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CLINICAL VIGNETTE

Doxycycline-induced Pseudotumor Cerebri

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Case Presentation

A 32-year-old female presented with daily headaches for 2 months, described as throbbing pain on the L temporal area, with photophobia, nausea and no fever. She has no numbness, weakness or vomiting. The headache improved temporarily with NSAIDs and sumatriptan.

She has a prior history of migraine 3-4 times a year, usually lasting for a few days but never more than 1 week. The pain responds to NSAIDs or sumatriptan. She has no other medical problems.

She has 2 children and family history of migraine in her mother and sister. She has been on doxycycline for 4 months for acne, does not smoke nor uses illicit drugs. She tries to avoid foods that trigger the migraine and drinks plenty of water, without improvement in headaches.

Her vitals are BP of 135/85 mm/hg, pulse 96, T 97 F, Weight 224 lb, height 162 cm, BMI 38. Exam including neurologic exam was normal except for bilateral papilledema. Because of papilledema, the patient was admitted to the hospital.

Labs included normal CBC, CMP, TSH, ESR, ANA.

MRI, MRA : normal

LP: revealed elevated opening pressure of 250 mmH₂O with normal cell count and protein.

The patient was diagnosed with Pseudotumor cerebri and her Doxycycline was held. She was started on acetazolamide and discharged on a low salt, weight reduction diet. On 2 week follow up the papilledema improved and headache gradually improved over 6 weeks. Acetazolamide was continued for 14 months, with monthly ophthalmology exams which have shown no permanent damage.

Discussion

Idiopathic intracranial hypertension (IIH) is also commonly called pseudotumor cerebri. It is defined by clinical criteria including symptoms and signs attributed to increased intracranial pressure, documented elevated intracranial pressure with normal cerebrospinal fluid composition, and no other cause of intracranial hypertension identified on clinical exam and neuroimaging.¹

The most common symptoms are headache, transient visual obscurations, intracranial noises (pulsatile tinnitus), photopsia, back pain, retrobulbar pain, diplopia, sustained visual loss.²

The annual incidence of IIH is 1 to 2 per 100,000 population.³ There is a higher incidence in obese women between the ages of 15 and 44 years old.⁴ Although IIH is, by definition, idiopathic, a number of systemic diseases, drugs, vitamin deficiencies and excesses, and hereditary conditions have been associated with IIH. However, patients with IIH do not have one of these conditions.

One of the medicines associated with IIH is the tetracyclines group. Minocycline and doxycycline have been linked to IIH, but other risk factors are often present.⁵ Tetracycline associated IIH often appears shortly after onset of treatment within a few weeks to months.

Diagnosis

Patients with headache and papilledema, undergo neuroimaging to exclude secondary causes of increased intracranial pressure.

Magnetic resonance imaging (MRI) with MR venography (MRV) is the preferred imaging and shows normal brain parenchyma without hydrocephalus, mass, structural lesion, or meningeal enhancement.

Elevated opening pressure on lumbar puncture (LP) is required to diagnose IIH long with normal cerebrospinal fluid (CSF) composition. For accurate pressure recording, the patient should be relaxed and lying in the lateral decubitus position with legs extended.¹

The goal of treatment of IIH is alleviation of symptoms, usually headache, some patients with normal vision and minimal symptoms require no treatment other than monitoring.⁶

Patients require regular follow-up until they are stable. Follow-up intervals are based on the severity, duration, and response to treatment, but initially should be at least monthly.

Indications that might cause or worsen IIH should be discontinued. However, this alone may not be sufficient to manage IIH. A low-sodium weight reduction program is recommended

for all obese patients with IIH and appears to alleviate symptoms and signs in many patients.⁷

Medical treatment for IIH typically starts with carbonic anhydrase inhibitors,⁸ but loop diuretics may also be used. Corticosteroids are not recommended for most patients with IIH.⁹ Iron supplementation in IIH patients with iron deficiency anemia was reported to be effective in a small case series of six patients.¹⁰

Indomethacin may be useful treatment of secondary intracranial hypertension¹¹ but further study is needed before it can be recommended in IIH.

Patients with IIH who fail, are intolerant to, or are non-compliant with maximum medical therapy with intractable headache or progressive visual loss may benefit from surgery. Optic nerve sheath fenestration, CSF shunting,¹² or venous sinus stenting are relatively new and somewhat controversial treatment options for IIH.

With treatment, there is usually gradual improvement and/or stabilization, but not necessarily full recovery. Many patients have persistent papilledema, or elevated intracranial pressure documented on lumbar puncture, and residual visual field deficits.

Permanent vision loss is the major morbidity associated with IIH.¹³ A recurrence of symptoms may occur in 8 to 38 percent of patients. Weight gain commonly precedes recurrent IIH.¹⁴

Our patient had two months of headache and a history of migraine, with papilledema on physical exam. MRI and MRA were normal. Because of papilledema, intracranial pressure was checked and was elevated.

The patient was morbidly obese which is associated with risk for IIH but recent doxycycline treatment was also a likely trigger factor.

Stopping Doxycycline and starting acetazolamide, significantly improved symptoms within 6 weeks.

Acetazolamide was continued for another 12 months and she lost 60 lbs in 12 months and she was free of any permanent eye damage.

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