Chapter 39

A Young Woman with a Changing Headache Pattern and Bilateral Papilledema

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Case History

S.G. is a 21-year-old young woman who presented to the emergency room for evaluation of headaches that she had had for 6 weeks. Her headaches were described as a global head pressure with a pulsatile pain behind both eyes. Along with the pulsatile pain, she was experiencing a pulsatile noise in her head. Her headaches had started gradually, with progressive worsening in their intensity. They were not made worse by any particular movements or activity. She was getting only minimal relief with the use of simple analgesics. In addition, she had intermittent horizontal diplopia on horizontal gaze in both directions. One day for a few hours, she reported having had some problems with her speech; that is, difficulties in finding her words and expressing herself in a fluent way. She had been seen in another hospital where a computed tomography (CT) scan of her head reportedly had been normal.

Since the age of 15 years, she had been prone to develop infrequent headaches of a few hours duration, usually associated at their onset with visual "sparkles." Those headaches were lateralized to either side of her cranium and were associated with nausea and vomiting. They were often active with her menses.

Her past medical history was quite unremarkable. She had been overweight for a number of years like many other members of her family. She had a regular menstrual cycle and had never been on any long-term medication. She was not taking any oral contraceptive.

Her general physical examination was unremarkable except for her obesity with a body mass index of 40. Her vital signs were normal. Her neurologic examination was normal including her speech and cognitive functions. Examination of her visual system showed normal extraocular movement, visual acuity, visual fields by confrontation, pupillary reflexes, and blind spots. She had bilateral swollen optic discs with blurring of their margins, concentric elevation of the discs, and retinal venous congestion.

Her general blood work was normal. A repeat CT scan of her brain was obtained and was reported as normal except for an empty sella turcica. A combined magnetic resonance imaging, magnetic resonance angiography, and magnetic resonance venography (MRV) scan of her brain confirmed the empty sella, with normal brain parenchyma, arterial system, and venous system. A hypoplastic right transverse sinus was documented but considered as an anatomic variant and probably not clinically significant.

Questions on the Case

Please read the questions, try to answer them, and reflect on your answers before reading the author's discussion.

- What are your diagnostic considerations at this point?
- Would you perform other investigations?

- Would you do a lumbar puncture (LP)?
- What treatment strategy would you favor?

Case Discussion

The only positive finding in this patient's neurologic examination was the presence of bilaterally swollen optic discs. In the absence of intraocular hypotony and in the context of normal visual acuity (abnormal with papillitis and central retinal arterial or venous thrombosis), the most common cause for bilaterally swollen discs is papilledema, and the predominant cause for papilledema is increased intracranial pressure. Increased intracranial pressure is often associated with headaches, but their absence does rule out increased intracranial pressure. In the case of this patient, although she had had previous infrequent headaches of the migraine type, her current headaches were of new onset and with a different pattern, raising the concern for a secondary headache disorder with increased intracranial pressure.

Her imaging studies had failed to document any space-occupying lesion or hydrocephalus to explain her state of raised intracranial pressure. An empty sella was reported. Empty sellae turcicae can be seen in association with usually longstanding intracranial hypertension. Chronically raised intracranial pressure seems to weaken the diaphragm sellae with subarachnoid herniation and progressive compression of the pituitary gland, with eventual enlargement of the sella turcica.

The clinical phenomenology and the imaging studies in this patient would fulfil all of the proposed diagnostic criteria for idiopathic intracranial hypertension (IIH), except for the absence of documented elevated intracranial pressure measured in lateral decubitus position with a normal cerebral spinal fluid (CSF) cytology and chemistry (Table 39-1).

Given the potential risks of tonsillar herniation or blindness (reversed optic disc herniation and optic nerve infarct) from an LP, can one avoid an LP in a context highly suggestive of isolated increased intracranial pressure presumably from IIH? Given that several causes can lead to secondary isolated increased intracranial pressure (Table 39-2), CSF cytology and chemistry should be documented using a small gauge LP needle, measuring the opening pressure, and removing the least necessary amount of CSF. If the lumbar CSF pressure taken with the patient in the lateral dorsal decubitus position is found to be elevated (200 mm H_2O in normal individuals and 250 mm H_2O in obese individuals) with normal CSF cytology and chemistry, then the appropriate blood work to rule out other secondary causes of isolated increased intracranial pressure should be obtained.

In the case of this patient, the initial LP showed a normal CSF cytology and chemistry, with an opening pressure in the lateral decubitus position at 370 mm H_2O. Her headache and pulsatile tinnitus improved after the procedure. Her parathyroid hormone, serum calcium, thyroid-stimulating hormone, free thyroxine, cortisol am, follicle-stimulating hormone, luteinizing hormone, insulin-like growth factor-1, estradiol, dehydroepiandrosterone-S, and androstenedione determinations had normal values. Her prolactin came back at 55.94 g/L (normal range, 0.0 to 30 g/L). Her elevated prolactin level was felt to be secondary to the increased intracranial pressure.

A diagnosis of IIH was confirmed. She was started on acetazolamide 500 mg bid.

A few days after the initial LP, the patient again became symptomatic with headache, pulsatile tinnitus, and upon

Table 39-1. Diagnostic Criteria for Idiopathic Intracranial Hypertension

I. Modified Dandy Criteria
1. Signs and symptoms of increased intracranial pressure (headaches, nausea, vomiting, transient obscurations of vision, papilledema)
2. No localizing neurologic signs otherwise, with the single exception being unilateral or bilateral nerve VI paresis
3. CSF can show increased pressure, but no cytologic or chemical abnormalities otherwise
4. Normal to small symmetric ventricles must be demonstrated (originally required ventriculography, but now demonstrated by CT)
II. International Headache Society Criteria (1988)
7.1.1 Benign intracranial hypertension
A. Patient suffers from benign intracranial hypertension fulfilling the following criteria:
1. Increased ICP (200 mm H_2O)
2. Normal neurologic examination except for papilledema and possible nerve VI palsy
3. No mass lesion and no ventricular enlargement on neuroimaging
4. Normal or low protein concentration and normal cell count in CSF
5. No clinical or neuroimaging suspicion of venous sinus thrombosis
B. Headache intensity and frequency related to variations of intracranial pressure with a time lag of less than 24 hours
III. IHS Diagnostic Criteria for Idiopathic Intracranial Hypertension (2004)
7.1.1 Idiopathic intracranial hypertension
A. Headache has at least one of the following characteristics: daily, diffuse, constant (nonthrobbing), aggravation by coughing or straining
B. Patient suffers from intracranial hypertension fulfilling the following criteria:
1. Alert patient with normal neurologic examination, except for possible papilledema (frequent), tinnitus (frequent), and nerve VI palsy (uncommon)
2. Increased CSF pressure (200 mm H_2O in the nonobese, 250 mm H_2O in the obese) measured by lumbar puncture or by epidural or intraventricular pressure monitoring
3. Normal CSF chemistry and cellularity
4. Intracranial diseases (including venous sinus thrombosis) ruled out by appropriate investigations
5. No metabolic, toxic, or hormonal cause of intracranial hypertension
C. Headache occurs in close temporal relation to increased intracranial pressure
D. Headache improves after withdrawal of CSF to reduce pressure to 120 to 170 mm H_2O or disappears within 72 hours of persistent normalization of intracranial pressure

CSF = cerebral spinal fluid; CT = computed tomography; ICP = intracranial pressure; IHS = International Headache Society.

Table 39-2. Causes of Secondary Isolated Increased Intracranial Pressure

1. Endocrine disorders
   a) Addison's and Cushing's diseases
   b) Hypoparathyroidism
   c) Hypothyroidism
2. Systemic diseases
   a) Chronic renal failure
   b) Iron deficiency anemia
3. Medications
   a) Vitamin A, retinoids
   b) Antibiotics: tetracyclines (minocycline), nalidixic acid, sulfa, nitrofurantoin
   c) Hormones or like: corticosteroids, anabolic steroids, tamoxifen, danazol, norplant
   d) Others: cimetidine, diphenylhydantoin, lithium, etc
4. Chronic meningitis
5. Cerebral venous sinus thrombosis, dural fistula

standing up she had brief visual blurring from her left eye. She had persistent papilledema with no hemorrhage. Her blind spots had remained normal in size, and her measured visual fields were normal. A repeat LP in the lateral decubitus position showed an opening pressure of 550 mm H_2O, with normal cytology and chemistry. Her acetazolamide dosage was adjusted to 500 mg tid, and she was started on furosemide 40 mg per day. She was advised to lose weight. Given her normal visual function, surgical procedures were not felt to be indicated at this point. Over the ensuing weeks, her headaches, pulsatile tinnitus, and visual obscurations resolved. There was also slow regression in her papilledema with retained normal visual fields.

Management Strategies

All possible secondary causes of isolated increased intracranial pressure should be ruled out (see Table 39-2).

Risk factors such as obesity, particularly in patients with a recent history of weight gain, should be treated vigorously. Indeed, weight loss has been associated with a more rapid resolution of papilledema and visual field recovery in patients with IIH.

Management of IIH should be based on the presence and progression of the visual loss. The routine testing with Snellen charts does not offer a high enough sensitivity to detect visual loss found by perimetry. Fundoscopic examination is certainly useful to document the presence of papilledema and to eventually follow its resolution, but in an individual patient, the severity of the visual loss cannot be predicted by the severity of the papilledema, since with the axonal loss from compression of the optic nerve head, the amount of papilledema tends to decrease. Goldman manual perimetry remains the most sensitive ophthalmologic evaluation tool to establish and follow the degree of visual loss in patients with IIH.

If no or mild visual loss (unlikely to be noticed by patient, but compromising visual function) is detected by perimetry, then treatment of IIH should be centered on the use of acetazolamide alone or in combination with furosemide. We usually use between 1,000 and 3,000 mg per day of acetazolamide, and if some progression in the visual loss is documented, we then add furosemide 40 to 80 mg per day. No randomized controlled trials are available to generate an evidence-based strategy in the treatment of IIH. Nonetheless, acetazolamide, a diuretic that reduces CSF production, has been shown to lower intracranial pressure when administered in doses of 2 to 4 g per day.

If moderate or severe visual loss (nearly always noticed by patient with significant interference with visual function) is detected at the time of diagnosis, or if despite medical treatment, there is progression of a mild visual deficit to a moderate one, then optic nerve sheath fenestration is recommended. Optic nerve sheath fenestration, in addition to effectively decompressing the optic nerve and protecting the visual function, offers many patients a temporary decompression of their CSF compartment.

At this stage of the disease, corticosteroids and/or repeated LPs have also been used. We rarely use corticosteroids, which could be associated with rebound papilledema and visual loss and worsening obesity. Corticosteroids have been shown in nonrandomized, noncontrolled studies to be effective in reducing intracranial pressure and preventing deterioration in the visual function. If they are to be used in specific cases, then patients should be treated with prolonged dose tapering.

We have infrequently used repeated LPs. Indeed, if no leak were created at the time of the LP, given the rate of formation of CSF, the decompressive effect of an LP would be very limited. Furthermore, in progressive cases of IIH, LPs may increase the risk of visual loss. Repeated LPs may be used in cases of no or mild visual loss when patients are intolerant to either acetazolamide or furosemide.

Lumboperitoneal shunts have long been used in the treatment of IIH. They are however not without complications, and they may not prevent the deterioration in visual function. They should probably be reserved for cases of persistent intractable headaches from IIH not responsive to medical therapy.

Case Summary

The patient was a 21-year-old young woman with a past history of infrequent headaches of the migraine without aura type, who presented with a changing headache pattern with bilateral papilledema. She had had a longstanding problem of obesity. Her investigations, aside from an increased pressure in her CSF compartment, disclosed no other abnormalities. A hypoplastic right transverse venous

sinus was documented on the MRV, but there were no signs of cerebral venous sinus occlusion or thrombosis. She was given a diagnosis of IIH. Given the absence of visual loss, she was treated medically with a weight reduction program, acetazolamide, and furosemide. Her symptoms and signs progressively resolved. Surgical management was not felt to be indicated.

Overview of Idiopathic Intracranial Hypertension

IIH has an annual incidence of 1 to 2 in 100,000 in the general population and 19 to 21 in 100,000 in young obese women, particularly between the ages of 21 and 34 years.

Headaches in IIH are commonly present (90%). They are often severe, daily, and pulsatile. Patients often complain of intense headache upon awakening, often exacerbated by Valsalva.

Next to headaches, visual obscurations and reduced visual acuity are commonly seen in IIH (72%), diplopia from nerve VI dysfunction comes next (23%), and pulsatile tinnitus has a variable incidence (0 to 80%). Pulsatile tinnitus, when present, appears to be an indicator of the activity of the condition, and often an early symptom of recurrence. Pulsatile tinnitus possibly reflects a hyperdynamic intracranial circulatory state.

The blackouts that occur with papilledema result from transient ischemia of the nerve head. They are described variously like "going into a darkened room" or like "a veil placed in front of the eyes." They are often bilateral, and often precipitated by head position or Valsalva maneuvers. Unlike the visual blackouts that come with central retinal artery ischemia that last for a few minutes, blackouts from IIH often last only for a few seconds. Visual obscurations are nonspecific and can be present in patients with IIH or elevated optic discs from other causes. Although reduced visual acuity or even loss of vision may be one of the consequences of IIH (25%), the presence of visual obscurations does not seem to have any specific prognostic significance for long-term visual acuity.

The term "idiopathic intracranial hypertension" was proposed in 1969 by Buchheit and colleagues as an alternate term for "benign intracranial hypertension." Indeed, benign intracranial hypertension, previously called pseudotumor cerebri, is often not so benign, with as much as 25% of the patients being left with functional blindness. The term IIH implies that once the secondary nontumoral and nonhydrocephalic causes of isolated increased intracranial pressure have been ruled out, then an element of unknown (idiopathic) is present, so far as the cause and pathogenesis of intracranial pressure increase in this syndrome goes.

Dandy in 1937 proposed a series of criteria for the diagnosis of intracranial pressure without brain tumor. These criteria were somewhat modified by Smith in 1985, and became known as The Modified Dandy Criteria. Others have also suggested diagnostic criteria for IIH. In 1988, the International Headache Society (IHS) recommended specific criteria for the diagnosis of benign intracranial hypertension. In 2004, the IHS produced a revised version of those criteria and adopted the term idiopathic intracranial hypertension (see Table 39-1).

With the advent of modern imaging techniques, more cases initially diagnosed as IIH have been associated with intracranial venous sinus thrombosis. In those cases, the increased intracranial pressure could possibly be explained from a partial blockage of CSF reabsorption through the arachnoid villae. If this was the only cause, however, hydrocephalus should be seen with all patients with IIH. On the contrary, slit-like ventricles have been reported not infrequently in association with IIH. Slit-like ventricles reflect an increase in the volume of the brain parenchyma, possibly secondary to an increase in the water content of the brain, as suggested by the presence of diffuse brain edema reported on some biopsy specimens and MR studies. Increased intracranial venous pressure may lead to a diffuse increase in the brain water content.

Increased intracranial venous pressure has been documented in patients with IIH. Obesity, often found in association with IIH, is known to increase intra-abdominal and intrathoracic venous pressure, thereby compromising cerebral venous return and perhaps maintaining the elevated intracranial venous pressure. That could lead to an increase in the intracranial cerebral blood volume, as suggested by some authors as a possible mechanism for IIH. However, obesity alone does not seem to increase the intracranial pressure in patients with normal MRV.

Using new sophisticated MR technology, recent studies have shown a consistent abnormality in more than 93% of the cases of IIH intracranial consisting of sinovenous obstruction, with only less than 7% of such obstruction being found in a control population.

The pathogenesis of IIH can therefore be viewed as a condition in which chronic interference with cerebral venous outflow leads to an increase in the cerebral blood volume, and consequently, in the water content of the cerebral parenchyma, with concomitant interference with CSF venous reabsorption leading to a synchronous pressure increase in the three intracranial compartments. Therefore, no shift in any of the intracranial compartments is to be expected, as observed in most IIH imaging studies.

The "incidental" hypoplastic right transverse sinus described in our patient may not be a trivial finding. It may represent a recanalized thrombotic obstruction with persistent cerebral venous outflow resistance, further worsened by the patient's obesity state.

Selected Readings

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Editorial Comments

Idiopathic intracranial hypertension continues to be an enigmatic disorder; however, as pointed out in this excellent review by Dr. Aubé, recent advances in neuroimaging are starting to provide valuable insights into its etiopathogenesis, particularly in relationship to the finding of sinovenous obstruction in most cases. This casts some welcome light on this entity, one that can also occur without papilledema. It is noted that CSF examination is part of the diagnostic criteria for IIH, especially to rule out secondary causes. However, caution and due diligence is required in performing this testing, and the use of a small bore needle, removal of small amounts of fluid, and testing in the lateral decubitus position seem reasonable, notwithstanding the concept that repeated LPs have been recognized to be a treatment of IIH for some time. The story of IIH, its mechanisms, and its management continue to evolve.

Final diagnosis:

Idiopathic intracranial hypertension