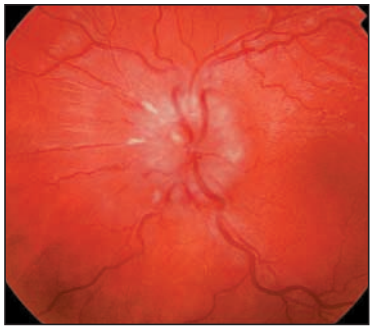
TEACHING CASE REPORT

The headache of teenage acne



THE CASE: A 15-year-old woman presented to hospital with a 1-month history of worsening bilateral headache and a perception of intracranial noise. The headaches were nonpulsatile, more severe in the morning and in the supine position and were associated with double vision on lateral gaze. On examination, she was alert, oriented and looked well. She was mildly overweight. There were no meningeal signs, and her vital signs were normal. There was dramatic bilateral papilledema (Fig. 1), with loss of physiologic cupping, indistinct disc margins and small retinal hemorrhages bilaterally. Visual acuity was reduced in the right eye (20/60), but her visual fields were full. She also had bilateral abducens palsies upon extreme lateral gaze. Her physical examination was otherwise normal.

A CT scan of the head was unremarkable, with no evidence of a space-occupying lesion, hemorrhage or hydrocephalus. On lumbar puncture, the cerebrospinal fluid (CSF) opening pressure, measured using bedside manometry, was found to be markedly elevated (> 55 cm of water; normal < 20 cm). Laboratory and microscopic analysis of the CSF was normal. The patient experienced significant improvement of her headache immediately after lumbar puncture; however, her double vision persisted. A diagnosis of intracranial hypertension was made and the patient was admitted to hospital for further investigation. She was prescribed 250 mg of acetazolamide twice daily.

Laboratory investigation revealed no endocrinopathy or hypercoagulable state. Magnetic resonance venography showed no signs of cerebral venous sinus thrombosis. Further questioning revealed that the patient had no significant menstrual irregularities but that she had begun taking minocycline for acne several days before the onset of her headache. Her only other medication was sertraline, which was prescribed for symptoms of depression about 2 weeks following the onset of headache. Minocycline was discontinued and the patient was discharged with near-complete resolution of her headache, although some residual visual abnormalities persisted. One month following discharge, she continued to report episodes of blurred vision. Funduscopic examination revealed indistinct disc margins, and acetazolamide therapy was continued.

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Intracranial hypertension (IH), also known as pseudotumour cerebri, is characterized by increased intracranial pressure without evidence of an intracranial space-occupying lesion, hydrocephalus, infection or hypertensive encephalopathy. The pathogenesis of IH is not completely understood, but proposed mechanisms include increased CSF production, reduced CSF absorption by the arachnoid villi and increased brain volume owing to increased volumes of extravascular fluid.[1] Idiopathic intracranial hypertension is a diagnosis of exclusion that is typically made among obese but otherwise healthy females of reproductive age.[1] Among prepubescent children, both sexes are affected equally and the association with obesity is not as strong.[2–3] Secondary causes of IH (Table 1) are relatively common in the general population and include several common medical conditions, disorders that impair cerebral venous outflow and numerous medications.[1] The annual incidence of IH is about 0.9 per 100 000 in the general population, although the rate may be as high as 7.9 per 100 000 among obese females aged 15–44 years.[2]

Minocycline is a tetracycline derivative commonly used for the treatment of acne. Numerous case reports describe its association with intracranial hypertension. Although the incidence of IH with minocycline use is not known, it is presumably low given the widespread use of the antibiotic. This suggests that other risk factors and possibly a genetic predisposition may contribute to the development of IH in susceptible people taking minocycline.[4]

Headache, papilledema, enlargement of the blind spot and elevated CSF pressure are the most common clinical features associated with IH (Box 1).[5] A temporary episode of blindness may be a harbinger of impending visual loss, increasing the urgency of diagnosis and treatment. However, symptoms may be absent and papilledema may be discovered incidentally during examination.[4]

Idiopathic IH is usually self-limited; however, it may recur. Weight loss may be associated with improved clinical outcomes.[6] Treatment for secondary IH includes treatment of underlying disorders and discontinuation of any offending medications. Medical treatment often includes acetazolamide, a carbonic anhydrase inhibitor that reduces CSF production. In more severe cases, dexamethasone is sometimes added to

reduce intracranial pressure. Failure of medical therapy may necessitate serial lumbar punctures, ventriculoperitoneal shunting and optic nerve sheath decompression. The prognosis for visual abnormalities is generally good with rapid diagnosis and treatment; however, persistent visual deficits occur in about 25% of cases after treatment.[6-8] Although the early clinical course of IH does not reliably predict whether vision loss will persist, poor visual outcome has been associated with significant obesity.[5-7] The risk of permanent visual sequelae underscores the importance of maintaining a high index of suspicion for symptoms and signs of IH in patients taking minocycline or other associated medications.

Table 1: Secondary causes of intracranial hypertension

Cause	Examples
Obstruction of cerebral venous drainage*	Cerebral or jugular venous thrombosis
Medical conditions	Addison's disease
	Chronic obstructive pulmonary disease
	Cushing's disease
	Hypoparathyroidism
	Hypothyroidism
	Iron deficiency anemia
	Pulmonary hypertension
Medications	Anabolic steroids
	Cimetidine
	Corticosteroid withdrawal
	Growth hormone
	Levonorgestrel (including implant systems)
	Lithium
	Nalidixic acid
	Nitrofurantoin
	Retinoids (including isotretinoin and vitamin A)
	Tamoxifen
	Tetracycline derivatives

*Obstruction may result from a hereditary thrombophilia or from an acquired illness that predisposes to a hypercoagulable state (e.g., malignant disease, systemic lupus erythematosus).

Box 1: Common clinical features of intracranial hypertension

Associated symptoms

- Headache, sometimes associated with nocturnal awakening
- Reduced visual acuity
- Episodic visual obscuration
- Double vision
- Pulsatile intracranial noise, tinnitus
- Nausea, vomiting
- Depression, anxiety*

Physical signs

- Papilledema
- Enlarged blind spot
- Retinal hemorrhages
- Impaired lateral gaze (abducens palsy)

*Patients with intracranial hypertension may experience symptoms of depression and anxiety related to their physical symptoms, particularly headache and visual impairment.[10]

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