our case.

It has been postulated that minocycline reduces CSF absorption at the arachnoid villi, inducing elevated intracranial pressure.[5] The higher lipophilicity of minocycline when compared to other tetracyclines allows greater penetration of the blood-brain barrier, resulting in higher CSF concentrations and perhaps its association with IIH.[6]

The prognosis of IIH after discontinuing the drug is ranges from complete resolution to permanent loss of vision.[7] At 3 months, our patient remained asymptomatic, displayed complete resolution of disc edema, complete visual recovery, and no residual field defect. IIH can present even without papilledema[8] and may need invasive procedures such as lumbar puncture and expensive investigations like magnetic resonance imaging to monitor or detect recurrence. Ultrasonographic ONSD correlates well with severity of papilledema and is very useful in detecting raised intracranial pressure even in the presence of optic atrophy.[9] Being a non-invasive procedure, it was chosen to monitor ONSD in our patient.

The average time lapse between minocycline intake and IIH presentation is variable, ranging from 1 month to 18 months.[10] In the literature, very few cases of minocycline-associated IIH have presented or been symptomatic as early as 1 week. Frasner *et al.*[5] reported a case of a 12-year-old girl who developed fulminant IIH with minocycline. She had a family history of hydrocephalus with ventriculo-peritoneal shunting procedures which may have had some association and precipitated the attack. Our patient had a 1-month history of minocycline intake and became symptomatic with complaints of headache 1 week after initiating the treatment.

Minocycline alone may induce severe IIH with persistently elevated intracranial pressure, and patients with this condition may require medical and surgical treatment beyond discontinuation of the medication.[7] Our patient needed oral acetazolamide therapy for a period of 3 months beyond discontinuation of the drug. There was no recurrence of disc edema and signs of raised intracranial tension as monitored with ONSD using B-scan ultrasonography at the last follow-up 3 months after stopping oral acetazolamide.

Our case suggests minocycline-induced IIH can have an early presentation; timely intervention may prevent visual loss. Ultrasound B-scan is a cheap, non-invasive tool for monitoring these patients.

Conclusion

Idiosyncratic reaction of intracranial hypertension with oral minocycline can be symptomatic and present as early as 1 week after initiating the therapy. Practitioners prescribing the drug should be aware of this potential adverse effect and educate patients about warning symptoms or preferably undertake periodic screening regimens with ophthalmologists for early detection and treatment when symptomatic. B-scan ultrasonography measuring ONSD can be used to detect and monitor these patients with IIH.

Declarations

Ethics approval and consent to participate

None required.

Consent for publication

The patient provided informed consent for the publication of the clinical data contained in this case report.

Competing interests

None to disclose.

Funding

None to disclose.

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None to disclose.

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