Diagnosis of pituitary disease

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Abstract

The prevalence of pituitary disease is increasing mainly because of advances in modern imaging techniques and an increased awareness among the medical community. Pituitary tumours constitute 10–15% of all diagnosed intracranial neoplasms, and their clinical manifestations result from local mass effects (mostly neurological, visual, hypopituitarism) and/or hypersecretion. Pituitary adenomas are the most common pituitary tumours and are clinically classified as functioning or non-functioning. Most are sporadic, but in rare cases they can be related to hereditary syndromes. Other lesions involving the (para)sellar region include inflammatory and infiltrative diseases, cysts, primary or metastatic neoplasms, abscesses and internal carotid artery aneurysms. The clinical manifestations of hypopituitarism depend mainly on the type, number and severity of hormonal deficits. Establishing the diagnosis requires hormonal measurements (basal or after dynamic tests), and management includes relevant hormonal replacement and life-long monitoring.

Keywords Craniopharyngioma; hypophysitis; hypopituitarism; pituitary adenoma; pituitary apoplexy; pituitary incidentaloma; pituitary stalk lesions; Rathke's cleft cyst

Key points

- Pituitary adenomas comprise the majority of pituitary tumours and can be functioning or non-functioning
- Clinical features of pituitary masses can result from local mass effects and/or hypersecretion
- Sellar or parasellar masses mainly include adenomatous and non-adenomatous tumours, inflammatory and infiltrative diseases, cysts, primary or metastatic malignancies, pituitary infections and internal carotid artery aneurysms
- All patients with pituitary masses should undergo testing for hypopituitarism and for hormonal hypersecretion (in cases of pituitary adenomas), radiological assessment and neuro-ophthalmological evaluation

Introduction

The pituitary gland, or hypophysis cerebri, is considered to be the 'master gland' of the endocrine system, integrating, together with the hypothalamus, hormonal signals that control a plethora of endocrine and metabolic functions.

The prevalence of pituitary disease has increased over the last 10 years because of advances in modern imaging techniques and hormonal measurements, as well as an increased awareness and rate of suspicion for these disorders on the part of the medical community. Fortunately, the improvements in pituitary surgery and radiotherapy techniques, combined with the development of medical treatments for pituitary tumours and advances in pituitary hormone replacement therapy, have led to more optimal outcomes.

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Pituitary anatomy

The pituitary gland consists of an anterior lobe (adenohypophysis), posterior lobe (neurohypophysis) and vestigial intermediate lobe. It lies at the base of the brain in the sella turcica, within the sphenoid bone, and is overlain by the dural sellar diaphragm, through which the pituitary stalk connects to the median eminence of the hypothalamus. The sellar diaphragm also protects the pituitary from compression by the cerebrospinal fluid (CSF). In both sides of the sella turcica, and lateral and superior to the sphenoid sinus, are the cavernous sinuses; the cavernous segments of the internal carotid arteries and the cranial nerves III, IV and VI are located in these. The optic chiasm is anterior to the pituitary stalk, and typically sits 5–10 mm above the sellar diaphragm.

The pituitary measures approximately 13 mm transversely, 9 mm anteroposteriorly and 6–9 mm vertically, and in adults weighs around 600 mg (range 400–900 mg). However, the size and volume of the gland change in different situations: the pituitary increases during pregnancy to almost twice its normal size, whereas it decreases in older people.

Anterior lobe (adenohypophysis)

The anterior lobe constitutes nearly 80% of the gland's mass and comprises five hormone-secreting cell types (Table 1):

- **somatotrophs**, which produce and secrete growth hormone (GH)
- **lactotrophs**, which produce and secrete prolactin (PRL)
- **corticotrophs**, which produce and secrete adrenocorticotrophic hormone (ACTH) and other pro-opiomelanocortin peptides
- **gonadotrophs**, which produce and secrete follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
- **thyrotrophs**, which produce and secrete thyroid-stimulating hormone (TSH).

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Hormone-producing cells in the anterior pituitary gland

Type of cell	Percentage of cells in anterior pituitary lobe	Distribution of cells
Somatotrophs	40–50%	Lateral wings of adenohypophysis
Lactotrophs	15–20%	Dispersed populations throughout the anterior lobe; mainly in the posterior part of the lateral wings
Corticotrophs	15–20%	Middle and posterior portion of anterior lobe
Gonadotrophs	10–15%	Distributed through anterior lobe
Thyrotrophs	5–10%	Anterior medial part of adenohypophysis

Table 1

The anterior lobe also includes the folliculostellate cells, which are not hormone-secreting but which play an important role in the integration of information in the anterior pituitary auto/paracrine loops.

Posterior lobe (neurohypophysis)

The posterior pituitary lobe comprises the distal axons of the magnocellular neurosecretory cells extending from the supraoptic and paraventricular nuclei of the hypothalamus. These cells synthesize the neurohypophyseal hormones oxytocin and vasopressin and store them in neurosecretory granules at their axon terminals; they are released from here into the neurohypophyseal capillaries and systemic circulation.

Blood supply

The anterior pituitary receives most of its blood supply from the hypothalamo-hypophyseal portal system, which originates from the capillary plexus of the median eminence and superior stalk, derived from the superior hypophyseal arteries. Through this system, the hypophysiotrophic hormones are delivered to the hormone-producing cells of the adenohypophysis. The remainder of the blood supply is via the pituitary capsular vessels, which also originate from the superior hypophyseal arteries. The posterior lobe and stalk are directly supplied with blood from the hypophyseal arteries.

The venous drainage from both lobes is through the cavernous sinuses into the petrosal sinuses and internal jugular veins.

Pituitary tumours

Pituitary tumours constitute 10–15% of intracranial neoplasms and are often discovered incidentally on imaging performed for an unrelated reason (pituitary incidentaloma). Their clinical features can result from local mass effects and/or hypersecretion.[1]

The local mass effects depend on the size of the tumour and its anatomical position and extensions. Headache is usually the consequence of dural stretching. The neuro-ophthalmological effects include visual field defects (usually bitemporal hemianopia) from compression of the optic pathways, and ocular nerve palsies caused by lateral extension to the cavernous sinuses. Erosion of the sellar floor can result in sinusitis, CSF rhinorrhoea and meningitis. The anterior pituitary hormone deficits tend to occur in a specific order, with GH and gonadotrophins affected first, followed by ACTH and TSH. PRL secretion is the most resistant, and decreased concentrations indicate severe pituitary damage.

All patients with a pituitary mass should undergo testing for hypopituitarism and neuro-ophthalmological evaluation. With pituitary adenomas, hormonal hypersecretion needs to be assessed. Careful neuroradiology review aiming to identify imaging features helpful for the differential diagnosis is also mandatory.

Pituitary adenomas

Pituitary adenomas account for 90% of pituitary tumours and have a prevalence of 77.6 cases per 100,000 inhabitants in the UK. They are benign lesions arising from adenohypophyseal cells and, based on their size, are classified as microadenomas (<10 mm in diameter) or macroadenomas (≥10 mm in diameter). They may hypersecrete hypophyseal hormones (functioning) or can be clinically non-functioning. Although most are sporadic, they are in rare cases related to hereditary syndromes, such as multiple endocrine neoplasia type 1, Carney complex or familial isolated pituitary adenomas.

Non-functioning pituitary adenomas: these comprise 15–37% of all pituitary adenomas and have a prevalence of 7–22 per 100,000 inhabitants. As they are not associated with hormonal hypersecretion, they usually escape early diagnosis, and are mostly recognized when they are large enough to exert pressure effects on surrounding tissues; thus, at the time of detection, 67–90% are macroadenomas. Additionally, at diagnosis, 60–85% of the patients have at least one pituitary hormone deficiency.

First-line treatment for macroadenomas is surgery, usually using a trans-sphenoidal approach; this aims to improve or resolve the mass effects on adjacent structures, especially the optic pathways. Radiotherapy can be offered as adjuvant treatment after surgery, aiming to prevent tumour regrowth. The management of regrown non-functioning pituitary adenomas includes observation, surgery, radiotherapy or a combination of surgery and radiotherapy.

Functioning pituitary adenomas: these release excessive amounts of active hypophyseal hormones into the systemic circulation, resulting in multiple clinical manifestations. Prolactinomas are the most prevalent hormone-secreting adenomas followed by GH-producing, corticotroph and thyrotroph adenomas. The clinical presentation, diagnosis and treatment of functioning adenomas depend on the type of hormone(s) secreted (Table 2).

Other sellar or parasellar masses

Rathke's cleft cysts: these are benign sellar and/or suprasellar lesions that arise from remnants of Rathke's pouch.[2] Their size varies, as does their content (ranging from clear CSF-like liquid

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