

About Pituitary Tumors

This article was provided to us by Daniel F. Kelly, M.D., Director of the Brain Tumor Center at the John Wayne Cancer Institute and Saint John's Health Center in Santa Monica, California. We appreciate his generous donation of time in preparing this material.

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 tumor types are almost always 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, a technique whereby a precise dosage of radiation is directed at the residual tumor either by stereotactic radiosurgery (SRS) delivered as a single dose or stereotactic radiotherapy (SRT) delivered in multiple doses over days to several weeks.

The information below explains pituitary adenomas, Rathke's cleft cysts, craniopharyngiomas, and hypopituitarism in more detail. We also offer images of pituitary tumors on the Pituitary Tumor portal of the ABTA web site, www.abta.org.

Pituitary Adenomas

Pituitary adenomas 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



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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, adrenocorticotrophic 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 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).



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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, T4, 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 performed 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 (e.g., 24-hour urinary free cortisol, midnight salivary cortisol, dexamethasone suppression testing) or acromegaly (e.g., oral glucose tolerance test), 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

Transsphenoidal surgery: Endonasal transsphenoidal surgery may be considered first-line treatment for pituitary adenomas except prolactinomas (as discussed below), as well as RCCs and many craniopharyngiomas. Today, at most centers that specialize in transsphenoidal surgery, the operation is



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performed through an endonasal approach. The operating microscope, an endoscope or both are used to provide high resolution and panoramic visualization during the procedure.

Transcranial surgery: A craniotomy is rarely used or indicated for removal of a pituitary adenoma or a RCC but may be used for relatively large craniopharyngiomas. Although a large fronto-temporal craniotomy or bifrontal craniotomy is effective, the more minimally invasive supra-orbital “eyebrow” craniotomy is being increasingly used for removing such 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. This approach is used instead of the endonasal approach when a craniopharyngioma is very large (typically over 4 cms) or extending too far away from the midline to be effectively accessed transphenoidally.

Medical and Radiation therapies: Please see below, under “Acromegaly treatment” section.

Adenoma sub-type 1: Acromegaly

Acromegaly is caused by a GH secreting adenoma. The problems associated with acromegaly include the effects of abnormally high GH and IGF-1 levels and in some instances by the tumor compressing the normal pituitary gland and optic nerves. Untreated acromegaly is a serious condition that can cause dramatic bone and soft tissue changes and serious cardiovascular problems. If the tumor develops before bone growth is completed in adolescence, gigantism is the result. Because of the serious changes resulting from GH excess, treatment is essential.

Symptoms

The most obvious changes of acromegaly are the external physical changes that typically include enlargement of the hands (increase in ring size) and feet (increased shoe size) as well as frontal bossing (enlargement of the forehead) and prognathism (jaw enlargement). There may also be development of an under bite, spreading teeth, an enlarging tongue, increased snoring and sleep apnea. Carpel tunnel syndrome and excessive sweating are also common. More serious problems can include development of hypertension, diabetes mellitus and an increased risk of colon cancer. With GH-secreting macroadenomas, there may be other problems of visual loss, headaches and problems associated with pituitary gland failure including fatigue, depression, impotence and loss of libido in men and menstrual irregularities and galactorrhea (milk discharge from the breast), in women.

Diagnosis

Acromegaly is diagnosed by documenting elevated levels of both GH and IGF-1. An oral glucose tolerance test (lack of suppression of GH to oral glucose administration) is often used to confirm excess GH production. Comparing old and recent photographs will often demonstrate dramatic changes in



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facial appearance. Following hormonal testing that confirms acromegaly, an MRI of the pituitary should be performed to confirm the presence of a pituitary adenoma.

Treatment

Transsphenoidal surgery: Considered the first-line treatment for a GH-secreting tumor. However, cure of acromegaly may not be possible in patients with large or invasive macroadenomas. In such instances, medical therapy and/or radiotherapy may be necessary to control GH levels. In general, the higher the pre-operative GH level, the lower the chance for cure. Long-term remission of acromegaly after surgery is seen in 80-90% of patients with microadenomas and in 40-60% of patients with macroadenomas.

Medical therapy: For patients with persistent GH elevation after surgery, octreotide or pegvisomant treatments, SRS, or both are generally indicated. Octreotide (given three times a day by injection or by one monthly injection) achieves long-acting suppression of GH in about 70% of patients. It causes some degree of tumor shrinkage in 30-50% of patients, and often improves soft tissue swelling, headache, joint pains and sleep apnea. Preoperative use of octreotide may facilitate tumor removal and lessen risks of general anesthesia. Side effects may include loose stools, malabsorption, cholelithiasis (gall stones), and local pain at the injection site. Pegvisomant, a GH receptor antagonist, is also effective in lowering IGF-1 levels although it does cause an elevation in GH levels. Bromocriptine is a "dopamine agonist" which lowers GH secretion in about 15% of acromegalic patients. The major side effect is gastrointestinal upset. Growth hormone lowering and tumor shrinkage are seen in only 10 - 15% of patients with acromegaly.

Radiosurgery (SRS) or Stereotactic Radiotherapy (SRT): For patients with uncontrolled acromegaly after surgery or who have failed medical therapy, 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.

Adenoma sub-type 2: Cushing's disease

Cushing's disease is caused by an ACTH-secreting adenoma. This serious endocrinopathy is a subset of Cushing's syndrome which refers to the presence of elevated blood cortisol levels. Cushing's syndrome may arise from tumors of the pituitary gland, adrenal glands or from tumors arising elsewhere in the body (ectopic ACTH producing tumors). The cause of Cushing's syndrome is a pituitary adenoma in over 70% of patients. Most ACTH-secreting adenomas are microadenomas. Cushing's disease is relatively uncommon, affecting 10 to 15 of every million people each year, and most commonly affects adults aged 20 to 50 years; women account for over 70% of cases. Given that Cushing's disease causes so many common problems affecting the general population such as obesity, hypertension and diabetes,



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it is possible that many patients with Cushing's disease are undiagnosed for years or perhaps never diagnosed.

Symptoms

Body changes including weight gain in the face (moon face), above the collar bone (supraclavicular) and on back of neck (buffalo hump) are commonly seen in patients with Cushing's disease. Skin changes may include easy bruising, with purplish stretch marks (stria) and red cheeks (plethora) as well as excess hair growth (hirsutism) on the face and body. The high cortisol levels also cause weakness, fatigue and muscle wasting. Women may develop menstrual disorders including amenorrhea (absence of menses) and decreased libido. Additional serious consequences may include hypertension, diabetes mellitus and depression.

Diagnosis

Patients are often diagnosed with Cushing's disease after several years of symptoms which might include progressive weight gain, new onset hypertension or diabetes and mood changes. Comparison of old and recent photographs will often demonstrate changes in appearance. Unfortunately, the diagnosis of Cushing's disease is often long delayed and can be difficult to make. An endocrinologist should always supervise the evaluation for Cushing's disease.

Hormonal diagnosis: The first step in diagnosing Cushing's disease is to confirm the presence of excessive cortisol secretion. This diagnosis is most easily made by performing a low-dose dexamethasone suppression test, a 24-hour urinary free cortisol collection, and/or a midnight serum cortisol level or a midnight salivary cortisol test. Once the diagnosis of Cushing's syndrome is established, the source of the excess cortisol should be determined: either from an adrenal gland tumor, an ectopic ACTH-producing tumor, or a pituitary ACTH-producing adenoma. Serum ACTH levels and a high-dose dexamethasone suppression test are typically used for this determination. Petrosal Sinus Sampling is an angiographic and endocrinological test used to distinguish between ectopic ACTH production and pituitary ACTH production (Cushing's disease). Petrosal sinus sampling should never be performed before the diagnosis of ACTH-dependent Cushing's syndrome is established.

Imaging: Once the diagnosis of Cushing's syndrome is confirmed hormonally, a pituitary MRI can detect the presence of an adenoma in approximately 70% of cases. Dynamic post-gadolinium coronal MRI is a recent technique that helps diagnose small adenomas that may not be seen on a conventional pituitary MRI. CT scans of the adrenal glands are very useful for determining the presence or absence of an adrenal tumor causing Cushing's syndrome.



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Treatment

Transsphenoidal Surgery: The only way to achieve long term remission of Cushing's disease is by transsphenoidal removal of the adenoma. Long-term remission or "cure rates" range from 80-90% for microadenomas and from 30-70% for macroadenomas and invasive adenomas.

Medical therapy: In patients who fail to have remission of their Cushing's disease or syndrome state after surgery, there are several medications that can lower cortisol levels. These include "adrenal-directed" medications ketoconazole and aminoglutethimide which inhibit steroid (cortisol) production in the adrenal glands. They are initially effective but have some side effects, and the overall long-term control of Cushing's disease with these drugs is rather poor.

Radiosurgery (SRT) or Stereotactic Radiotherapy (SRS): For patients whose Cushing's disease is not controlled with surgery, SRT (multiple doses) and SRS (one dose), which provide precise doses of radiation directly to the tumor, are effective in controlling cortisol levels and tumor growth in 50 – 70% of patients. However, the lowering of cortisol levels generally takes significantly longer with SRT compared to SRS. Also, SRT and SRS may result in loss of normal pituitary function over 5 to 10 years. Neurologic complications such as visual loss and temporal lobe damage rarely occur with SRT and SRS.

Adenoma sub-type 3: Prolactinoma

Prolactinomas are the most common adenoma and secrete excessive prolactin. They generally have different presentations in women and men. The normal prolactin level is less than 20-25 ng/ml.

Symptoms

In most women with prolactinomas, the tumors are detected when they are microadenomas and the prolactin level is moderately elevated (50 - 300 ng/ml). In contrast, in men prolactinomas are typically detected when they are macroadenomas, with prolactin levels over 500 - 1000 ng/ml. In women, relatively small elevations in prolactin will cause irregular menstrual periods or amenorrhea and galactorrhea. Most men diagnosed with a prolactinoma have some degree of pituitary failure (hypopituitarism, especially hypogonadism. Women and men also typically have a reduced sex drive (decreased libido). With larger tumors, headaches and visual loss (from compression of the optic nerves or optic chiasm) can occur. A minority of patients with large tumors may have acute hemorrhage into the tumor (pituitary apoplexy) causing relatively sudden onset of headache, visual loss, double vision, and/or pituitary failure.

Diagnosis

Prolactinomas are typically diagnosed because of problems related to high prolactin and associated hypogonadism.



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Hormonal diagnosis: A prolactinoma is diagnosed by demonstrating elevated blood levels of prolactin. A prolactin level of over 150-200 ng/ml is almost always due to a prolactinoma. It is important to note that moderate elevations of prolactin (30 - 200 ng/ml) can occur from other causes, including pregnancy, the post-partum period, stress (discomfort, exercise), low thyroid function (hypothyroidism), kidney or liver failure, psychiatric medications (haloperidol, antidepressants, verapamil), hypothalamic\ pituitary "stalk effect". Therefore, other types of pituitary adenomas, craniopharyngiomas, RCCs or other brain tumors may cause modest elevations in prolactin.

Imaging: Almost all prolactinomas can be visualized on a pituitary MRI performed with and without gadolinium.

Treatment

Medical therapy: In general, the first line of treatment for patients with a prolactinoma is medication rather than transsphenoidal surgery. Approximately 80% of patients will have prolactin levels restored to normal with dopamine agonist therapy and many will have marked tumor shrinkage. The most commonly used agent is cabergoline (Dostinex) which has replaced bromocriptine (Parlodel) as the drug of choice given cabergoline's higher success rate and lower side-effect rate. Most women, following treatment, have a return of menses and many become fertile again. The size of the prolactinoma will be reduced in the majority of patients to varying degrees, which often results in rapidly improved vision and resolution of headaches. Dostinex has the advantage of only being taken twice per week and generally has fewer side effects than bromocriptine. It has also been shown to be effective in patients whose prolactinomas are resistant to bromocriptine therapy. The usual starting dose is 0.5 mg twice per week. The dose may be increased up to 1.0 mg twice per week. Bromocriptine is less often used for prolactinomas given the higher rate of side-effects. If used, it should be started at a low dose to minimize nausea and other gastrointestinal side effects, usually 2.5 mg tablet per day at mealtime. The dose is then increased over several days or weeks to a daily maximum usually not exceeding 10 mgs.

Recent reports indicate that long-term high-dose therapy with a dopamine agonist like cabergoline or bromocriptine can result in heart disease that affects the valves specifically. Although this risk of valvular heart disease appears to be relatively low with standard doses of cabergoline and bromocriptine typically used to treat a prolactinoma, it remains a potential risk of this therapy.

Transsphenoidal Surgery: Surgery is a reasonable first-line therapy in patients with micro-prolactinomas that do not invade the cavernous sinus and whose prolactin level is less than 250 ng/ml. In these patients, long term remission is generally 80-90%. Surgery is also effective for lowering prolactin levels in patients intolerant of Dostinex. For macroadenoma patients, the surgical cure rate is generally low. In men with large invasive prolactinomas, it is particularly low, averaging less than 30%. For this reason, Dostinex is usually tried first. In patients with long-standing visual loss, dopamine agonist therapy can be tried first. However, if the visual loss has occurred relatively rapidly



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over a period of less than two weeks, or if there is evidence on MRI of subacute hemorrhage or degeneration in the tumor, transsphenoidal surgery is generally recommended. For the minority of patients who do not respond well to cabergoline or bromocriptine, surgery should generally be performed within 6 months of starting dopamine agonist therapy. After more than six months of such therapy the tumor may become more fibrotic and more difficult to remove.

Radiosurgery (SRS) or Stereotactic Radiotherapy (SRT): Because most patients with prolactinomas respond so well to dopamine agonist therapy and/or surgery, radiation therapy is rarely required.

Adenoma sub-type 4: Endocrine-inactive (non-functional) adenoma

Endocrine-inactive adenomas do not result in excess hormone production. Instead they typically cause symptoms due to pressure on the normal pituitary gland and/or on structures near the pituitary such as the optic nerves and optic chiasm.

Symptoms

Typical complaints of patients with an endocrine-inactive adenoma are those of hypopituitarism, vision loss and headache. Hypopituitarism may manifest itself as fatigue, decreased mental function, weight gain, lethargy, joint pains, and loss of sex drive, infertility and in women, irregular periods or amenorrhea. Almost all of the symptomatic endocrine-inactive adenomas are macroadenomas when diagnosed. Occasionally, they grow quite large and into the cavernous sinus, causing nerve compression and double vision. Some patients with large tumors may have acute hemorrhage into the tumor (pituitary apoplexy) causing a relatively sudden onset of headache, vision loss, double vision, and/or pituitary failure.

Diagnosis

Endocrine-inactive adenomas are best diagnosed by imaging studies and hormonal testing. An MRI of the pituitary gland performed without and with gadolinium provides the most detail, although a brain MRI or brain CT scan will also reveal most pituitary macroadenomas. Hormonal Testing is also essential to evaluate for pituitary gland failure (hypopituitarism). A complete pituitary hormonal analysis should be performed as described above and is ideally overseen by an endocrinologist.

Treatment

Transsphenoidal Surgery: Endonasal transsphenoidal surgery is recommended for the great majority of patients with symptomatic endocrine-inactive adenomas. The long-term cure or control rate is approximately 70-80% overall. The cure rate is generally higher for smaller tumors and those that do not invade the cavernous sinus; conversely, the cure rate is lower for larger tumors (over 3 cm) and those that invade the cavernous sinus. Overall, transsphenoidal tumor removal improves visual acuity and visual field deficits in 75-90% of patients and headache resolution is seen in 80-90% of patients.



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Pituitary function is restored in only 20-50% of patients. Patients who do not have hormonal recovery after surgery will require long-term hormone replacement therapy. Because the transsphenoidal approach is so effective and relatively safe, it is rare that even large macroadenomas warrant a transcranial operation as the initial procedure.

Medical therapy: There is no effective medical therapy that reliably halts growth of endocrine-inactive adenomas.

Radiosurgery (SRS) or Stereotactic Radiotherapy (SRT): For patients who have residual tumor after the initial transsphenoidal surgery, SRT, SRS, or both (which provide precise dosage of radiation directly to the tumor) may be recommended if the tumor grows. Both SRT and SRS are effective in controlling tumor growth in at least 80-90% of patients. However, SRT and SRS may result in loss of normal pituitary function over 5 to 10 years. Neurologic complications such as visual loss and temporal lobe damage rarely occur with SRT and SRS.

Craniopharyngiomas

Craniopharyngiomas are benign tumors that arise near the pituitary gland and pituitary stalk and are typically both cystic and solid in structure. They occur most commonly in childhood and adolescence and in later adult life, after age 50. They account for 10-15% of sellar and suprasellar tumors (tumors that occur in and above the pituitary gland) and 50-60% of sellar and suprasellar tumors in children. They are usually not discovered until they impinge upon important structures around them, and are frequently quite large (over 3 cm) when detected. Although they are benign (not malignant), these tumors tend to become adherent to structures around the pituitary gland and stalk, including the optic nerves, optic chiasm, intracranial arteries and the brain itself. They are thought to arise from remnants of the craniopharyngeal duct or Rathke's pouch which are developmental structures related to the primitive gut. These tumors are thought to be closely related to Rathke's Cleft Cysts (RCCs).

Symptoms

Craniopharyngiomas can cause a variety of symptoms depending upon their location. If the tumor compresses the pituitary stalk or gland, the tumor can cause partial or complete pituitary hormone deficiency which may lead to growth failure, delayed puberty, loss of normal menstrual function or sexual desire, increased sensitivity to cold, fatigue, constipation, dry skin, nausea, low blood pressure, and depression. Pituitary stalk compression can also cause diabetes insipidus (DI), and increase prolactin levels causing a milky discharge from the breast (galactohhrea). If the tumor compresses the optic chiasm or nerves, then visual loss can result. Involvement of the hypothalamus, an area at the base of the brain, may result in obesity, increased drowsiness and temperature regulation abnormalities. Other symptoms especially with larger tumors may include personality changes, headache, confusion, and vomiting.



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Diagnosis

The best means of visualizing a craniopharyngioma is with a magnetic resonance imaging (MRI) scan of the pituitary region performed without and with contrast. Many craniopharyngiomas will also be well seen on a computer tomography (CT) scan especially since some are partially calcified (containing calcium deposits). A complete pituitary hormonal blood evaluation should also be performed. Other possible diagnoses to consider when a cystic mass is seen in the area of the pituitary include a cystic pituitary adenoma or an arachnoid cyst.

Treatment

The best initial treatment for a craniopharyngioma is surgical removal. The goal of surgery is to completely remove the tumor while improving vision and brain function. Craniopharyngiomas can be removed by either an endonasal transsphenoidal approach or a craniotomy. Because of their tendency to be adherent to the optic chiasm, other nerves and important blood vessels, a total removal may not be possible in up to 50% of patients. With incomplete removal, stereotactic radiotherapy (SRT) or stereotactic radiosurgery (SRS), in which special equipment provides a precise dose of radiation directly to the tumor to prevent further growth, is often used. Because hormonal deficiencies can develop many years after radiation treatment, patients treated with radiation should have periodic hormonal evaluations throughout their lifetimes. Additionally, because of the tendency for craniopharyngiomas to recur, repeat MRIs or CT scans should be obtained at least every six months for the first 5 years after surgery or radiation therapy and then at least annually thereafter.

Rathke's Cleft Cysts (RCCs)

Rathke's Cleft Cysts are not true tumors or neoplasms; instead they are benign cysts. Rathke's pouch forms as part of normal development and eventually forms the anterior lobe, pars intermedia and pars tuberalis, of the pituitary gland. This pouch normally closes in fetal development, but a remnant often persists as a cleft that lies between the anterior and posterior lobes of the pituitary gland. Occasionally, this remnant enlarges to form a cyst, the RCC that can cause pituitary failure, headaches and in some instances, vision loss.

Symptoms

Symptomatic RCCs are relatively common pituitary lesions, accounting for 5-10% of surgically removed pituitary masses. RCCs can be seen at any age, although most are identified in adults. Intracellular RCCs are usually asymptomatic and are found incidentally at autopsy or on a magnetic resonance imaging (MRI) scan. However, larger RCCs may cause visual disturbances, symptoms of pituitary dysfunction, and headaches.



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Diagnosis

The best means of visualizing a RCC is with an MRI or a computer tomography (CT) scan of the pituitary region performed without and with contrast. A complete pituitary hormonal blood evaluation should also be performed. Other possible diagnoses to consider when a cystic mass is seen in the area of the pituitary include a cystic pituitary adenoma, craniopharyngioma or arachnoid cyst.

Treatment

The best treatment for a symptomatic RCC causing pituitary failure, headache or visual loss is surgical removal through an endonasal transsphenoidal approach. The goal of surgery is to completely remove the cyst contents while improving or preserving pituitary function vision and alleviating headache and visual loss if present. Attempts to remove the cyst lining should be avoided because this can result in pituitary gland damage. A complete removal of RCCs is possible in 80-95% of cases although they can recur at a rate of 5 – 15% over 5 to 10 years.

Hypopituitarism (Pituitary Failure)

Hypopituitarism is a term that refers to under-function of the pituitary gland. This clinical term means that one or more functions of the pituitary gland are deficient. The term refers to both anterior and posterior pituitary gland dysfunction. Hypopituitarism may be temporary or permanent.

Panhypopituitarism refers to complete loss of all pituitary function. Patients with panhypopituitarism should carry a Medic Alert Bracelet with them to notify health care personnel of this problem in case of an emergency.

Causes of Hypopituitarism

Loss of pituitary function can result from damage to the pituitary gland, the pituitary stalk or the hypothalamus. The hypothalamus contains releasing and inhibitory hormones that control the pituitary and reach the gland via the pituitary stalk. Injury to the pituitary gland, pituitary stalk or hypothalamus can occur from an enlarging pituitary tumor or brain tumor, pituitary or brain tumor surgery, radiation to the pituitary, pituitary apoplexy (hemorrhage), pituitary inflammation (hypophysitis) and head injury. There appears to be a predictable loss of hormonal function: the growth hormone (GH), luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secreting cells appear to be the most vulnerable while thyroid stimulating (TSH) and adrenocorticotrophic hormone (ACTH) secreting cells are less vulnerable. Approximately 50% of patients will have some recovery of pituitary function after surgical removal of a pituitary adenoma. Approximately 45% will have no recovery or change, and 5% will have diminished pituitary function.

Deficiency of ACTH and cortisol: Adrenocorticotrophic hormone deficiency resulting in decreased cortisol production by the adrenal glands can be serious and life- threatening. With gradual onset of deficiency over days or weeks, symptoms may include weight loss, fatigue, weakness, depression,



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apathy, nausea, vomiting and loss of appetite. As ACTH deficiency becomes more severe or has a more rapid onset, (Addisonian crisis) symptoms may include confusion, stupor, psychosis, serum electrolyte changes (low serum sodium and/or elevated serum potassium), vascular collapse, shock and death. Treatment consists of glucocorticoid administration (hydrocortisone, dexamethasone or prednisone). For patients with acute adrenal insufficiency (Addisonian crisis), rapid intravenous administration of high dose steroids is essential to reverse the crisis.

Deficiency of TSH and thyroid hormone: Thyroid stimulating hormone deficiency causes decreased energy, increased need to sleep, cold intolerance, dry skin, constipation, muscle aches and decreased mental capacity. This is a very serious and disabling hormonal deficiency that often causes patients with pituitary disease to seek medical attention. Treatment with thyroxin (Synthroid) reverses the symptoms and signs over several days or weeks and requires careful monitoring of free T4 or total T4 (thyroid function levels).

Deficiency of LH and FSH (Hypogonadotropic Hypogonadism): Women with hypogonadism (sexual dysfunction, loss of libido, and/or impotence) develop ovarian suppression with menstrual irregularities or absence of periods (amenorrhea), infertility, decreased libido, decreased vaginal secretions and osteoporosis. Blood levels of estradiol decrease and can be replaced as oral Premarin or estrace, or given as a patch applied twice weekly. Women on estrogen also need progesterone. Men with hypogonadism develop decreased libido, impotence, decreased ejaculate volume, loss of body and facial hair, weakness, fatigue and often anemia. Blood testosterone levels are low and should be replaced as a daily patch or gel or as an injection every 2-3 weeks.

Growth Hormone Deficiency: Growth hormone is necessary in children for growth, and in adults to maintain body composition, muscle mass, energy level, cardiovascular status and possibly some mental functions. Symptoms of GH deficiency in adults include fatigue, poor exercise tolerance, decreased muscle mass, increased fat mass and poor quality life. GH is only available in injectable form that must be given daily.

Antidiuretic Hormone Deficiency (ADH) and Diabetes Insipidus (DI): Patients with DI have excessive thirst and urination. This lack of ADH results in copious and diluted (unconcentrated) urine. Such patients can become rapidly dehydrated unless they are adequately hydrated or the ADH is replaced. Diabetes insipidus results from damage to the pituitary stalk, posterior pituitary gland or hypothalamus. It may occur transiently in up to 25% of patients after transsphenoidal (through the nasal passage) pituitary adenoma surgery and is permanent in 1-3% of patients. It occurs more commonly because of a craniopharyngioma or after surgery for a craniopharyngioma which often arises along the pituitary stalk. Replacement of ADH resolves the high urine output of DI. Treatment with DDAVP (a synthetic type of ADH) can be given by subcutaneous injection, intranasal spray, or a tablet taken once or twice a day.



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This information is not intended as a substitute for professional medical advice and does not provide advice on treatments or conditions for individual patients. All health and treatment decisions must be made in consultation with your physician (s), utilizing your specific medical information. The American Brain Tumor Association does not endorse any of the organizations listed or guarantee that individuals will qualify for the services they provide. Please contact each organization for their specific guidelines

August 2010



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