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Pituitary Adenomas: Insights into the Recent Trends

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Abstract Pituitary adenoma is a type of pituitary neoplasms that is typically a benign, slow-growing tumor that arises from cells in the pituitary gland. Pituitary adenomas are classified according to their secretory products into functioning (Endocrine-active) tumors that represent almost 70% of pituitary tumors, and non-functioning adenomas (Endocrine-inactive). Because of physiologic effects of excess hormones, the functioning tumors present earlier than non-functioning adenomas. Patients with pituitary adenomas usually present with symptoms related to hormonal disturbances. However, pressure symptoms, such as headache, visual field defects, cranial nerve palsies and hypopituitarism may occur due to the mass effect of large tumors. Treatment of pituitary adenomas include transsphenoidal surgery and adjunctive therapy including supervoltage radiation and pharmacologic agents. This review throws light on pituitary adenoma regarding its prevalence, predisposing factors, types, clinical presentation, diagnosis and possible lines of management in view of the recent trends.

Keywords: *pituitary, adenomas, hypopituitarism, diagnosis, management*

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1. Introduction

Cancer is a broad term that refers to a wide variety of diseases characterized by development of abnormal cells that divide uncontrollably and have the ability to invade and destroy the surrounding normal body tissues [1]. Pituitary adenomas are the most common type of pituitary disorders [2]. The pituitary is a small gland in the brain that is located behind the back of the nose. It releases different types of hormones that affect other glands and many functions in your body [3]. Most pituitary tumors are not cancerous. They don't spread to other parts of your body but they can cause the pituitary to make too few or too many hormones, causing problems in the body [2].

Pituitary tumors that make too many hormones will cause other glands to make more hormones [4]. That will cause symptoms related to each of the specific hormones. Many pituitary tumors will also press against the nearby optic nerves. This can cause vision problems [5].

Prevalence of pituitary adenomas ranges from 1 in 865 adults to 1 in 2688 adults [2]. About 50% are microadenomas (<10 mm); the remainder are macroadenomas (≥10 mm). Prolactinomas account for 32% to 66% of adenomas. Growth hormone-secreting tumors account for 8% to 16% of tumors [6]. Adrenocorticotropic hormone (ACTH)-secreting tumors account for 2% to 6% of adenomas. Clinically nonfunctioning adenomas account for 15% to 54% of adenomas [7]. This review throws light on pituitary adenoma regarding its prevalence, predisposing factors, types, clinical presentation, diagnosis and possible lines of management in view of the recent trends.

2. Classification of Pituitary Adenomas

Pituitary adenomas are classified according to the primary cell origin and the type of the hormone secreted by the tumor [8]. If adenoma does not secrete a sufficient level of hormones to be detectable in the blood or to result in clinical manifestations, it is considered nonfunctioning [9]. Also, tumors are also categorized based on their size. If the tumor is 10 mm or larger, it is considered as macroadenoma. Microadenoma occurs if the tumor is less than 10 mm [8]. The main types of pituitary tumors include growth hormone-secreting tumors, null cell adenomas, prolactinomas and adrenocorticotropic hormone secreting tumors [10] (Figure 1).

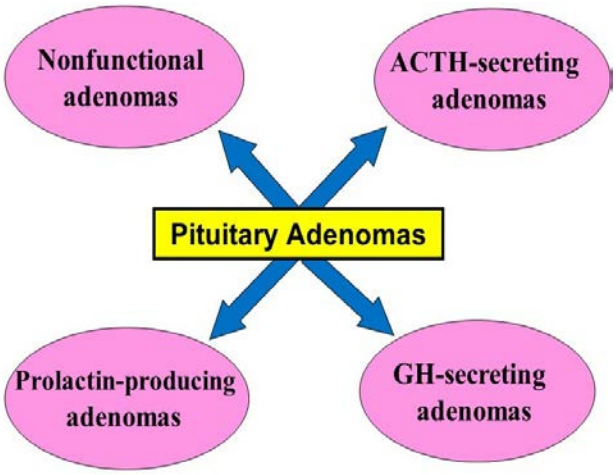

Figure 1. Classification of pituitary adenomas

2.1. Nonfunctional Adenomas (Null Cell Adenomas)

These tumors are the most common type of pituitary adenomas. They don't make extra hormone and may be asymptomatic until the tumor reaches a certain size [7]. When the tumor is big enough, it may cause headaches and vision problems. Large pituitary tumors can crush normal pituitary cells. This leads to symptoms caused by decreased hormone production [11].

2.2. Prolactin-producing Tumors (Prolactinomas)

These are common benign tumors that produce too much prolactin. Women with this tumor will have high prolactin levels and this can make menstrual irregularities or even amenorrhea [2]. These tumors can also cause leucorrhea, even if the patient is not pregnant or nursing. Males may have erectile dysfunction or a lack of interest in sexual relations. Also, he may also have gynecomastia, low sperm count, less body hair, headaches and vision problems [12].

2.3. ACTH-secreting Tumors

ACTH (adrenocorticotropic hormone) stimulates the adrenal gland to make steroids that affect metabolism. They reduce redness and inflammation all over the body. They also slow down the immune system [2,3]. Too much ACTH can cause Cushing's disease. This disease causes fat buildup in face, neck, back, abdomen, and chest. Also the arms and legs tend to become thin. may also have purple stretch marks and high blood pressure. These tumors can also weaken the bones leading to osteoporosis [13].

2.4. Growth Hormone-secreting Tumors

These tumors make too much growth hormone. In children, too much growth hormone stimulates the growth of almost all the bones in the body [14]. When that occurs, the result is called gigantism. Gigantism can include increased height (over 7 feet), very quick growth, joint pain, and heavy sweating. In adults, too much growth hormone causes a condition called acromegaly [3].

3. Etiology of Pituitary Adenomas

Up till now, the exact etiology of uncontrolled cell growth in the pituitary gland, which creates a tumor, remains unknown [4]. A small percentage of pituitary tumor cases run in families, but most have no apparent hereditary factor. Researchers suggest that genetic alterations play an important role in how pituitary tumors develop [15]. Patients with a family history of certain hereditary conditions, such as multiple endocrine neoplasia type 1 (MEN 1), have an increased risk of pituitary tumors. In MEN 1, multiple tumors occur in various glands of the endocrine system. Genetic testing is available for this disorder [16].

4. Clinical Presentation of Pituitary Adenomas

Early signs of pituitary adenomas usually depend on whether the tumor is functioning (making excess hormones) or non-functioning (not making excess hormones) [17]. Functioning adenomas may cause problems because of the hormones they release. Most of the time, a functional adenoma makes too much of a single pituitary hormone. These tumors are often found while they are still fairly small (microadenomas) [18]. Tumors that aren't making excess hormones (non-functioning adenomas) often become large (macroadenomas) before they are noticed. These tumors don't cause symptoms until they press on nearby nerves, parts of the brain, or other parts of the pituitary gland [19]. Non-functioning adenomas that cause no symptoms are sometimes found accidentally while an MRI or CT scan is done for other reasons. These might be the most common pituitary tumors. As long as they aren't causing symptoms, they're often just watched closely without requiring any intervention [7].

Pituitary macroadenomas and carcinomas, whether functional or not, can be large enough to press on nearby nerves or parts of the brain. This can lead to symptoms such as weakness of muscles of the eye, blurred or double vision, blindness, headaches, facial numbness or dizziness [3]. Macroadenomas and pituitary carcinomas may also press on and destroy the normal parts of the pituitary gland leading to deficiency of one or more pituitary hormones [20]. Low levels of some body hormones such as cortisol, thyroid hormone, and sex hormones may cause symptoms. Depending on which hormones are affected, symptoms might include nausea, weakness, unexplained weight loss or weight gain, loss of body hair, fatigue, nenstrual disturbances in females and sexual dysfunction in males [21].

5. Complications of Pituitary Adenomas

One of the most serious pituitary tumor complications is blindness. This occurs when a tumor puts too much pressure on the optic nerve which is very close to the pituitary gland. Not everyone who has a pituitary tumor will have vision problems, however. Tumor growth and vision loss usually occur very gradually [3].

Other potential complications include diabetes insipidus, permanent hormonal deficiency and pituitary apoplexy [22]. Diabetes insipidus is mostly associated with macroadenomas and occurs when the pituitary gland and the hypothalamus don't produce enough vasopressin, a hormone that maintains the body's water balance. The most common symptom is constant thirst. This is because without vasopressin, the kidneys aren't able to hold onto water leading to dehydration. This condition can also be a complication of some pituitary tumor treatment [23]. Also, pituitary tumors may cause permanent hormonal imbalance such as thyroid-stimulating hormone deficiency which requires thyroid hormone replacement therapy [24]. Pituitary apoplexy is a rare but serious complication that causes sudden bleeding into the pituitary tumor and needs immediate treatment, usually with corticosteroids or surgery [22].

6. Fate of Pituitary Adenomas

Prognosis of pituitary adenoma depends on the type of tumor and whether the tumor has spread into other areas of the central nervous system or outside of the central nervous system to other parts of the body [21]. The choice of the lines of treatment depends on the type and size of the tumor, the hormones secreted by the tumor, the presence of problems with vision, the presence of metastasis and whether the tumor has just been diagnosed or has recurred [25].

7. Management of Pituitary Adenomas

Pituitary adenomas may hypersecrete hormones or cause mass effects. Therefore, early diagnosis and treatment are important. Prevalence of pituitary adenomas ranges from 1 in 865 adults to 1 in 2688 adults. Approximately 50% are microadenomas (<10 mm); the remainder are macroadenomas (>10 mm) [2]. Lines of treatments include transsphenoidal surgery, medical therapies, and radiotherapy [25]. Prolactinomas account for 32%to 66% of adenomas and present with amenorrhea, loss of libido, galactorrhea, and infertility in women and loss of libido, erectile dysfunction, and infertility in males. They are generally treated with the dopamine agonists cabergoline and bromocriptine [26]. Growth hormone-secreting tumors account for 8% to 16% of pituitary tumors and usually present with enlargement of the lips, tongue, nose, hands, and feet and are diagnosed by elevated insulin-like growth factor 1 levels and growth hormone levels [27]. Initial treatment of this type of tumors is surgical. Medical therapy with somatostatin analogues, cabergoline, and pegvisomant may be also needed [28]. Adrenocorticotropic hormone secreting tumors account for 2% to 6% of adenomas and are associated with obesity, hypertension or diabetes mellitus. Measurement of a late-night salivary cortisol level is the best screening test but petrosal sinus sampling for ACTH may be necessary to distinguish a pituitary from an ectopic source [29]. The primary treatment of Cushing disease due to ACTH-producing adenomas is surgical resection and medical therapies including ketoconazole, mifepristone, and pasireotide [30]. Hyperthyroidism due to thyroid-stimulating hormone secreting tumors accounts for 1% of the pituitary tumors and is treated with surgery and somatostatin analogues if not surgically cured [31]. Nonfunctioning adenomas are usually presented with mass effects. Surgery is the primary treatment of this type of tumors, although incidentally found tumors may require no treatment if they are asymptomatic [32].

Patients with pituitary adenomas should be identified at an early stage so that effective treatment can be planned [3]. For prolactinomas, initial therapy is generally dopamine agonists. For all other pituitary adenomas, initial therapy is generally transsphenoidal surgery with medical therapy being reserved for those not cured by surgery [26].

Management of pituitary tumors is multidisciplinary, with medical therapy playing an increasingly important role [33]. Except for prolactin-secreting tumors, surgery is considered the first-line therapy for the majority of pituitary adenomas. However, pharmacological therapy plays an important role in controlling hormone-producing pituitary adenomas, especially for patients with acromegaly and Cushing disease [34]. In non-functioning pituitary adenomas, pharmacological therapy plays a minor role [32]. For pituitary carcinomas and atypical adenomas, medical therapy, including chemotherapy, acts as an adjuvant to surgery and radiation therapy [35]. Improvement in patient selection and determination of the prognostic factors largely helped to individualize therapy for patients with different types of pituitary adenomas [4].

8. Conclusion

Pituitary adenomas are the most common form of neoplasms that originate from the pituitary gland. They may be functioning or nonfunctioning tumors. Symptoms generally depend on the type of the tumor and its size. Management of functioning pituitary adenomas often requires the collaboration of different treatment modalities to achieve rapid and durable remission and thus improve the morbidity and mortality rates. Recent studies should be directed towards development of effective medical therapies that are suitable for patients with uncontrolled disease or intolerance to the traditional medications.

Conflict of Interest

The author has no conflict of interest to declare.

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