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Pituitary Tumors - Overview

Introduction: Pituitary tumors and related growths that arise around the pituitary gland are relatively common. The most common of these are pituitary adenomas, followed by Rathke's cleft cysts (RCCs) and craniopharyngiomas. Fortunately, these three tumors types are almost always non-malignant (benign). However, given their location they can cause significant health problems and disability including abnormal pituitary gland hormonal function, vision loss, headaches and bleeding in or around the pituitary gland. Pituitary tumors are best diagnosed by imaging studies, typically a magnetic resonance imaging (MRI) or computer tomography (CT) scan of the brain and pituitary, as well as pituitary hormonal blood tests. The treatment and management of pituitary tumors is usually coordinated by a neurosurgeon and an endocrinologist because the majority of patients with a symptomatic pituitary adenoma, RCCs or craniopharyngioma, will warrant surgical removal of the tumor, and many patients will also have pituitary hormonal problems before and possibly after surgery. The preferred route for removing almost all adenomas, RCCs, and many craniopharyngiomas is through the endonasal transsphenoidal route (through a nostril without facial or lip incisions) as opposed to a craniotomy (surgical removal of a section of the skull, called a bone flap, to access the brain) which is used for removing most other brain tumors. Some types of pituitary adenomas can also be treated with medications to shrink the tumor and lower abnormally elevated hormone levels. Additionally, some pituitary adenomas and craniopharyngiomas that cannot be completely removed surgically are effectively treated with radiotherapy, in which special equipment is used to provide precise dosage of radiation directly to the tumor, either by stereotactic radiosurgery (SRS - one dose) or stereotactic radiotherapy (SRT - multiple doses).

Pituitary Adenomas

Pituitary adenomas are by far the most common growth associated with the pituitary gland; they account for 15-20% of primary brain tumors and are the third most common intracranial tumor after gliomas and meningiomas. Over 99% of pituitary adenomas are benign (not malignant) and are relatively slow growing. From autopsy studies and magnetic resonance imaging (MRI) scans of normal individuals, it is known that 10-20% of the general population has a pituitary adenoma. Most of these tumors remain small and do not cause the patient significant harm or symptoms. However many progress and grow to cause major hormonal and neurological problems.

Adenomas are classified by size and whether they produce pituitary hormones; those less than 1 cm in diameter are called microadenomas, those over 1 cm in diameter are called macroadenomas. Adenomas that make excess hormones (endocrine-active adenomas) include prolactin secreting adenomas known as prolactionomas, adrenocorticotropic hormone (ACTH) secreting adenomas causing Cushing's disease, growth hormone (GH) adenomas causing acromegaly, and the least common endocrine-active adenoma, thyroid stimulating hormone (TSH) secreting adenomas causing hyperthyroidism. Adenomas that do not make excess hormones are called endocrine-inactive or non-functional adenomas.

Most adenomas are not genetically inherited and cases of familial pituitary tumors are rare. Multiple Endocrine Neoplasia (MEN) type I accounts for less than 5% of cases of pituitary adenomas. This autosomal dominant condition is characterized by multiple and sometimes simultaneous tumors of the pituitary, pancreas and parathyroid glands. Pituitary adenomas develop in 25% of patients with MEN I.

Pituitary adenomas may cause problems because of hormonal hypersecretion, pituitary hormonal failure, vision loss, headaches and/or bleeding.

Symptoms

Hormonal hypersecretion: The three most common hormonally active adenomas are prolactinomas, GH-secreting tumors causing acromegaly, and ACTH-secreting tumors causing Cushing's disease. Thyroid stimulating hormone (TSH) tumors are relatively rare.

Pituitary failure (hypopituitarism): This problem typically occurs only with macroadenomas and results from progressive compression and damage to the normal pituitary gland. Manifestations may include hypogonadism (sexual dysfunction, loss of libido, and impotence), hypothyroidism (fatigue, weakness, weight gain, coarse dry hair and dry skin, cold intolerance, depression), adrenal insufficiency (fatigue, weakness, loss of appetite, dizziness, nausea and vomiting), growth failure

(in children and adolescents), hyperprolactinemia due to "stalk effect" (seen in diseases within or near the pituitary gland and stalk, interfering with the delivery of dopamine, a neuron-transmitter, from the hypothalamus to the prolactin secreting cells of the pituitary gland), which can result in hypogonadism and its associated problems. Rarely posterior pituitary gland damage occurs with diabetes insipidus, which is caused by the inability of the kidneys to conserve water leading to frequent urination and thirst.

Neurological problems: The most common neurological problems from a pituitary macroadenoma are loss of visual acuity and loss of peripheral vision termed a bitemporal hemianopsia. This visual loss results from pressure on the optic nerves and optic chiasm which is directly above the pituitary gland. Visual loss is typically seen only with larger macroadenomas (> 1 - 2 cms in size). Macroadenomas may on occasion also result in ocular palsies (double vision).

Headache: Typically headaches are seen in patients with macroadenomas and they are usually located in the frontal/ forehead and temporal area.

Bleeding (pituitary apoplexy): This condition develops over hours to several days from hemorrhage and/or infarction of a macroadenoma. Symptoms may include headache, nausea, visual loss, double vision and confusion. Most patients have undiagnosed hormone insufficiency prior to the apoplectic event. Pituitary apoplexy is best confirmed with an MRI of the brain and pituitary. A head CT scan will also show an abnormality in the majority of cases. Other conditions to consider that might mimic pituitary apoplexy are a ruptured aneurysm, meningitis, a stroke, intracerebral hemorrhage and migraine headache.

Diagnosis

Pituitary adenomas are best diagnosed by imaging studies and hormonal testing.

Imaging: The imaging study of choice is an MRI of the pituitary gland performed without and with gadolinium (a contrast agent). A brain MRI or CT scan will also reveal most pituitary macroadenomas but may not reveal smaller microadenomas. In a minority of patients it may be difficult to distinguish an adenoma of the pituitary from other masses which may include Craniopharyngioma, Rathke's Cleft Cyst, Meningioma, Hypophysitis (pituitary inflammation), Glioma of the suprasellar region, Metastatic tumor or Chordoma.

Hormonal Testing: Evaluation of pituitary gland function either for under-production (hypopituitarism, or pituitary failure) or over-production of hormones should include an assessment of ACTH levels, cortisol, TSH, free T4 (thyroid function), LH (luteinizing hormone), FSH (follicle-stimulating hormone), estradiol in women, testosterone in men, GH (growth hormone), IGF-1 (insulin-like growth factor, growth hormone's target hormone, also known as somatomedin-C), and prolactin. Given that some of these tests need to be preformed at a certain time of the day, and additional tests may be needed to diagnose an endocrine-active tumor such as with Cushing's disease or acromegaly, such testing is best overseen by an endocrinologist.

Ophthalmological Evaluation: Patients with a macroadenoma and visual complaints should receive a full ophthalmological evaluation. This evaluation should include acuity (vision quality) testing of each eye and formal visual field testing to determine if there is loss of peripheral vision.

Treatment

Endonasal Endoscopic surgery: The first-line treatment for all pituitary adenomas except prolactinomas (as discussed below), as well as RCCs and many craniopharyngiomas is endonasal transsphenoidal surgery. Because of improved tumor visualization, the endonasal endoscopic approach is rapidly becoming the preferred method for removal of the great majority of pituitary adenomas, RCCs, most craniopharyngiomas and chordomas as well as many midline meningiomas. Surgical success rates are generally quite high (80-90%) with smaller and non-invasive pituitary tumors, and lower with larger and/or invasive tumors (30-70%). Major surgical complications such as vision loss, bleeding, stroke, cerebrospinal fluid leak and meningitis are low when performed by experienced endonasal transsphenoidal neurosurgeons who often work collaboratively with a Head & Neck surgeon. The success rates of surgery are described further in the sections below for specific tumor types.

Transcranial Surgery: Although rarely used for removal of a pituitary adenoma or a RCC, a supraorbital eyebrow craniotomy is used frequently for craniopharyngiomas with far anterior or lateral extension. We also routinely use this minimally invasive eyebrow craniotomy for some meningiomas and metastatic brain tumors. Through an incision within the eyebrow, a small (1.5 - 2 cm x 2.5 - 3 cm) craniotomy is placed above the eyebrow to access tumors lying under or within the frontal lobes and around the pituitary gland. This "eyebrow" craniotomy requires minimal brain retraction and muscle dissection, promoting a rapid neurological recovery with less pain; the cosmetic result is generally excellent.

Medical and Radiation Therapies: Radiosurgery (SRS) or Stereotactic Radiotherapy (SRT): For patients with uncontrolled acromegaly after surgery, SRS (one dose) or SRT (multiple doses), provide precise radiation directly to the tumor, are relatively effective in lowering GH and IGF-1 levels and stopping tumor growth. However, the lowering of GH and IGF-1 levels takes longer with SRT (average 7 years) compared to SRS (average 18 months). Pituitary gland failure often occurs in the years after SRS or SRT. Complications such as visual loss are rare with either SRS or SRT.

For a visual tour of endonasal and keyhole surgery for brain, pituitary & skull base tumors, visit our BTC YouTube channel: *www.youtube.com/user/BrainTumorCenter*