1 Poor Growth With Presence of a Pituitary Lesion in an 11-year-old Boy

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EDITOR'S NOTE

Beginning with our January 2017 issue, *Pediatrics in Review* will publish three additional Index of Suspicion cases each month. All cases will be available in their entirety online, but only the Presentation for each case will be published in the print edition of the journal. We anticipate the move to online will encourage authors to use more images and video in their case submissions.

PRESENTATION

An 11-year-old boy presents to his primary pediatrician due to poor growth. His height was at the 25th percentile between ages 6 and 10 years and now has fallen to the 10th percentile. He also complains of fatigue and has a 1-month history of polyuria, polydipsia, and nocturia. Review of symptoms is negative for weight loss, headaches, vision changes, gynecomastia, breast discharge, nausea, vomiting, and cold and heat intolerance. His past medical and family histories are not contributory and his development has been normal.

On physical examination, his temperature is 96.8°F (36°C), blood pressure is 86/52 mm Hg, heart rate is 59 beats/min, respiratory rate is 18 breaths/min, and oxygen saturation is 100% in room air. His standing height is 138.23 cm (10th percentile), weight is 31.5 kg (10th percentile), and body mass index is 16.5 (10th-50th percentile). His neurologic examination yields unremarkable results. His pubic hair is at Sexual Maturity Rating stage 2 and testicular volume of both testes is 10 mL.

Laboratory evaluation shows free thyroxine (T4) of 0.76 ng/dL (9.78 pmol/L) (normal range 0.93-1.60 ng/dL [11.97-20.59 pmol/L]), total T4 of 4.3 μg/dL (55.35 nmol/L) (normal range 4.5-12 μg/dL [57.92-154.45 nmol/L]), thyrotropin (TSH) of 1.97 mIU/L (normal range 0.45-4.5 mIU/L), and insulinlike growth factor (IGF-1) of 103 ng/mL (13.49 nmol/L) (normal range for an 11-year-old male: 112-454 ng/mL [14.67-59.47 nmol/L]). His complete blood cell count, urinalysis results, and electrolyte values are within normal limits, and his evaluation for celiac disease is negative. Due to these results, the pediatrician orders magnetic resonance imaging (MRI) of the pituitary, which shows a lesion within the

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We invite readers to contribute Index of Suspicion cases through the PIR manuscript submission system at: https://mc.manuscriptcentral.com/pir.

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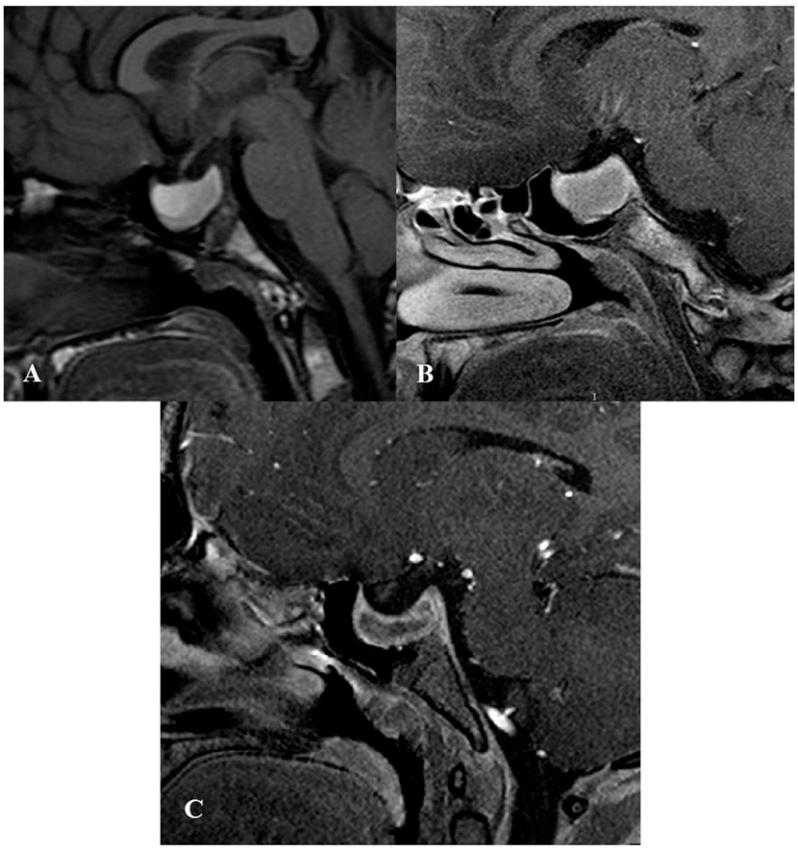

Figure. A and B. Initial magnetic resonance imaging of the brain showing a pituitary mass within the sella and suprasellar cistern. C. Pituitary mass 3 months after therapy.

sella and suprasellar cistern. The greatest vertical, anterior-posterior, and transverse diameters of this lesion measure 19, 21, and 25 mm, respectively (Fig).

The Case Discussion and Suggested Readings appear with the online version of this article at http://pedsinreview.aappublications.org/content/38/1/44.

DISCUSSION

The patient underwent imaging immediately after initial results became available, without further referrals or additional laboratory evaluation. Clinicians could have considered referral to pediatric endocrinology before proceeding with imaging to evaluate pituitary function with further tests. However, the presence of low free T4 with normal TSH and low IGF-1 values suggested central hypothyroidism and growth hormone deficiency, which justify the decision for pituitary imaging, especially taking into consideration the patient's symptomatology.

The patient was subsequently referred to neurosurgery for trans-sphenoidal resection of the pituitary mass that was suspected to be a craniopharyngioma. Before the scheduled surgery, the patient's family asked for a second opinion. Although a prolactinoma was considered as a possibility for his pituitary tumor, his prolactin values had never been measured. Therefore, the biochemical evaluation was repeated, and the prolactin measurement was added. His prolactin was found to be substantially elevated at 996 μg/L (43,304.09 pmol/L) (normal range 2-25 μg/L [86.96-1,086.95 pmol/L]), which led to the diagnosis of a prolactin-secreting macroadenoma.

Differential Diagnosis

Craniopharyngiomas are the most common pituitary tumors in children, accounting for approximately 90% of all pituitary neoplasms and 6% to 13% of all intracranial tumors. Pituitary adenomas are rare and account for less than 3% of all supratentorial tumors, with prolactinomas being the most common (48%-52%). Other conditions that could present with similar symptoms and lesions on imaging studies are cystic lesions, such as Rathke cleft cysts, teratomas, or ependymomas, and even more rarely blastomas, germ cell tumors (50% of which are usually germinomas), and metastases from other primary tumor locations (a relatively common event in adult patients with pituitary tumors but very rare in children).

Taking into consideration the fact that our patient did not present with galactorrhea or any neuro-ophthalmologic signs, which may occur in a boy with a prolactinoma, craniopharyngioma or another cystic lesion was considered as the most likely initial diagnosis. In addition, the noncontrast MRI showed a nonhomogeneous appearance of the tumor with an enhancing spot, which is more characteristic of a craniopharyngioma. However, most probably this was due to hemorrhage because it completely resolved in subsequent imaging studies.

The Condition

Prolactinomas are the most common hormone-secreting pituitary tumors and have been reported to occur at all ages. In girls with prolactinomas, microadenomas are encountered more frequently, and their clinical presentation is associated with galactorrhea and hypogonadotrophic hypogonadism. Interestingly, males have a greater incidence of macroadenomas, which can cause neuro-ophthalmologic signs and symptoms. Prolactinomas in adult males have been associated with hypopituitarism, with the most common form being growth hormone deficiency and hypogonadism; hypocortisolism is less common. The diameter of the adenoma and its prolactin secretion have been shown to affect the degree of both hypogonadism and hypothyroidism.

Diagnosis of a prolactinoma requires both the laboratory results of persistent hyperprolactinemia and imaging studies showing an adenoma. Prolactin values can be related to the size of the tumor. Most patients with prolactin concentrations greater than 150 μg/L (6,521.70 pmol/L) (normal range 2-25 μg/L [86.96-1,086.95 pmol/L]) have a prolactinoma, but clinicians cannot rule out prolactinoma if the prolactin values are only moderately increased. The abnormal expression of genes such as the pituitary tumor-transforming gene (*PTTG*) and high mobility group A2 gene (*HMGA2*) has been associated with the development of pituitary tumors, including prolactinomas.

Management

Prolactinomas are treated conservatively with dopaminergic agonists as the initial therapy of choice to shrink the pituitary mass. Such treatment offers the best chance for normal pubertal development, gonadal function, and future fertility. Surgery (usually with a trans-sphenoidal approach) is only performed in cases of drug therapy failure or for neurosurgical emergencies such as apoplexy. Radiotherapy is very rarely used and only after failed medication therapy and/or surgery.

Patient Course

The patient was started on 0.5 mg cabergoline, a dopamine receptor agonist that blocks prolactin secretion from the pituitary gland, twice a week and 25 μg levothyroxine once daily. After 1 month of cabergoline treatment, his prolactin concentrations had substantially decreased to 15.1 μg/L (656.52 pmol/L). During his follow-up evaluation 3 months later, the pituitary MRI showed a decrease in the size of the adenoma (1.6 × 1.7 cm) (Fig 1C), the prolactin values dropped to 5.5 μg/L (239.12 pmol/L), and his thyroid hormones and IGF-1 values returned to normal range. He had grown 1.2 cm during those 4 months, and his puberty had progressed, with more pubic hair and increase in testicular size. Use of cabergoline, especially long-term, has been associated with mild-to-moderate tricuspid regurgitation and subtle changes in cardiac valves such as calcifications,

thickening, and increased mitral tenting. Because of this concern for potential cabergoline-associated valvulopathy, baseline echocardiography was also performed and results were normal.

Lessons for the Clinician

- Patients with prolactinomas do not always present with characteristic clinical manifestations.
- Prolactin must be measured in all patients suspected to have a pituitary mass, even if the patient does not present with typical clinical manifestations of prolactinoma.
- A proper diagnosis of pituitary mass lesions can avoid unnecessary surgery and/or radiotherapy and, thus, reduce morbidity and mortality.

Suggested Readings

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