

# Graves' disease in an adolescent presenting with increased intracranial pressure and bilateral papilledema

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## Summary

Increased intracranial pressure (ICP) can present with symptoms of headache, vomiting, visual changes, and tinnitus. Papilledema may be seen on physical exam. Thyroid disease has been a rare secondary cause of increased ICP. We present a 16-year-old female who had a worsening headache for 6 months. She was found to have signs, symptoms, physical exam findings, and diagnostic studies consistent with both increased ICP and previously undiagnosed Graves' disease. The patient was treated with a 19-month course of methimazole 40 mg daily. Her headache and papilledema resolved shortly after medication initiation. The timeline of symptoms and resolution of her increased ICP symptoms with treatment of Graves' disease suggests that hyperthyroidism was the underlying cause of her increased ICP. Clinicians should consider Graves' disease as the etiology in pediatric patients presenting with signs and symptoms of increased ICP with papilledema.

## Learning points:

- Symptoms of increased intracranial pressure (ICP) include headache, vomiting, transient visual changes, and tinnitus.
- Secondary causes of increased ICP should be considered in males, young children, older patients, and those not overweight.
- Clinicians should consider Graves' disease as the etiology in pediatric patients presenting with signs and symptoms of increased ICP with papilledema. They should assess for orbitopathy and thyromegaly and inquire about symptoms that would be indicative of hyperthyroidism.

## Background

Idiopathic intracranial hypertension (IIH), also known as Pseudotumor Cerebri, is a condition diagnosed using the Dandy criteria. These criteria include increased intracranial pressure (ICP) but normal cerebrospinal fluid (CSF) analysis, signs and symptoms of increased ICP, unremarkable neurologic exam except for occasional cranial nerve VI palsy, unremarkable imaging studies, and no other cause of increased ICP. IIH is most often seen in obese women of childbearing age with an average age of

31 years old. Secondary causes of increased ICP should be considered in males, young children, older patients, and those not overweight (1, 2). Signs and symptoms of increased ICP include headache, vomiting, transient visual changes, and tinnitus. Papilledema is almost always present in adults but is less commonly observed in children and adolescents. Brain tumors should especially be ruled out before diagnosing IIH in the pediatric population. Brain tumors may present with a constant headache that



is worse in the morning, seizures, focal neurologic deficits, and changes in behavior (3, 4, 5).

A secondary cause of increased ICP is identified in most cases of IIH seen in the pediatric population, whereas secondary causes are less frequently identified in adults (4). Common secondary causes include medications (e.g. tetracyclines, vitamin A, corticosteroids, indomethacin, and phenytoin) and systemic diseases (e.g. anemia, multiple sclerosis, chronic kidney disease, sarcoidosis, and systemic lupus erythematosus) (3). Both hyperthyroidism and thyroid hormone replacement for hypothyroidism have rarely been linked to increased ICP (6). Only a handful of cases of increased ICP secondary to Graves' disease have been reported. Fewer have been reported in those under the age of 18 (6). Symptoms of Graves' disease include nervousness, palpitations, sweating, heat intolerance, weight loss, fatigability, and increased bowel movements (7). Other endocrine etiologies reported in children include corticosteroid withdrawal, primary adrenal insufficiency, and recombinant growth hormone replacement (4).

We describe an adolescent with no significant past medical history who was found to have signs and symptoms of increased ICP that was believed to be secondary to undiagnosed Graves' disease – a rare potential cause.

## Case presentation

A 16-year-old nonpregnant female, noted only to have a past medical history of asthma, presented to her general practitioner complaining of a worsening headache over the last 6 months. Her family history was notable of her mother having hyperthyroidism. The patient denied alcohol, tobacco, or illicit drug use. The patient was referred to optometry for an eye exam and was found to have significant bilateral papilledema with normal visual acuity. MRI of the brain with and without contrast revealed no acute intracranial process, concerning findings, or enhancing lesions. MRI of the orbits with and without contrast revealed no acute pathology. Neurosurgery was consulted to perform a diagnostic and therapeutic lumbar puncture. Opening pressure was found to be elevated at 33 cm of water. After draining 15 mL of clear spinal fluid, the final pressure was 18 cm of water. Lumbar puncture transiently alleviated her symptoms. The patient was noted to have thyromegaly at the time of the lumbar puncture and was referred to endocrinology.

Evaluation by endocrinology 2 days post-lumbar puncture revealed a history of heat intolerance, tremors, diaphoresis, palpitations, increased frequency of bowel movements, and neck soreness without dysphagia over the

last several months. Physical exam revealed an enlarged thyroid, sweaty palms, and tremor; the patient had no focal neurologic deficits, orbitopathy, skin changes, or mood changes. Vital signs included BMI-for-age in the 86th percentile, blood pressure of 123/79 mmHg, and heart rate of 117 per minute.

## Investigation

Thyroid ultrasound revealed an enlarged, heterogeneous, and hypervascular goiter. Laboratory findings showed increased thyrotropin receptor antibodies (TRAb) (39.10 IU/L, normal range 0.00–1.75), suppressed thyroid-stimulating hormone (TSH) (<0.015 uIU/mL, normal range 0.47–4.68), increased free T4 (6.32 ng/dL, normal range 0.78–2.19), and free T3 (30.3 pg/mL, normal 2.3–5.0). A diagnosis of Graves' disease was made.

## Treatment

Methimazole 40 mg PO daily and atenolol 25 mg PO daily were initiated.

## Outcome and follow-up

Her headache completely resolved within 2 weeks of initiating methimazole. Papilledema was no longer present when evaluated by the optometrist about 3 weeks after initiating methimazole. Methimazole was eventually discontinued after about 19 months of therapy due to being clinically and biochemically euthyroid (TSH 2.63 uIU/mL, free T4 1.08 ng/dL, and free T3 3.1 pg/mL) and TRAb being undetectable. At the most recent follow-up about 6 months after discontinuing methimazole, the patient continued to be asymptomatic. Her thyroid function tests remained normal, and TRAb remained undetectable, indicating remission of Graves' disease.

## Discussion

With essentially no past medical history, our patient presented with signs and symptoms of both increased ICP and Graves' disease for about 6 months. The patient's symptoms only transiently improved with a lumbar puncture. The patient was diagnosed with Graves' disease based on history and physical exam combined with laboratory and imaging studies. Pharmacologic treatment with methimazole was initiated; the patient did not receive acetazolamide, mannitol, topiramate, or methylprednisolone (4). One of the drawbacks of this case



report was the lack of CSF analysis being performed at the time of the lumbar puncture. However, the timeline of symptoms and resolution of her increased ICP symptoms with treatment of Graves' disease is strongly indicative that hyperthyroidism was the underlying cause of her increased ICP.

The mechanism behind IIH in Graves' disease is unknown. Thyroxine contributes to sodium transport and likely decreases the driving pressure gradient of CSF from the subarachnoidal space to the venous system – thus impeding CSF absorption. Alternatively, the increased ICP leads to increased central venous sinus pressure and arachnoid villi compression causing decreased CSF absorption. Hence, hyperthyroidism can theoretically contribute to the increased ICP as seen in our patient (3, 4, 5).

Unlike adults, most cases of IIH in juveniles have an identifiable secondary cause. Clinicians should consider Graves' disease as the etiology in pediatric patients presenting with signs and symptoms of increased ICP with papilledema. They should assess for orbitopathy and thyromegaly and inquire about symptoms of nervousness, palpitations, sweating, heat intolerance, weight loss, fatigability, and increased bowel movements.

#### Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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#### Patient consent

Written informed consent for publication of their clinical details and/or clinical images were obtained from the patient/parent/guardian/relative of the patient.

#### Author contribution statement

Both J N and D J substantially contributed to the drafting of this manuscript, including surveying the literature, identifying relevant articles, and incorporating supporting comments. D J provided details about the patient's clinical presentation and course of treatment. J N and D J have read and approve the final manuscript and agree to the journal's submission policies. The authors would like to thank Dr. Kristen Gilbert, MD and Dr. Piyush Patel, MD for offering constructive feedback.

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