Pituitary Incidentaloma

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Brian, 46, is referred to endocrinology for evaluation of a pituitary "mass." The mass was an incidental finding of head and neck CT performed three months ago, when Brian went to an emergency department following a motor vehicle accident. He has fully recovered from the accident and feels well. He describes himself as a "completely healthy" person who has no chronic medical conditions and takes neither prescription nor OTC medications.

Brian denies significant headache, visual disturbance, change in appetite, unexplained weight change, skin rash (wide purple striae) or color changes (hyperpigmentation), polyuria or polydipsia, dizziness, syncopal episodes, low libido, erectile dysfunction, joint pain, and changes in ring or shoe size. He does not wear a hat or cap and is unaware of head size changes. He has not experienced changes in his facial features or trouble with chewing.

He is a happily married engineer with two healthy children and reports that he feels well except for this "brain tumor" finding that has been a shock to him and his family. There is no family history of pituitary adenoma or multiple endocrine neoplasia syndrome.

His vital signs, all within normal ranges, include a blood pressure of 103/65 mm Hg. His height is 6 ft and his weight, 180 lb. His BMI is 24.4.

TABLE
The Patient's Lab Test Results

Study	Value (reference range)
Prolactin	7 ng/mL (2-18)
Growth hormone	< 1 ng/mL (< 10)
Insulin-like growth factor 1	128 ng/mL (52-328)*
Adrenocorticotropic hormone	15 pg/mL (6-50)
Early-morning cortisol	14 μg/dL (5-23)
TSH	1.87 mIU/L (0.4-4.5)
Free T4	1.3 ng/dL (0.8-1.8)
Luteinizing hormone	4.2 mIU/mL (1.5-9.3)
Follicle-stimulating hormone	5.7 mIU/mL (1.6-8.0)
Total testosterone	493 ng/dL (250-1100)

* Z score, –0.2

HOW COMMON IS PITUITARY INCIDENTALOMA?

A pituitary incidentaloma is a lesion in the pituitary gland that was not previously suspected and was found through an imaging study ordered for other reasons. Pituitary incidentaloma is surprisingly common, with an average prevalence of 10.6% (as estimated from combined autopsy data), although it has been found in up to 20% of patients undergoing CT and 38% undergoing MRI.[1,2] Most are microadenomas (< 1 cm in size).[1]

SHOULD AN ASYMPTOMATIC PATIENT BE EVALUATED FURTHER?

Endocrine Society guidelines[2] recommend that all patients with pituitary incidentaloma, with or without symptoms, should undergo a complete history and physical examination and laboratory evaluation to exclude hypersecretion and hyposecretion of pituitary hormones.

The "classic" presentation of pituitary hormone hypersecretion—in the form of prolactinoma, adrenocorticotropic hormone (ACTH) excess (Cushing disease), growth hormone (GH) excess (gigantism/acromegaly), and TSH excess (secondary hyperthyroidism)—may be readily detectable on history and physical examination. Subtle cases, so-called *subclinical disease*, however, may exhibit little or no signs and symptoms initially but can be detrimental to the patient's health if left untreated. For example, the estimated time from onset to diagnosis of acromegaly is approximately seven to 10 years—a delay that can significantly impact the patient's morbidity and mortality.[3]

Prolactinoma can be more clinically apparent in premenopausal females due to irregular menstrual cycles (oligomenorrhea/amenorrhea). However, galactorrhea, or "milky" nipple dis-

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charge, occurs in only about 50% of women with prolactinoma and is extremely rare in men. Furthermore, the clinical presentation of prolactinoma in men is vague and related to hypogonadism, resulting from increased prolactin levels. Since men are essentially asymptomatic, these tumors can grow extensively (macroadenoma) and cause "mass effect," such as headaches and visual impairment.

Therefore, without laboratory testing, abnormal pituitary function may go unrecognized.

WHAT LABS SHOULD I ORDER FOR THIS PATIENT?

Guidelines suggest an initial screening panel of prolactin, GH, insulin-like growth factor 1 (IGF-1), ACTH, early-morning cortisol, TSH, free T4, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone.[2]

Note the use of "suggest" rather than "recommend." Even among guideline task force members, there were differences in opinion as to whether certain tests (eg, TSH, LH, and FSH) should be included in initial screening. Those tests can be ordered at the clinician's discretion, according to the level of suspicion, or can be added later if necessary.

Brian's sample for laboratory testing is drawn at 7:50 AM. Results can be found in the table (previous page).

ARE THERE ANY CAVEATS TO THE INTERPRETATION OF LAB VALUES?

It is important to note that in postmenopausal women who are not taking hormone replacement therapy, LH and FSH will be elevated and estradiol may provide an additional clue in the detection of abnormal function. Conversely, low LH and FSH in postmenopausal women should raise a flag for hypopituitarism.

Another caveat is that GH secretion is pulsatile and serum levels are undetectable between pulses. Therefore, low/undetectable GH does not necessarily suggest deficiency. The GH measurement would only be helpful if it is significantly elevated (suggestive of hypersecretion—gigantism/acromegaly). Otherwise, GH has little value as a screening test.

Instead, IGF-1, which is secreted from the liver in response to GH secretion, has a longer half-life and serves as a better screening tool. IGF-1 has age- and sex-adjusted reference ranges, which are often reported by the lab or given as a Z score.

WHAT IS THE PREFERRED IMAGING STUDY FOR THE PITUITARY GLAND?

The best choice is MRI of the pituitary gland (not the whole brain) with gadolinium. If the incidentaloma was initially diagnosed by a CT, additional testing with MRI should be performed, unless contraindicated.[2]

Brian is referred for MRI with gadolinium. The radiologist's report describes a 5 x 4 x 4–mm pituitary microadenoma without sellar extension or involvement of the optic chiasm.

AT WHAT POINT SHOULD OPTIC CHIASM BE A CONCERN?

Since the pituitary gland is located directly beneath the optic chiasm, any compressive effect of growth against the optic nerve(s) can cause visual impairment. This includes bitemporal hemianopsia (loss of peripheral vision) or ophthalmoplegia (abnormal movement of the ocular muscle). Since clinical signs and symptoms can be subtle or absent, all patients with evidence of a pituitary lesion abutting or compressing the optic chiasm should have a formal visual field exam.[2]

WHO REQUIRES SURGICAL INTERVENTION?

Patients with mass effect (headache, increased intracranial pressure, compromised optic chiasm) and those with hyperfunctioning nonprolactin adenomas, some (but not all) macroprolactinomas, or pituitary apoplexy should be referred for surgery.[2] Almost all cases involve macroadenomas rather than microadenomas.

The preferred treatment for GH-secreting tumors and ACTH-secreting tumors is surgery. However, prolactinoma can be well controlled with pharmacologic agents (dopamine agonists) in most cases. For prolactinomas refractory to these medications, surgical resection is recommended. (Detailed treatment approaches are available elsewhere; those for hyperprolactinoma can be found on the *Clinician Reviews* website: http://bit.ly/1HOb9Jf.)

Pituitary apoplexy, a life-threatening emergency that requires prompt surgical decompression, is an infarction of the gland due to abrupt cessation of the blood supply, caused by either pituitary artery hemorrhage or sudden hypovolemia. Increased blood supply is needed due to the extra tissue and volume of the pituitary mass; this may stress the pituitary arteries, which are not equipped for this increased flow, causing them to rupture. Hemorrhage anywhere else in the body can lead to hypovolemia and decrease the blood supply to the

pituitary gland. A classic example would be postpartum hemorrhage causing pituitary infarct, called *Sheehan syndrome*.

Due to increased estrogen levels, the pituitary gland doubles in size during pregnancy.[4] A preexisting mass may further develop and compress the optic chiasm. Therefore, women of childbearing age should be engaged in discussion of the potential risks and benefits of decompression surgery before actively pursuing pregnancy—especially if the lesion is close to the optic chiasm.

Surgery can also be considered for patients with significant growth in adenoma size during monitoring, loss of endocrinologic function due to mass effect on other pituitary cells, or unremitting headache.[2]

HOW SHOULD PATIENTS BE MONITORED?

Those who do not meet criteria for surgery can be closely monitored with periodic testing. Imaging can be repeated six months after the first scan for macroadenoma and in one year for microadenoma. If there is no change in the size of the mass, imaging can be done yearly for macroadenoma and for microadenoma, every one to two years for three years and then gradually less often thereafter.[2]

Unless the lesion is abutting the optic chiasm (seen via imaging) or the patient reports symptoms, visual field testing does not need to be repeated.

Lab testing should be repeated six months after initial testing for macroadenoma and yearly thereafter. No further testing is suggested for nonsecretory microadenoma, unless clinically indicated.[2]

If there are any changes in status—noted clinically or via imaging—more frequent testing is suggested.

Brian is reassured that pituitary adenoma is not an uncommon finding and that his adenoma is relatively small in size and nonsecretory. Repeat pituitary MRI in one year is recommended.

CONCLUSION

Most pituitary incidentalomas have no consequences to a patient's health. However, patients often become highly anxious about the "brain tumor" they were told they have. Appropriate patient education and thorough evaluation can reassure patients and alleviate their concerns. **CR**

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