PITUITARY TUMOR

Pituitary Adenoma, Pa

An abnormal growth that develops in the pituitary gland that could impair the hormonal balance needed for fertility function.

 sağlanabilir.

Related Diagnoses:
Non-obstructive azoospermia

About Pituitary tumor

Pituitary tumors (adenomas) are abnormal growth that develop in the pituitary gland (Pic. 1) and can lead to destruction of some of the hormone-secreting cells (Pic. 2) the pituitary gland, causing cessation of menstrual periods in women and reduced sperm production in men.

Pituitary tumor is not a cancer in 99% of patients; it is benign. However, it can cause problems because of its size, causing loss of vision, loss of normal pituitary function (hypopituitarism) and/or headache or because of excessive hormone production by the tumor. If the gonadotropins (LH and FSH) that regulate the ovaries are not produced adequately by pituitary gland due to tumor, it is unlikely for a woman to become pregnant without additional medical treatment. Male patients with pituitary tumor may seek from decreased production of testosterone and low sperm count, thus they are treated with hormonal therapy to balance a hormonal level.

The cause of most pituitary tumors remains unknown, although a genetic contribution is recognized for some. The scientists investigated the co-prevalence of other independent primary tumors in patients with known pituitary tumors, both benign and malignant, and in the relatives of these patients. The information about genetic contribution is useful for counseling patients in whom pituitary tumors have been diagnosed and suggests strong genetic or environmental co-risks for the development of other tumors.

Pituitary adenomas are generally divided into three categories dependent upon their biological functioning:

- **benign (non-invasive) adenoma**
  Non-invasive and non-secreting pituitary adenomas are considered to be benign in the literal as well as the clinical sense. A benign tumor is a mass of cells (tumor) that lacks the ability to invade neighboring tissue or metastasize. These characteristics are required for a tumor to be defined as cancerous and therefore benign tumors are non-cancerous.

- **invasive adenoma**
  Tumor that has spread beyond the layer of tissue in which it developed and is growing into surrounding, healthy tissues.

- **carcinomas**
  Carcinoma is a type of cancer that develops from epithelial cells. Specifically, a carcinoma is a cancer that begins in a tissue that lines the inner or outer surfaces of the body. Carcinomas occur when the DNA of a cell is damaged or altered and the cell begins to grow uncontrollably and become malignant.

Pituitary adenomas may also be classified according to size (microadenomas are < 1 cm, macroadenomas are ≥ 1 cm) or may be classified as functional (active) or non-functional (endocrine inactive) according to their ability to produce hormones, for example prolactinoma is the pituitary cancer producing prolactin.
The diagnosis is confirmed by testing hormone levels, and by radiographic imaging of the pituitary for example, by a magnetic resonance imaging (MRI) or computed tomography (CT). CT scan has insufficient resolution to show small tumors and does not confer the anatomic detail found in MRI.

However, pituitary tumors often can be treated to return hormone levels to normal and alleviate signs and symptoms. Treatments include surgical removal of the tumor, radiation therapy, hormone replacement therapy or a combination.

**Associated diseases**

**Hypogonadotropic hypogonadism**

Pituitary tumor could result in acquired hypogonadotropic hypogonadism which is a condition of low serum testosterone due to a decrease in the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary gland.

The clinical characteristics of hypogonadotropic hypogonadism are androgen deficiency and a lack/delay/stop of pubertal sexual maturation. Moreover, the development of gamets (sperm or ovum) is impaired and the fertility is decreased. Thus, it is important to remember that the fertility of patients with hypogonadotropic hypogonadism is only reduced and that fertility may be restored through hormone therapy.

**Hypopituitarism**

Hypopituitarism is the decreased (hypo) secretion of one or more of the eight hormones normally produced by the pituitary gland at the base of the brain which could be caused by tumor of pituitary gland. As a result of the absence of pituitary hormone action, the production of eggs and sperm could be affected.

**Hyperpituitarism**

Hyperpituitarism is a disease of the anterior lobe of the pituitary gland which is usually caused by a functional pituitary adenoma and results in hypersecretion of hormones such as growth hormone, prolactin (associated with prolactinoma), thyrotropin, luteinizing hormone (LH), follicle stimulating hormone (FSH), and adrenocorticotropic hormone (ACTH). Thus, hormonal balance is impaired and patients could seek from fertility problems such as irregular periods, low sex drive and erectile dysfunction.

**Cushing disease**

Cushing’s disease is a life-threatening illness defined by the chronic excess of serum cortisol in the presence of an ACTH-secreting pituitary adenoma and accounts for approximately 80% of newly diagnosed cases of Cushing’s syndrome. High cortisol level may also interfere with the function of glands, mainly thyroid and gonads. Thus, the consequent damage of fertility may occur, such as loss of menstrual period.

**Complications**

**Permanent hormone deficiency**

The presence of a pituitary tumor or the removal of a part of pituitary gland may permanently alter hormone supply, which may need to be replaced with hormone medications. Deficiency in LH and FSH leads to sex hormone abnormalities and insufficient egg and sperm maturation.

**Pituitary tumor apoplexy**

Very rare but potentially serious complication is pituitary tumor apoplexy. Pituitary tumor apoplexy is a medical emergency due to acute infarction or bleeding in the pituitary gland that is associated with infertility due to deficiency or insufficiency of hormones.

**Osteoporosis**
If the excess production of prolactin is prolonged, osteoporosis (decreased bone density) becomes an issue as well. Thus, bone density testing should be performed on patients with incompletely treated prolactinomas and intervene pharmacologically if density is shown to be insufficient. Osteoporosis itself does not affect fertility and does not prevent a woman from becoming pregnant, but in severe cases women get fractures in their spine during pregnancy. These are painful but do not harm the baby.

**Morbidity**

Pituitary adenomas are endowed with significant clinical morbidity related to hormonal hypersecretion, neurological symptoms due to intracranial mass effects or invasion of the surrounding structures and/or secondary hypocpituitarism. Long-term uncontrolled pituitary hormone hypersecretion, leading to potential severe systemic diseases, and tumour recurrence or aggressiveness still represent a difficult clinical challenge.

**Risk factors**

There are few risk factors for pituitary tumors and these are all related to genetics, but there are no known environmental or lifestyle-related risk factors for pituitary tumors.

**Impact on fertility**

The pituitary tumor imparts the function of pituitary gonadal axis. The pituitary gonadal axis is the hormone system that is most vulnerable to extrinsic pressure. Even small disturbances of pulsatile rhythms of follicle-stimulating hormone (FSH), luteinizing hormone (LH) or prolactin production causes loss of menstrual periods and infertility in women and causes loss of sexual function, a low blood testosterone level and infertility in men.

When low levels of FSH and/or LH can be shown, the search for pituitary tumors should be part of any infertility workup. Low levels of prolactin are not considered to be significant or to require intervention.

**Female fertility**

Non secretory tumor often causes loss of regular menses and infertility in premenopausal women. Although nonfunctioning tumors do not secrete hormones, their size or position can damage the pituitary gland and prevent it from secreting enough of certain hormones (hyposecretion) which can lead to decreases in the sex steroids required for pregnancy. Menstrual cycles may be disrupted even without frank hypogonadism, particularly in the case of hormone-secreting adenomas.

High levels of prolactin (hyperprolactinemia) may cause galactorrhea (milky discharge from the breasts), which can be the presenting symptom of this condition. If high prolactin is the only reason for infertility in pituitary tumor patient, lowering prolactin to normal results in the same chances for pregnancy as the general age-matched population.

Advances in ovulation induction or medical and surgical therapy has allowed pregnancy to occur in many of women with pituitary tumor. Although it requires more effort, pregnancy is very possible in a woman who has pituitary deficiency of the hormones that control ovarian function. Women with high levels of prolactin are usually infertile due to inhibition of pulsatile gonadotropin-releasing hormone secretion. Normalization of prolactin levels is required before ovulation and conception can occur.

**Male fertility**

A lack of stimulation by gonadotropins could result in failure of sperm development (spermatogenesis) within the testis, called non-obstructive azoospermia, diagnosed in approximately 10% of infertile men. Nonobstructive azoospermia refers to a lack of sperm production, whereas obstructive azoospermia (Pic. 4) implies adequate sperm production but failure to deliver the sperm into the ejaculate because of a ductal obstruction.

In many cases, men with nonobstructive azoospermia typically have small-volume testes and elevated FSH. Although treatment may not completely restore the quality of semen from men with subnormal fertility, in some cases, a successful pregnancy can still be achieved through assisted reproductive technology (ART).
Hyperprolactinemia may also cause infertility by inhibiting the hypothalamic secretion of gonadotropin-releasing hormone (GnRH) and also through a direct inhibition of the binding of LH to the Leydig cells in the testis that produce testosterone in the presence of LH.

**Prevention**

If anyone develops signs and symptoms that might be associated with a pituitary tumor, he should see doctor. To the present day, there is no known way to prevent these tumors.

**Symptoms**

Symptoms of an adenoma are unspecific and depend on their size and secreting activity thus delaying timely diagnosis of such lesions. Most commonly they include headaches, vision problems, menstrual cycle abnormality, erectile dysfunction or weight change.

**Therapies**

**Self therapy**

There is no self or alternative therapy for pituitary tumor, but it is necessary to seek medical attention when observing symptoms.

**Conventional medicine**

The current clinical management is based on pharmacological treatment, surgery and radiotherapy. Patients with pituitary tumors come to surgery for several reasons. Rapid deterioration of vision is considered as an immediate indication for surgery to relieve pressure produced by an expanding tumor mass. The transsphenoidal microsurgical approach to a pituitary lesion is the most widely employed surgical approach to pituitary lesions and represents a major development in the safe surgical treatment of both hormonally active and nonfunctioning tumors.

Prolactin producing tumors are most successfully treated with medical therapy (pills) in over 90% of patients. The best treatment for other types of pituitary tumors is removal of the tumor by an experienced neurosurgeon that performs pituitary surgery frequently.

In some, the drug is ineffective or produces debilitating side effects. In others, drug therapy has been successful but not completely so, and debulking the tumor is felt to be helpful in allowing medical therapy a better chance to work on a smaller volume of disease. Finally, a number of patients present for surgery because of what one might term "medication fatigue," namely a desire to free themselves of the necessity for taking what may amount to lifelong medication requirement.

Despite considerable progress in the management of pituitary adenomas, a significant subset of patients is not satisfactorily controlled.

**Pharmacotherapy**

Medical therapy generally consists of replacing hormones when levels are low or of suppressing them when they are high, mainly dopamine-agonists (DA) and somatostatin analogues (SSA).

Pituitary tumors producing prolactin (prolactinomas) are generally treated with medical therapy as the first line approach due to the fairly good success achievable with Dopamine agonists such as Bromocriptine (Parlodel) or Cabergoline (Dostinex).
Since sperm cycle in men is long (over 70 days) and a year or more of treatment may be required for a man to achieve a sperm count adequate to father a baby. If the patient has an adequate sperm count at diagnosis, sperm can be collected and frozen for future use.

**Surgical therapy**

Patients with hypersecreting pituitary tumors (such as acromegaly or Cushing’s disease), are subjected to undergo surgical resection (Pic. 3). In prolactinomas, however, surgical resection is considered when there is treatment failure with dopaminergic medications and/or experience severe side effects, tumoral mass effect and/or elect to undergo surgery.

On the other hand, patients with non-functional pituitary adenomas undergo surgery when clinically manifest mass effects are noted like visual disturbances, headaches, or hypopituitarism.

**Other therapies**

**Radiotherapy**

Radiotherapy (or radiation therapy) is the use of high-energy x-rays or other particles to destroy tumor cells. In general, radiotherapy is used when there is tumor remaining after surgery or when surgery is cannot be performed. Varying intervals between radiotherapy and decline in hormone levels have been published, ranging from one to more than ten years. Also, distinct threshold doses for the various hormone-secreting cells have been described, resulting in characteristic clinical courses, commonly starting with loss of growth hormone.

Radiotherapy does not have an immediate effect to lower excess hormone production and it may take several years to be effective. Moreover, controversial data on when to irradiate (primary vs. postoperative vs. salvage), whom to irradiate (secreting vs. non-secreting) and how to irradiate have occupied scientists, clinicians and patients. Several authors have addressed short- and medium-term outcome in irradiated pituitary adenoma patients, however little data is available on long results and toxicity.

**Assisted reproduction**

Fertility is possible in patients with pituitary tumor but it takes effort and time. Most of patients with pituitary tumor may have problems with natural conceiving due to imbalance in hormone levels. Thus, hormones usually need to be corrected before conception can occur by fertility drugs that stimulate the ovaries to produce eggs and testes to produce sperm assuming the ovaries and testes are otherwise normal.

If conservative medical treatments fail to achieve a full term pregnancy, the physician may suggest the patient undergo assisted reproductive technology (ART). After stimulation, the physician surgically extracts one or more eggs from the ovary, and unites them with sperm in a laboratory setting, with the intent of producing one or more embryos. Fertilization takes place outside the body, and the fertilized egg is reinserted into the woman’s reproductive tract, in a procedure called embryo transfer.

The fertilized eggs (embryos) are cultivated under very stringent conditions and examined every day by the embryologist to evaluate their progress. The embryos are usually cultured for 3 to 5 days, before the best one(s) are selected to be put (transferred) in to the womb.

Intracytoplasmic sperm injection (ICSI) is beneficial in the case of male factor infertility where sperm counts are very low or failed fertilization occurred with previous IVF attempt(s). The ICSI procedure involves a single sperm carefully injected into the center of an egg using a microneedle.
Non-obstructive azoospermia
Complete absence of sperm in the ejaculate due to testicular failure.
Learn more at: www.fertilitypedia.org/therapy/diag/non-obstructive-azoospermia

Therapies

Egg donation
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: www.fertilitypedia.org/edu/therapies/egg-donation

ICSI
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: www.fertilitypedia.org/edu/therapies/icsi

Sperm donation
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: www.fertilitypedia.org/edu/therapies/sperm-donation

Standard IVF
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: www.fertilitypedia.org/edu/therapies/standard-ivf

Gallery

Pic
The major parts of the brain, including the pineal gland, cerebellum, spinal cord, brain stem, pituitary gland, and cerebrum are labeled.

Pic
The anterior pituitary contains several different types of cells that synthesize and secrete hormones. Usually there is one type of cell for each major hormone formed in anterior pituitary.

<table>
<thead>
<tr>
<th>Type of cell</th>
<th>Hormone secreted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatotropes</td>
<td>Human growth hormone (HGH)</td>
</tr>
<tr>
<td>Corticotropes</td>
<td>Adrenocorticotropic hormone (ACTH)</td>
</tr>
<tr>
<td>Thyrotropes</td>
<td>Thyroid stimulating hormone (TSH)</td>
</tr>
<tr>
<td>Gonadotropes</td>
<td>Gonadotropins: luteinizing hormone (LH) and follicle stimulating hormone (FSH)</td>
</tr>
<tr>
<td>Lactotropes</td>
<td>Prolactin (PRL)</td>
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Pic
Surgery is a common treatment for pituitary tumors. The normal approach is Trans-sphenoidal adenectomy, which usually can remove the tumor without affecting the brain or optic nerves.

Pic
Routes Used to Remove Pituitary Tumor
Non-obstructive azoospermia refers to no sperm in the semen because of abnormal sperm production, instead, obstructive azoospermia refers to no sperm in a man's semen, as a result from problems with sperm delivery.

Sources

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