

Pituitary incidentaloma

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Background

Detection of a pituitary incidentaloma is a recent clinical problem resulting from the increased use of high-resolution cranial imaging, particularly magnetic resonance imaging (MRI). From a clinical standpoint, pituitary incidentaloma is defined as a pituitary lesion discovered unexpectedly in an individual with no obvious symptoms to suggest pituitary disease. In this situation, cranial imaging has typically been undertaken for evaluation of headache, other neurological complaints or following head trauma. By convention, a lesion measuring <10 mm is termed a micro-incidentaloma and a lesion measuring ≥10 mm is a macro-incidentaloma. This is a useful subdivision to guide clinical management.

Epidemiology, aetiology and natural history

Pituitary incidentaloma is common. In a systematic review, Ezzat *et al* estimated the prevalence of pituitary incidentaloma to be between 14% (autopsy series) and 23% (imaging series).¹ Most are small pituitary microadenomas (<5 mm), of which approximately 40% immunostain for prolactin. The prevalences are similar between sexes and across all ages. Larger lesions are referred more commonly for specialist endocrine evaluation; most will still be pituitary adenomas, but there is a differential diagnosis to be considered (Table 1).

Only limited information is available on the natural history of pituitary incidentaloma. In a meta-analysis of studies including a total of 865 patients with nonfunctioning incidentaloma, lesions ≥10 mm in diameter were four times more likely to increase in size during follow-up than those <10 mm in diameter (12.5% vs 3.3% per 100 person years).² Karavitaki *et al* demonstrated a 44% 4-year probability of enlargement for untreated, (presumed) nonfunctioning pituitary macroadenomas.³

Investigations

Hyperfunction

All patients with pituitary incidentaloma should be investigated for pituitary hyperfunction. The single most important test is measurement of serum prolactin (PRL). Elevated PRL can indicate either direct tumour secretion (levels are typically 800–2,000 mU/l for microprolactinoma, >2,000 mU/l for macroprolactinoma and <600 normally) or ‘disconnection’ of the hypothalamus and normal pituitary gland by a large nonfunctioning pituitary mass (PRL usually <2,000 mU/l). In patients with raised PRL, it is important to consider PRL-elevating drugs (eg domperidone), hypothyroidism and ‘macroprolactin’ (an assay artefact caused by PRL-binding immunoglobulin G, which is present in approximately 1% of normal individuals). Hypogonadism (with implications for bone thinning as well as sexual dysfunction) can occur with any degree of hyperprolactinaemia.

Although acromegaly is a rare cause of pituitary incidentaloma, it is an important diagnosis to make as early as possible; insidious symptoms of acromegaly might have been overlooked until the time of incidentaloma discovery. The best single test for acromegaly is measurement of serum

Table 1. Differential diagnosis of pituitary incidentaloma.

Diagnosis	Typical radiological and clinical features
Pituitary adenoma (most common)	<ul style="list-style-type: none"> • Microadenoma: hypodense lesion within the pituitary gland (<10 mm in diameter) • Macroadenoma: usually smooth contoured lesion, arising from within the sella, and often with suprasellar extension (≥10 mm in diameter)
Craniopharyngioma	<ul style="list-style-type: none"> • Calcification on CT scan • Cystic change • Diabetes insipidus • ‘Hypothalamic’ features (eg hyperphagia and weight gain)
Meningioma	<ul style="list-style-type: none"> • Homogeneous, increased signal (before and after MRI contrast) • Dural ‘tail’ and adjacent hyperostosis
Metastasis	<ul style="list-style-type: none"> • Epicentre often suprasellar • Unusual, irregular shape • Carotid artery compression • Diabetes insipidus
Hypophysitis	<ul style="list-style-type: none"> • Other pointers to malignancy: weight loss, breast lump, smoker, abnormal chest X-ray • Increased and homogeneous MRI contrast enhancement • Female gender • Recent pregnancy • Associated autoimmune diseases, eg type 1 diabetes mellitus
Carotid artery aneurysm (intrasellar)	<ul style="list-style-type: none"> • Markedly increased and homogeneous MRI contrast enhancement

CT = computed tomography; MRI = magnetic resonance imaging.

insulin-like growth factor 1 (IGF1); in patients with borderline IGF1, suppression of growth hormone (GH) after glucose loading should be checked. Thyroid function testing is routine and relatively inexpensive. The relationship between free-thyroxine and thyroid-stimulating hormone (TSH) should be examined carefully. If thyroxine is elevated and TSH is either normal or raised, the rare but important possibility of TSH-secreting pituitary adenoma should be considered. Cushing's syndrome is rare and often difficult to diagnose. If there are suggestive clinical features, overnight dexamethasone suppression testing or measurement of urinary free cor-

tisol can be undertaken in selected cases.⁴ However, it should be remembered that pituitary micro-incidentoma is common and might be present in patients with Cushing's syndrome not resulting from pituitary pathology. Two examples of hyperfunctioning pituitary incidentomas are shown in Fig 1.

Hypofunction

Significant hypopituitarism is unlikely to be present in a patient with a pituitary micro-incidentoma. By contrast, patients with macro-incidentomas should undergo full pituitary function testing.⁵ A simple thyroid

profile might be informative; low thyroxine associated with normal or reduced TSH is likely to indicate secondary hypothyroidism. Adrenal reserve can be conveniently assessed by short Synacthen® testing, whereas more detailed assessment of adrenocorticotrophic hormone (ACTH) and GH is usually undertaken at a later stage in management. It should be noted that 50% of GH-deficient adults have normal IGF1 levels. Gonadotropin deficiency is common in patients with pituitary macro-incidentomas but irrelevant in postmenopausal women. The presence of diabetes insipidus should alert a clinician to pathology other than a pituitary adenoma (Table 1).

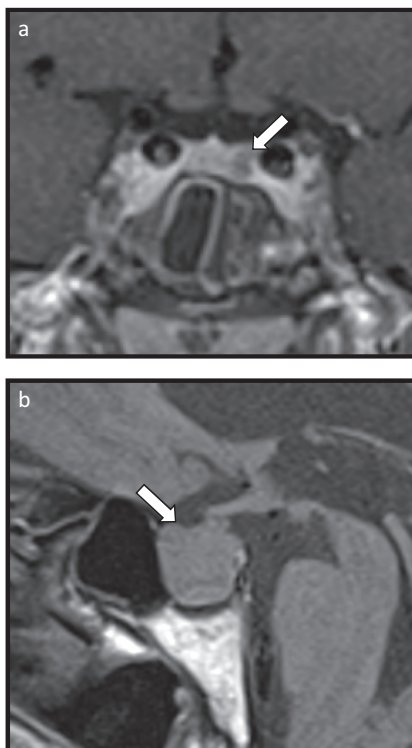


Fig 1. Examples of pituitary incidentoma. (a) Microadenoma (6 mm, arrow), revealed on MRI (coronal slice) in a 56-year-old man whose sole complaint was 'dizziness'. Serum prolactin was raised (1,250 mU/l, normal <300) and testosterone reduced (5.2 nmol/l, normal 10–35). Both hormones normalised with low-dose dopamine agonist therapy (cabergoline). (b) Macroadenoma (18 mm, arrow), revealed on MRI (sagittal slice) in an 84-year-old man with 'cognitive decline'. Serum IGF1 was raised (130 nmol/l, normal 7–22). The pituitary tumour shrank and sleep apnoea improved following somatostatin analogue therapy (lanreotide). IGF = insulin growth factor; MRI = magnetic resonance imaging.

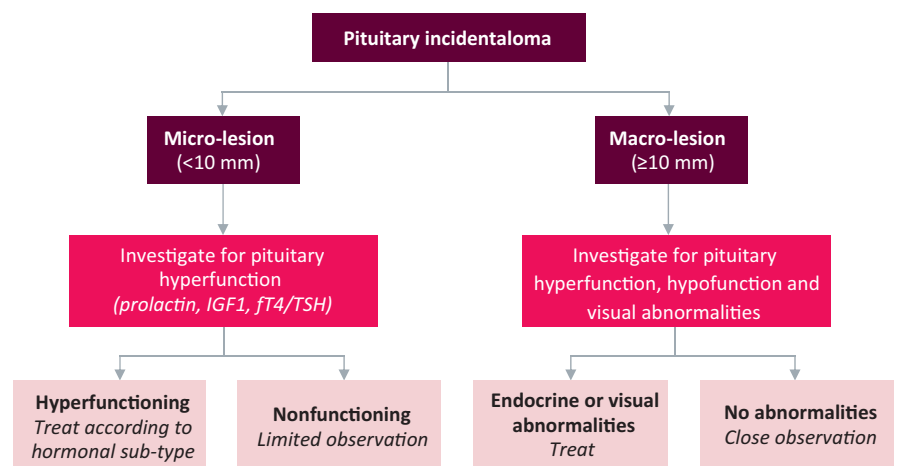


Fig 2. Summary of investigation, treatment and follow-up of pituitary incidentoma. fT4 = serum free T4, IGF1 = insulin-like growth factor 1, TSH = thyroid-stimulating hormone.

Key points

Increased use of high-resolution cranial magnetic resonance imaging (MRI) has led to the detection of pituitary incidentoma in up to 20% of patients without obvious pituitary symptoms

Most incidentomas are small, benign, pituitary adenomas that can be either functioning or nonfunctioning, the latter being the most common

Measurement of serum prolactin concentration is the most important test and recommended in all cases

Macro-incidentomas (≥ 10 mm in diameter) are four times more likely than are micro-incidentomas (< 10 mm) to increase in size with time

Close surveillance of nonfunctioning pituitary macro-incidentomas should be undertaken, with endocrine, ophthalmological and MRI monitoring, annually for at least 5 years, and less frequently thereafter

KEY WORDS: Pituitary incidentoma, pituitary adenoma, magnetic resonance imaging (MRI), prolactin, pituitary apoplexy

Box 1. Typical clinical features of pituitary apoplexy.

Emergency presentation:

- Sudden-onset headache
- Vomiting
- Diplopia
- Visual impairment
- Meningism
- Reduced conscious level
- Haemorrhage on CT scan of brain (± blood in CSF)

Consider: could this be pituitary apoplexy, rather than aneurysmal subarachnoid haemorrhage?

If there is a pituitary mass on head scan:

- ✓ Check serum cortisol
- ✓ Start hydrocortisone replacement (without waiting for cortisol result)
- ✓ Refer urgently to specialist neuroendocrine team
- ✓ Request MRI scan of pituitary

CSF = cerebral spinal fluid, CT = computerised tomography, MRI = magnetic resonance imaging.

Vision

Patients with pituitary macro-incidentoma, particularly those with suprasellar extension, should have careful ophthalmological assessment and recording of visual acuities and visual field perimetry. This can confirm normal vision as a baseline for future follow-up or reveal an asymptomatic visual defect requiring active intervention.

Management

Evidence of hormone excess, chiasmal compression and ‘significant’ extrasellar disease are all clear indications for appropriate medical and/or surgical interventions (Fig 2). Most prolactinomas of all sizes are treated successfully with dopamine agonist therapy alone. GH-secreting adenomas can sometimes be treated with primary medical therapy (combinations of somatostatin analogues, dopamine agonists and GH-receptor antagonists), but surgery still has an important place in the management algorithm. Nonfunctioning pituitary macroleions producing visual failure require surgery to debulk the lesion and provide a histological diagnosis (Table 1).

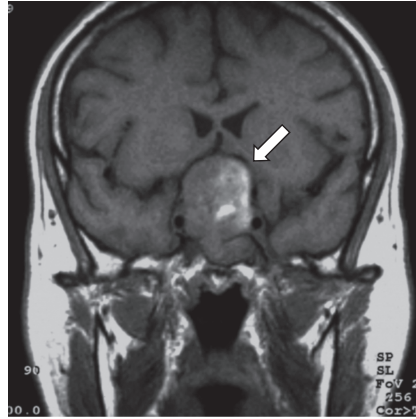


Fig 3. Pituitary apoplexy. Unenhanced MRI showing a heterogeneous and previously unsuspected pituitary mass (arrow) – histology confirmed infarction and haemorrhage within a pituitary adenoma. MRI = magnetic resonance imaging.

Micro-incidentaloma

Patients with nonfunctioning lesions <5 mm in diameter require no further testing. Those with lesions 5–9 mm in diameter should have a repeat serum PRL and MRI after 1 year; if there has been no change, the patient can be discharged with reassurance. This approach is less rigorous than the recently published US Endocrine Society guideline, which recommends annual MRI for 3 years and ‘gradually less frequently’ thereafter.⁶

Macro-incidentaloma

Patients with nonfunctioning macroleions that are well separated from optic structures (mostly 10–20 mm in diameter) require careful follow-up because of the increased risk of tumour growth. Endocrine testing, MRI and visual assessment should be repeated after 6 months and then annually for at least 5 years. If the lesion has been stable, monitoring frequency can be reduced, but not stopped completely. This is in line with the US Endocrine Society guideline for larger lesions.⁶ Managing ‘tumour anxiety’ can be a clinical challenge during ‘watchful waiting’. Naturally, any hormonal deficiencies should be fully corrected with appropriate replacement therapies.

Pituitary apoplexy

Although not strictly a pituitary incidentoma, pituitary apoplexy is mentioned here for two reasons. First, it produces a clinical syndrome often indistinguishable from acute aneurysmal subarachnoid haemorrhage and the discovery of a pituitary mass on computerised tomography (CT) scan is usually an unexpected finding. Second, it is crucially important for acute-care physicians and radiologists to appreciate that pituitary apoplexy is a medical emergency and timely glucocorticoid administration can be life saving. UK guidelines on diagnosis and management of acute pituitary apoplexy have been recently published.⁷ The typical clinical features and an illustrative MRI scan are shown in Box 1 and Fig 3 respectively.

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