"Help, my headaches keep getting worse!"

Hayder Kubba, MBChB, LMCC, CCFP, FRCS(UK), DFFP, DPD

Alissa, 20, presents to my office to continue her isotretinoin treatment, which was started three months ago for her severe cystic acne.

She was very well informed about the isotretinoin side-effects and aware of the possible teratogenic effects. Also, she wanted to continue her monthly blood tests, which were ordered by her previous doctor.

Alissa was very happy with the isotretinoin results on her acne, despite some dry skin. However, she mentioned that she was bothered with diffuse worsening headaches that started about two months ago, woke her up at night on few occasions and were worse in the morning. The headaches were nonpulsatile, but associated with a perception of intracranial noise.

She was surprised that they got better as the day progressed, in spite of the stress of leaving her family and her physically demanding job. She denies any vomiting, but has increased nausea, which she thought was stress related. She also noticed bilateral double vision on lateral gaze. Her headache did not respond to the OTC treatment including acetaminophen and ibuprofen.

Her father takes anti-hypertensive medications, but otherwise her family is very healthy.

Apart from the isotretinoin, she has been taking minocycline MR 100 mg q.d. for the last nine months. She was advised to stop it when she was started on the isotretinoin, but she continued as she thought that the drug combination will help to clear her face quicker.

She is not on any birth control, is not aware that she is allergic to any medication and has never smoked.

Physical examination reveals that she is alert, fully-oriented and looks well. She is overweight at 82 kg and her height is 172 cm. There are no meningeal signs and her vital signs are normal.

Visual acuity was reduced on the left side (20/60), but her visual fields were full. She also has bilateral abducens palsies upon extreme lateral gaze. Her physical examination was otherwise normal.

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Initial investigations

The lab results revealed normal complete blood count (CBC), liver function tests, TSH, serum pregnancy test, creatinine and urinalysis.

What's your diagnosis?

a. Tension headache
b. Temporal arteritis
c. Migraine
d. Idiopathic intracranial hypertension

Figure 1. Lateral skull x-ray.

Figure 2. Sagittal brain CAT scan.

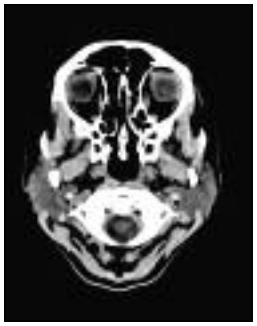

Figure 3. Sagittal brain CAT scan.

Answer: d. Idiopathic intracranial hypertension

Additional investigations

I was unsure about the reason for the headache, but was concerned about the possibility of increased intracranial pressure as her history was suggestive of that.

I repeated her blood tests adding erythrocyte sedimentation rate and calcium, which all came back normal.

I arranged an urgent brain CAT scan, which was unremarkable, with no evidence of a space-occupying lesion, hemorrhage or hydrocephalus.

I requested the local neurologist to see her on urgent basis after the normal CAT scan and he performed a lumbar puncture, which revealed a markedly elevated cerebrospinal fluid (CSF) pressure of > 55 cm water (normal level is < 20 cm). Alissa experienced significant improvement of her headache immediately after the lumbar puncture. A diagnosis of idiopathic intracranial hypertension (IIH) was made.

She was advised to stop the minocycline and was started on acetazolamide in a dose of 250 mg b.i.d. She was reviewed after a month and was doing very well with no further headaches. The acetazolamide was stopped and she was returned back to my care for further follow-up for her acne.

Dr. Kubba graduated from the University of Baghdad, where he initially trained as a Trauma Surgeon. He moved to Britain, where he received his FRCS and worked as an ER Physician before specializing in Family Medicine. He is currently a Family Practitioner in Mississauga, Ontario.

Making the case

The diagnosis criteria for IIH include the following:

- Symptoms and signs restricted to those of elevated intracranial pressure
- Normal findings on neuroimaging studies, excluding nonspecific findings of raised intracranial pressure
- Increased cerebrospinal fluid pressure with a normal composition

The pathophysiology of the disorder is unclear. A relative resistance to the absorption of cerebrospinal fluid across the arachnoid villi is widely presumed to be present. Other theories support an abnormality in the cerebellar circulation with a resulting increase in the brain's water content. The subsequent increase in the intracranial pressure is transmitted to the structures within the intracranial cavity, including the optic nerves.

The disease commonly occurs in women who are overweight. The role of obesity in this disorder is unclear. Obesity has been proposed to increase intra-abdominal pressure, which, in turn, raises cardiac filling pressures. This rise in pressure leads to impeded venous return from the brain (due to the valveless venous system that exists from the brain to the heart) with a subsequent elevation in intracranial venous pressure. If not treated appropriately, chronic interruption of the axoplasmic flow of the optic nerves with ensuing papilledema due to this pressure may lead to irreversible optic neuropathy.

Causes

Most cases of IIH occur in young women who are obese and, less frequently, in men who are otherwise healthy. Patients with higher BMIs and recent weight gain are at an increased risk for this disorder.

A myriad of illnesses are associated with IIH such as:

- anemia,
- chronic respiratory insufficiency,
- familial Mediterranean fever,
- hypertension,
- multiple sclerosis,
- polyangitis overlap syndrome,
- psittacosis,
- renal disease,
- Reye's syndrome,
- Sarcoidosis,
- systemic lupus erythematosus and
- thrombocytopenic purpura.

The list of exogenous substances associated with IIH is extensive and includes:

- Vitamin A and retinoids (including isotretinion)
- Minocycline and tetracycline
- Human growth hormone (incidence of up to 6.5 per 1,000 children)
- Other drugs include lithium, amiodarone and corticosteroid withdrawal

How to diagnosis

Brain CAT scan is needed to rule out structural lesion (space-occupying lesion) causing raised intracranial pressure. Typically, but not always, one would see slit-like ventricles, empty sella and flattening of posterior globe. MRI with magnetic resonance venography may be optimal to rule-out occult venous thrombosis as cause.

Treatment

Weight loss for obese patients is the only proven therapy, even mild reductions in weight can lead to improvements in signs and symptoms.

Any potentially offending medication should be discontinued. Acetazolamide should be started at 250 mg b.i.d. up to 1.5 g to 3 g q.d. (unless sulfa allergy). Warn patients about a change in taste or tingling of lips or extremities while taking this medication. Furosemide can be used as a second-line or adjunctive agent (or if sulfa allergy is present). Corticosteroids appear to work in some cases, but can also cause weight gain. Dx

Resource

1. Friedman DI, Jacobson DM: Diagnostic Criteria for Idiopathic Intracranial Hypertension. Neurology 2002; 59(10):1492-5.