West Yorkshire & Harrogate Cancer Alliance

Guidelines for the Management of Pituitary Tumours

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1 Pituitary tumours

1.1 Purpose of the guidelines

Pituitary tumours represent a heterogeneous group of disorders, both clinically and pathologically.

These guidelines relate to the management of patients with all types of pituitary tumour whose care falls under the Pituitary MDT, they are supplementary to the Guidelines for the Management of Brain and Central Nervous System (CNS) Tumours

The pituitary guidelines are not intended to offer a rigid protocol, but to provide a framework for the delivery of high quality specialist care.

1.2 Introduction

Pituitary tumours are common with an estimated prevalence of 16.7% in the general population[1]. Although the majority of these lesions are clinically silent, a subgroup of patients manifest endocrine and/or neurological sequelae due to one or more of:

(i) hormone hypersecretion
(ii) hypopituitarism
(iii) local mass effect (e.g. optic chiasm compression)

Most pituitary tumours are pituitary adenomas (PA): based on size, PA are traditionally classified as microadenomas (<1 cm maximum diameter) or macroadenomas (>1 cm maximum diameter), each of which may be either hormone-secreting (i.e. functional) or non-functional (non-functioning pituitary adenomas – NFPA).

Common functional tumours secrete prolactin (PRL – prolactinomas), growth hormone (GH – somatotropinomas – acromegaly) or adrenocorticotrophic hormone (ACTH – corticotropinomas – Cushing's disease).

Tumours secreting thyroid stimulating hormone (TSH) or biologically active follicle stimulating hormone (FSH) and/or luteinizing hormone (LH) are rarer.

1.3 Epidemiology

Both autopsy and radiological series indicate that pituitary tumours are common: 14.4% prevalence at autopsy (systematic review of 3375 subjects in 7 studies)[1]; mean prevalence in radiological series 22.3% (systematic review of 202 subjects in 3 studies)[1]; yielding a 'combined final prevalence' of 16.7%[1]. The majority of these tumours are clinically silent, with clinically relevant PA (i.e. those presenting with hyperfunction, hypopituitarism and/or mass effect) estimated to occur in 1:1000 to 1:1500 of the general population[2,3]. Pituitary tumours account for 10% of all diagnosed intracranial tumours (Cancer Registry data) and are the third most common intracranial neoplasm[4]. Overall the sex incidence is equal, but with a difference for certain tumour types (e.g. microprolactinomas are more commonly diagnosed

in women and macroprolactinomas are more common in men). Prolactinomas are the most common PA in subjects <60 years, and NFPA in those >60 years. There is no known racial difference in prevalence.These tumours are rare in childhood and prevalence increases with age[5].

1.4 Aetiology

The majority of pituitary tumours are benign PA with pituitary carcinomas comprising 0.2% of surgically resected specimens[6,7]. Although there have been recent advances in the understanding of the aetiology of pituitary tumours, knowledge remains sparse. Factors implicated include those intrinsic to the pituicyte, and altered availability of regulatory factors and autocrine/paracrine growth factors[8]. Pituitary tumours are thought to arise as a result of monoclonal expansion of a single transformed cell, rather than polyclonal proliferation[8]. Most PA are sporadic tumours, but a small proportion may have an underlying genetic cause (see below).

1.5 Genetics

It is estimated that pituitary tumours arise in a familial setting in approximately 4 to 5% of cases.

Currently, four conditions are known to be associated with familial pituitary tumour syndromes:

- multiple endocrine neoplasia type 1 (MEN-1)
- multiple endocrine neoplasia type 4/type X (MEN-4/MEN-X)
- Carney complex (CNC)
- familial isolated pituitary adenomas (FIPA)[9]

Over half of these familial cases are due to MEN-1 or CNC[3]. Prolactinomas predominate amongst MEN-1 associated PA, and are typically macroadenomas (80%), with higher rates of invasion than in non-MEN-1 prolactinomas – their response to dopamine agonists is often poor, with <50% of cases exhibiting normalisation of serum prolactin[10]. Other pituitary tumours also tend to be larger and more aggressive in MEN-1[10].

Approximately 10% of patients with CNC manifest overt acromegaly, which often develops insidiously[13]. and is caused by multifocal hyperplasia of somatomammotrophic cells[14].

The remaining familial cases are termed FIPA[15,16], which tend to occur at younger age and often present with larger tumours. Germline mutations in the aryl hydrocarbon receptor-interacting protein gene (AIP) are found in 15% of families[16].

If a familial pituitary tumour syndrome is suspected, consider referring to Genetics service for MEN1 screening, or entering patient into the FIPA study.

1.6 Clinical features and differential diagnosis

As outlined above, apart from those pituitary tumours that are discovered incidentally during radiological investigations undertaken for other clinical indications, or as part of a screening programme in familial disorders, the mode of presentation largely depends on whether the tumour is functional or not[17].

1.6.1 Who to suspect pituitary disease in?

Many patients with pituitary tumours will present insidiously or with an incidental finding on MR imaging for another reason. However, there are certain categories of patients in whom the index of suspicion should be raised, and an endocrinology referral should always be considered.

- Visual field defects (classically bitemporal hemianopia or superior quadrantopia)
- Hypogonadotropic hypogonadism (low testosterone or oestradiol, with low or normal LH/FSH)
- Unusual thyroid function tests: low Thyroxine plus low or normal TSH, or high thyroxine plus high or normal TSH
- Unexplained hyponatraemia
- Unexplained weight loss, malaise, dizziness
- Sudden onset headache, vomiting and visual disturbance (apoplexy)
- Other cranial nerve palsies (III, IV or VI from parasellar extension)
- Incidental lesion discovered on MRI scan
- Excess sweating, increase in the size of hands and feet, change in appearance (acromegaly)
- Central obesity, proximal myopathy, purple striae, hypertension, impaired glucose tolerance (Cushing's disease)
- Amenorrhoea and galactorrhoea (Prolactinoma females)
- Loss of libido, erectile dysfunction, visual field defect (Prolactinoma males)

1.6.2 Who requires urgent referral to an endocrinologist?

In the absence of visual field defects, patients with suspected pituitary failure should be referred for urgent assessment by an endocrinologist.

1.6.3 Who requires urgent referral to an Neurosurgeon?

All patients with significant visual field loss (usually temporal and classically bitemporal superior quadrantopia / hemianopia) should have MR scanning of the brain with contrast enhancement locally. If this reveals a pituitary tumour they should be referred urgently through the channels described below.

If the visual loss is significant over a few days the patient should have an urgent local scan and be referred to the neurosurgical service on call at Leeds Teaching Hospitals. The on call phone number is 07979 928120, this is for emergencies only.

1.6.4 Craniopharyngiomas and other parasellar lesions

Other conditions may also manifest as sellar/suprasellar/parasellar lesions, causing local mass effects and hypopituitarism (Table 1). The presence of diabetes insipidus (DI) should alert the clinician to the possibility of these other disorders (especially cranipopharyngioma, metastasis (e.g. breast, bronchus), autoimmune (lymphocytic) hypophysitis and other infiltrative conditions) as DI is rarely,if ever, a presenting manifestation of PA.

Craniopharyngiomas are often unpredictable and require detailed and prolonged follow up including regular MRI scans (at least annually for the first five years) over many years. Debulking surgery is usually required at first presentation, with appropriate hormone replacement therapy instituted perioperatively. However, radiotherapy and further surgery are frequently required during long term follow up.

Germ cell tumours usually respond well to chemotherapy and require long term oncology follow up.

The treatment and investigation of metastases depends on the underlying malignancy, though replacement therapy is usually required.

Autoimmune and infiltrative conditions must always be discussed at an MDT to help define a precise diagnosis and exclude more serious conditions. Long term management is dependent upon the underlying aetiology.

Rathke's cleft and other cysts always require monitoring, frequently require replacement therapy, but may not require further treatment.

Table 1: Examples of conditions that may present with sellar/suprasellar/parasellar lesions.

Cysts	**Tumours**	**Miscellaneous**
Rathke's cleft cyst	Pituitary adenoma	Aneurysm
Arachnoid cyst	Craniopharyngioma	Autoimmune hypophysitis
Epidermoid cyst	Meningioma	Infection
Dermoid	Chordoma	Granulomatous disorders
	Metastasis	Langerhans histiocytosis
	Sarcoma/glioma/Schwanoma/ hamartoma	

1.7 Diagnosis

Establishing the diagnosis of pituitary tumours depends on careful history and clinical examination, targeted endocrine testing, high quality imaging and histopathological assessment of surgically resected specimens.

1.7.1 History

The history should include questions to assess for functionality, hypopituitarism and compressive symptoms. If the history is suggestive of a PA then questioning should include reference to potential familial pituitary disorders.

1.7.2 Clinical examination

Similarly, clinical examination is predominantly focussed on looking for evidence of hormone hypersecretion, hormone hyposecretion, and compressive signs (visual deficits, cranial nerve deficits) (see above).

If other disorders are suspected, then the history and examination should be targeted appropriately.

1.7.3 Endocrine testing

Urgent assessment required in all patients with confirmed pituitary disease

- Prolactin
- 9am Cortisol
- Visual field assessment (for macroadenomas or those complaining of visual symptoms)
- MRI scan

As first line dopamine agonist therapy is preferred in patients with prolactinomas. Serum prolactin should be determined urgently in all patients before considering pituitary surgery.

Cortisol deficiency must also be excluded urgently before considering surgery in all patients, and can often be screened for by a single 9am cortisol. If the result is unclear and dynamic testing is not practical, the patient should be assumed to be cortisol deficient, and formal assessment deferred until after their surgery.

Visual field assessment may be clinical in the urgent setting as this informs the decision on the timing of surgery. This should always be confirmed with formal visual perimetry once practical.

MRI scan is the imaging of choice at diagnosis.

1.7.4 Baseline blood tests:

Initial evaluation should include baseline blood tests in all patients with suspected pituitary disease.

- Full blood count (anaemia and eosinophilia are associated with cortisol deficiency; a mild anaemia is frequent in androgen deficiency)
- Urea and electrolytes (hyponatraemia is associated with cortisol deficiency, hypernatraemia is associated with diabetes insipidus; and hypokalaemia with Cushing's disease)
- Liver function (useful to aid interpretation of borderline testosterone results)
- Bone profile (useful as a basic screen for MEN1)

1.7.5 Baseline pituitary function tests:

- Prolactin (consider screening for macroprolactin, and dilution to exclude hook effect with large tumours)
- Free T4 (FT4) and TSH
- Luteinising hormone (LH), follicle stimulating hormone (FSH)
- 9am testosterone (in men), plus SHBG if available
- Oestradiol (in women)
- 9am cortisol (+/- adrenocorticotrophic hormone (ACTH) if Cushing's syndrome is suspected)
- Insulin-like growth factor 1 (IGF-1) [+ growth hormone (GH) if acromegaly is suspected)
- Paired serum and urine osmolalities (if diabetes insipidus is considered a possibility).

Depending on the clinical suspicion and the results of baseline investigations, further endocrine evaluation may be required to confirm/refute evidence of hormone hypersecretion and/or hypopituitarism.

Peg precipitation of prolactin should be performed at baseline in cases of 'asymptomatic' hyperprolactinaemia to exclude biologically inactive 'macroprolactin' which of itself requires no further investigation or treatment. Very high levels of prolactin may also lead to falsely low or normal levels (the hook effect). In the presence of large tumours, apparently normal prolactin levels should be diluted and rechecked to detect this phenomenon[19].

Table 2. Examples of Investigations used to confirm/exclude hormone hypersecretion and hypopituitarism.

Disorder	**Investigations**
Acromegaly	Oral glucose tolerance test IGF-I
Cushing's disease	Urinary free cortisol (UFC) Dexamethasone suppression testing – overnight, low dose, Midnight serum cortisol/late night salivary cortisol Dexamethasone-CRH test ACTH Inferior petrosal sinus sampling (IPSS)

Disorder	Investigations
Thyrotropinoma (TSHoma)	alpha-subunit (alpha -subunit:TSH molar ratio) Sex-hormone-binding globulin (SHBG) TRH test T3 suppression test
GH deficiency	Glucagon stimulation test Insulin tolerance test Combined GHRH-arginine test*
Cortisol deficiency	Glucagon stimulation test Insulin tolerance test Short synacthen test
Diabetes Insipidus	9am urine osmolality (fluid restricted overnight) Water deprivation test

* Not generally available at LTHT

The majority of currently available serum cortisol assays measure total as opposed to free cortisol. Hence, it is necessary to withdraw exogenous oestrogen therapy for six weeks before undertaking assessment for hypo- or hyper-cortisolism in female subjects.

Modest hyperprolactinaemia may be seen with pituitary stalk compression (e.g. due to a NFPA or other lesion causing local mass effect). However, recent studies suggest that serum prolactin in such cases rarely exceeds 2000 mU/L[20].

Other causes of hyperprolactinaemia (e.g. drugs (especially certain antipsychotics), renal failure, stress) should also be excluded before making a diagnosis of prolactinomas or 'stalk disconnection' syndrome.

1.7.6 Imaging

MRI Scanning

The current gold standard imaging modality for pituitary tumours is magnetic resonance imaging (MRI). Ideally thin sections (e.g. 2mm) targeted to the pituitary fossa in both the sagittal and coronal planes should be performed. T1 weighted sequences before and after intravenous contrast are the main-stay of pituitary imaging[21]. T2 weighted images may provide additional useful information in certain settings (e.g. Rathke's cleft cyst).

There may be additional benefit in performing the post-contrast MRI sequences in a dynamic fashion (within the first 60 seconds) after contrast injection for patients with Cushing's disease as these tumours are frequently difficult to identify[22]. This can help visualise small PA, which typically enhance less than normal pituitary tissue, and this differential enhancement is sometimes best appreciated within the early arterial phase post-contrast injection[22].

Post contrast images are not always necessary during follow-up scanning.

CT Scanning

In patients who cannot undergo MRI scanning (e.g. pacemakers, extreme claustrophobia) computed tomography (CT) of the pituitary with 1mm slices should be performed, accepting the lower resolution compared with MRI. Wherever possible, MRI/CT should be reported by a Neuroradiologist with particular expertise in the assessment of sellar/parasellar disorders.

Interventional Radiology

Inferior petrosal sinus sampling (IPSS) is usually performed in patients with ACTH-dependent Cushing's syndrome[25]. IPSS helps to distinguish between a pituitary and ectopic source of ACTH secretion. Corticotroph PA are typically small and often cannot be localised with confidence even with high quality MRI.

In addition, pituitary 'incidentalomas' are common in the general population (see above) and may erroneously be assumed to be the source of ACTH excess. Hence, IPSS is useful as it typically provides a clear distinction between a central (pituitary) and peripheral (ectopic) origin: if the central to peripheral gradient of ACTH before and after injecting CRH are >2:1 and >3:1 respectively, then this is strongly suggestive of a pituitary source of ACTH[25].

More recent reports also suggest that in cases with no obvious baseline central to peripheral gradient, a peak stimulated central to peripheral gradient at 5 minutes post CRH >2 is 97% sensitive and 100% specific in diagnosing pituitary dependent disease. IPSS may also aid lateralisation of a PA within the pituitary fossa in approximately two thirds of cases[25].

As with MRI/CT, IPSS should be performed by a Radiologist with appropriate expertise, and it should be undertaken before commencing agents such as metyrapone or ketoconazole.

1.7.7 Ophthalmic assessment

Visual acuity and visual fields must be assessed formally (ideally through an Ophthalmic service) if imaging reveals suprasellar extension or if there is clinical evidence of visual impairment.Visual fields should also be formally tested prior to radiotherapy or radiosurgery. Assessment for other cranial nerve deficits [especially III, IV, VI] should also be performed if there is clinical suspicion of neuropathy and/or if imaging reveals parasellar extension into the cavernous sinuses.

1.7.8 Histopathology

Various histopathological classification systems have been proposed for PA[26]. The WHO 2004 system of immunohistochemical profiling primarily classifies PA according to secretory granule content which is highly useful clinically (Table 3). In addition, examining for immunoreactivity for certain transcription factors and keratins such as the Ki-67 labelling index (detected by MIB-1) is widely used as a marker of proliferation and potential for recurrence.

Histopathological findings should be reported by a Neuropathologist with particular expertise in sellar/parasellar disorders.

Table 3. WHO 2004 classification of pituitary tumours.

GH producing adenoma Densely granulated Sparsely granulated Mixed adenomas Mammosomatotroph adenoma Acidophil stem cell adenoma	Gonadotroph producing adenoma
PRL producing adenoma Densely granulated adenoma Sparsely granulated adenoma Acidophil stem cell adenoma	Unusual Plurihormonal adenoma Silent subtype 3 adenoma
TSH producing adenoma	Null cell adenoma Hormone immuno-negative adenoma Oncocytoma
ACTH producing adenoma Silent ACTH cell adenoma Subtype 1 – densely granulated Subtype 2 – sparsely granulated	Others Carcinoma Atypical adenoma

2 Treatment

The optimal choice of treatment for a pituitary tumour in any given patient is dependent on a number of factors including: mode of presentation, size of the tumour, functionality, compressive symptoms, new diagnosis/recurrence, previous treatment and patient preference.

Current therapeutic modalities include surgery, radiotherapy, medical treatment, chemotherapy (rarely), and 'watchful waiting' (with clinical, ophthalmic and radiological surveillance).

2.1 Medical treatment

2.1.1 Prolactinomas

Microprolactinomas almost always respond to oral dopamine agonist therapy and do not require discussion at the MDT.

Treatment is titrated to restore regular menses, and control other symptoms although restoration of a completely normal prolactin is not always necessary.

Echocardiographic scanning is currently recommended at baseline and annually when using ergot derived dopaminergic drugs (cabergoline, bromocriptine).

An attempt to withdraw treatment is usually made every two years or at the natural menopause. Repeat imaging is not usually required.

A greater remission rate is observed in patients where prolactin levels have been successful suppressed to less than 160 mu/l, or the tumour has reduced in size more than 50%

Macroprolactinomas also frequently respond to medical treatment but should always be discussed at MDT to consider other treatment modalities, and to ensure a full assessment has been made. Scanning is usually repeated at 6 weeks post treatment initiation and then at 12, and 24 months or as determined by MDT discussion.

2.1.2 Acromegaly

For GH-secreting tumours causing compressive symptoms/signs, surgery remains the preferred first line definitive treatment option. However, somatostatin analogue (SSA) therapy also affords control of tumour growth and hormone hypersecretion in a substantial proportion of patients and may be used as an adjunct to surgery and/or radiotherapy or as primary medical therapy in selected cases[28].

There is limited evidence that pre-surgical treatment with both Lanreotide Autogel and Sandostatin LAR may improve surgical outcomes in patients with macroadenomas, though further studies are required. Up to 30% of subjects with acromegaly are reported to respond to cabergoline, most notably those with only marginally increased GH levels. Pegvisomant, a GH receptor antagonist, is licensed for use in those with persistent active disease despite

surgery, radiotherapy and other medical therapy, but has significant cost implications. Pasireotide, a somatostatin analog with affinity at multiple somatostatin receptor subtypes, is likely to be available for use in treatment of acromegaly at the end of 2013.

2.1.3 Cushing's disease

For ACTH-secreting tumours, metyrapone and ketoconazole can help to control/normalise cortisol levels by inhibition of the cortisol synthetic pathway in the adrenal gland. Around 75% of corticotrophomas express the D2 receptor, and control of cortisol secretion occurs in up to 30% of patients with cabergoline.

Pasireotide has recently been licensed for use in Cushing's disease with normalisation of urinary free cortisol levels in around a third of cases.

Notably 60-70% of patients develop adverse events relating to hyperglycaemia.

Medical therapy is frequently administered to patients with a high cortisol burden for at least 6 weeks to aid medical optimisation pre-operatively.

They are also appropriately used following non-curative surgery while awaiting the benefits of radiotherapy and/or bilateral adrenalectomy

2.1.4 Thyrotropinomas

These are rare tumours in whom less data are available. Tumours causing compressive symptoms/signs should be offered surgery, though they may also respond to SSA therapy, radiotherapy or radiosurgery.

2.2 Surgery

For sudden and serious visual deterioration surgery may be required urgently.

For GH-, ACTH- and TSH-secreting PA and all NFPA causing compressive symptoms/signs surgery remains the preferred first-line 'definitive' treatment option in most centres.

Surgery also has a key role to play in some patients with prolactinomas (e.g. intolerance of/refractory to dopamine agonists). Medical pre-treatment may be indicated in some patients as above.

Most Surgeons have adopted a minimally invasive endoscopic approach to pituitary surgery , but there are a number of different other surgical approaches that can be used to resect/debulk pituitary tumours including: transsphenoidal (most commonly performed transnasal/transseptal with or without endoscopic assistance) and transcranial (e.g. subfrontal, pterional, transcallosal).

The decision to offer surgery, and choice of approach, should be made following careful discussion between the members of the pituitary MDT, taking in to account those individual factors highlighted above, and patient preference.

UK guidelines for the management of pituitary apoplexy have recently been published, and it is anticipated that these recommendations will be adopted .

2.3 Radiotherapy

Radiotherapy is most often employed as an adjunct to medical or surgical therapy.

Fractionated conformal external beam radiation therapy reduces excessive hormone production and prevents further growth/regrowth of residual tumour.The doses most commonly used are the order of 45Gy in 25 fractions of 1.8Gy[29].

Alternative modalities (e.g. Gamma Knife stereotactic radiosurgery) may have a role to play in a small number of highly selected cases, specifically for small, radiologically well defined tumours, located at a distance from the optic apparatus sufficient to limit the dose to the optic chiasm and nerves to ≤8Gy[30].

Following surgery the main indications for consideration of radiotherapy in non functioning pituitary adenomas are where there is a significant tumour remnant, particularly with an extrasellar component. Reported 10-year local control rates with adjuvant radiotherapy are usually in the range 80–97%[32,33,34,35].

Where there is no residual tumour or a small intrasellar remnant an expectant policy may be adopted, as up to 80% of these will be controlled at 5years[36].

In functioning tumours pituitary tumours the goals are similar across tumour types ie tumour control and suppression of hormone secretion., generally as an adjunct or salvage following surgery and medical management.There is often a delay before the benefits of radiotherapy are observed, especially with respect to control of hormone hypersecretion, and hence patients typically need to continue suppressive medical therapy for a variable period of time following treatment For example.In patients with acromegaly treated with radiotherapy serum GH levels can fall by 50% within two years, with mean levels less than 2.5 ng/ml in 60% by 10 yr, and 77% by 20 yr in one large series[37].

Radiotherapy also carries with it a risk of developing/evolving more widespread hypopituitarism, which can present several years down the line[38].

In a small number of cases, second tumours (e.g. meningioma) may occur within the radiation field[39] and an increased rate of cerebrovascular disease has also been reported in some studies[40]. However two recent Dutch studies did not show excess mortality or reduced quality of life following pituitary irradiation[41,42].

2.4 Chemotherapy

Chemotherapy is only rarely used in the management of pituitary tumours.

Recent case reports have detailed the successful use of temozolomide, an orally administered alkylating agent licensed to treat malignant gliomas, in the management of pituitary carcinomas and aggressive pituitary tumours.

The outcome of treatment might depend on the expression of O(6)-methylguanine-DNA methyltransferase (MGMT), a DNA repair enzyme that potentially interferes with drug efficacy.

Temozolomide should be considered in the treatment of these difficult pituitary tumours.Because of the inconsistency of published data, MGMT expression should not be taken as a reason to deny the potential benefit of temozolomide treatment, taking into account the paucity of other available treatments[43,44,45].

2.5 Watchful monitoring

Watchful monitoring with periodic assessment of visual status and interval MRI/CT scanning may be appropriate for some cases, e.g. incidentally discovered NFPA without compressive features.

2.6 Follow-up

For most patients periodic reassessment of endocrine, ophthalmic and radiological appearances will be required, especially in those who have undergone surgical intervention and/or received radiotherapy.

A typical follow up regime for a patient with intact pituitary function post surgery for a non functioning pituitary adenoma is outlined in Table 4.

Endocrine re-evaluation is likely to involve a similar combination of tests to those outlined above (1.7.3), and should be tailored to the individual. For example, an annual assessment for biochemical cure is undertaken initially in all patients with functioning tumours. Baseline reassessment is also indicated annually in all patients, and other measures may be used to help gauge the adequacy of pituitary replacement therapy periodically. However, dynamic pituitary function testing may also required on an ongoing basis (eg on alternate years) in patients apparently eupituitary following radiotherapy.

All patients should undergo repeat ophthalmological assessment post-surgery, and periodically (e.g. annually) thereafter (which may be undertaken via their optician) as dictated by their initial presentation and extent of residual tumour.

The timing of follow-up MRI/CT scans should be determined on a case by case basis. As a general rule of thumb the first postoperative scan is typically carried out between 3 to 6 months (early post-operative scans may be difficult to interpret due to post-operative

inflammatory changes). Thereafter, it is reasonable to perform 'routine' surveillance scans at 12, 24 48 and 72 month intervals after surgery. The interval between scans may then be increased (eg to 5 yearly), and the decision to continue long-term radiological surveillance should be made on an individual case basis.

Patients with small functioning tumours that are completely excised, with biochemical remission demonstrable post-operatively and no evidence of residual tumour on follow-up MRI, may be recommended for a combination of clinical and biochemical surveillance with repeat imaging only in the event of clinical concern.

Table 4: Follow-up regimen

Interval	**Tests**
1 week	U+E
6 weeks	Baseline +/- Dynamic pituitary function
3 months	Baseline MRI Formal visual field testing – in macroadenomas
6 months	Baseline pituitary function
12 months	1y follow up MRI Baseline pituitary function (+/- Dynamic pituitary function following radiotherapy, or of functional tumours to assess for cure)
18 months	Baseline pituitary function
2 years	2y follow up MRI Baseline +/- Dynamic pituitary function as above Consider formal visual field testing
3 years	3 y follow up MRI Baseline +/- Dynamic pituitary function
4 years	4y follow up MRI Baseline +/- Dynamic pituitary function Consider formal visual field testing
5 years	5 y follow up MRI Baseline +/- Dynamic pituitary function
7 years	7 y follow up MRI Baseline +/- Dynamic pituitary function Consider formal visual field testing

Conversely, earlier imaging is indicated if there is clinical/ophthalmic concern regarding possible tumour recurrence, interval growth or atypical tumours (eg craniopharyngiomas: section 1.6.3)
If a patient receives radiotherapy, then a return to a scanning interval of 3-6 months post-treatment, followed by further scans at years 1, 2,3,5, and 7 (as outlined above) is advised, but again with tailoring to the individual case.

3 Local arrangements for delivery of IOG compliant service

3.1 Pituitary MDT meetings

The pituitary MDT occurs every Wednesday at the Leeds General Infirmary

It is held to facilitate the discussion of patients with pituitary and parasellar disorders in order to provide guidance on the definitive management of newly diagnosed patients, and those receiving active treatment in line with Improving Outcomes Guidance. It also advises on follow up plans for patients under long term surveillance.

It is recommended that referring physicians attend and we are particularly pleased to invite all endocrinologists in the Yorkshire region.

3.2 Patients discussed at the MDT Meeting

All patients with sellar and parasellar disorders should be considered for discussion at the pituitary SMDT. However the following patients in particular should be referred for review:

- All new functional and non-functional pituitary macroadenomas post initial radiological diagnosis, pre- potential histological confirmation;
- All new functional microadenomas apart from prolactinomas post initial radiological diagnosis, pre- potential histological confirmation;
- All new sellar-related lesions with suprasellar and/or parasellar extension(s) – including those detected incidentally post initial radiological diagnosis, pre-potential histological confirmation;
- All patients with pituitary disease post histological confirmation pre-potential definitive surgical procedure
- All patients with pituitary disease post definitive surgical procedure, pre- potential adjuvant treatment
- Previously treated (surgery/radiotherapy or both) functional and non-functional macroadenomas where there is a need for ongoing advice regarding possible further treatment and/or radiological surveillance intervals especially those within 5 years of undergoing surgery and/or radiotherapy.
- All macroprolactinomas (including those being considered for medical therapy) at presentation, and again at 3-6 months following commencement of dopamine agonist treatment. These patients should be discussed again whenever a change in management is necessary eg patients intolerant of medical therapy, patients with a poor response to medical treatment or those requiring high dose medical therapy when the consideration of radiotherapy or surgery may be appropriate.
- All suspected/confirmed cases of pituitary carcinoma
- Pregnancy with pituitary adenomas (aside from microprolactinoma)
- Patients with a microprolactinoma desiring surgery
- Pituitary apoplexy with neurological signs and symptoms or where there is other clinical concern
- Malignancy elsewhere with an incidental pituitary lesion

3.3 MDT Referral guidelines

Cases are discussed after referral from cancer units. Given that the local managing team are not able to attend in person, it is vital that as much clinical information is available as possible. Access to relevant imaging is also essential.

Referral is done by completing the MDT Pituitary referral form which is available from www.leedsneurosurgery.com

Go to downloads and the Pituitary MDT Form is available there.

Please complete this form and send it via email to leedsth-tr.LeedsCancerCentre@nhs.net
Brain/CNS MDT Admin Office telephone number is : 0113 3928461/3928547

Imaging should be sent by image link from the referring hospital to Leeds Teaching Hospitals NHS Trust

Cases will NOT usually be discussed at the Wednesday MDT meeting unless this form and the relevant imaging and Endocrinology/ opthalmology results are received by 3.30pm on the preceding MONDAY.

Please note the Pituitary MDT is held EVERY Wednesday

If any patient needs discussion before the next MDT meeting, the relevant core members should be contacted immediately, and the patient discussed retrospectively at the next MDT.

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