

Neurological Aspects of Sellar and Parasellar Tumours



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Introduction

Pathology in the sellar and parasellar regions accounts for several disabling and distinctive neurological syndromes characterised by visual failure and upper cranial neuropathies. These features have a major impact on functional outcome and can be more intrusive for the patient than the commonly associated endocrine morbidity.

Recent advances in this field include the emphasis on multidisciplinary team (MDT) working, skull base endoscopy and stereotactic radiation therapy. This paper summarises the presentation, treatment and prognosis of sellar and parasellar lesions with particular reference to their neurological presentation and outcome.

The optic nerves and chiasm

Sellar and parasellar lesions commonly cause loss of visual acuity and visual field defects. Visual acuity tends to be progressively impaired in chiasmal or optic nerve compression; ultimately optic atrophy from chronic compression occurs with associated disc cupping and pallor on ophthalmoscopy. The patterns of visual field defect caused by parasellar lesions have been of diagnostic value for well over a century, since visual field perimetry pre-dated X-ray as a diagnostic tool.¹ Visual fields still provide valuable information about visual function and a means of measuring the progress and outcome of treatment.

Clinical Assessment

Visual acuity and fields

Visual acuity is best measured with the LogMAR charts now standard in eye clinics. These have several advantages over the historically familiar Snellen chart, though the test is more time consuming. The scale is linear with equal increments of difficulty between the lines of characters, there are the same numbers of letters on each line, and the notation is a single figure which lends itself to statistical analysis. This is especially helpful for comparison of pre and postoperative patient groups.

Beside confrontational testing of the four quadrants of each eye with a red target can be useful for screening for field defects. Formal assessment requires the use of a binocular Esterman program (10dB stimulus intensity) on the Humphrey visual field analyser. It is important to establish whether patients with visual field defects are driving and advise them according to the criteria specified by law. In the UK the Driver and Vehicle Licencing Agency (DVLA) sets the requirements for safe driving, outlined in Table 1.²

Features of visual impairment

Symmetrical chiasmal compression from an enlarging sellar lesion produces an upper temporal quadrantanopia progressing to a complete temporal hemianopia. Whilst an early upper quadrantic defect (Figure 1) from impaired inferior retinal fibres in the inferior chiasm often goes unnoticed, symptoms from a bitemporal hemianopia may cause involuntary collision with objects, sometimes when driving. The hemi-fields

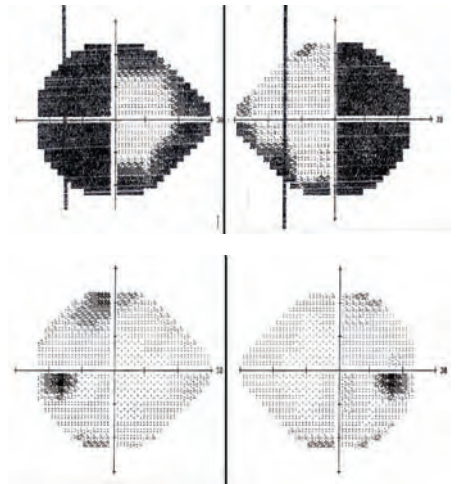


Figure 1a and 1b: Humphrey visual fields pre and postoperative.

affected are blank not black. The site of the lesion and the degree of pre or post-fixation of the chiasm with reference to the pituitary stalk, determine the scale of the defect. Preferential impairment of the inferior temporal quadrants implies superior chiasmal compression. Asymmetric lesions such as the case of neurosarcoidosis demonstrated in Figure 2 produce asymmetric field defects.

Other visual symptoms may develop because of dissociation of the two visual fields from lack of overlapping information, known as the hemi-slide phenomenon. This causes 'slippage' - the breaking up of a line of text when reading, or 'post-fixational blindness' which occurs when focussing on an object causes those behind it to disappear. This produces difficulty threading a needle, or the tendency to cut one's fork with the knife.³

The rate of deterioration of visual impairment may suggest the pathology. In pituitary apoplexy deterioration may develop over hours or even minutes. Malignant lesions may produce subacute deterioration whilst benign pathology such as

Table 1 : DVLA guidelines with reference to visual fields and diplopia

	Group 1 (motor car ; motorcycle)	Group 2 (HGVs ; buses)
Visual field impairment	Driving must cease unless confirmed able to meet recommended national guidelines: The minimum field of vision for safe driving is defined as “a field of at least 120° on the horizontal measured using a target equivalent to the white Goldmann III4e settings. In addition, there should be no significant defect in the binocular field which encroaches within 20° of fixation above or below the horizontal meridian”	Normal binocular field of vision is required, i.e., any area of defect in a single eye is totally compensated for by the field of the other eye.
Diplopia	Cease driving on diagnosis. Resume driving on confirmation to the Licensing Authority that the diplopia is controlled by glasses or by a patch which the licence holder undertakes to wear while driving. (If patching, must meet additional requirements for monocularity). Exceptionally a stable uncorrected diplopia of 6 months' duration or more may be compatible with driving if there is consultant support indicating satisfactory functional adaptation.	Permanent refusal or revocation if insuperable diplopia. Patching is not acceptable.

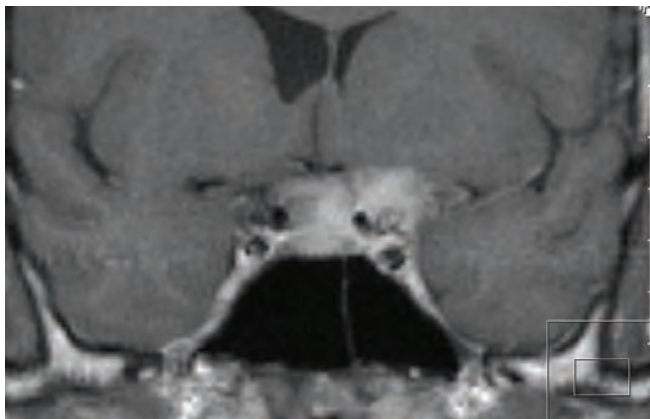


Figure 2: Coronal T1W + contrast. Neurosarcoidosis.

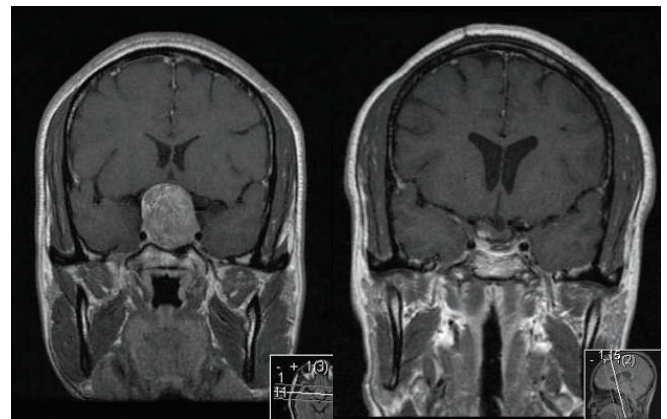


Figure 3a and b: Coronal MRI T1+Contrast. Pituitary adenoma pre and postoperative.

pituitary adenoma or meningioma may cause slow or imperceptible deterioration. Positive visual symptoms such as flashes of light can result from focal demyelination at the site of compression of the optic apparatus.³

External ocular movements

The III, IV and VI cranial nerves lie in the parasellar region. Careful examination is required to assess the integrity of these nerves. Eye movements are normally tested in a H-pattern. Movement of the globe in the horizontal plane is achieved by the medial rectus (adduction) and lateral rectus (abduction) muscles. The fully abducted globe enables isolation of superior rectus (elevation) and inferior rectus (depression) muscle action due to the anatomical location of the tendons of these muscles. Similarly, the adducted globe enables the superior oblique (depression) and inferior oblique (elevation) muscle function to be isolated.

Management

The management of sellar and parasellar lesions is dependent upon the pathology of the lesion. MRI scanning is very useful at determining the likely disease process.

Pituitary adenoma

Transsphenoidal surgery has an important role in the management of pituitary adenomas (Figure 3). The conventional transnasal transsphenoidal approach is undertaken via a submucosal tunnel adjacent to the nasal septum. The sphenoid sinus is opened enabling access to the pituitary fossa. The adenoma can usually be distinguished from the underlying gland by its soft, friable consistency. 72% of patients with macroadenomas had visual field defects with 58% having bitemporal hemi-

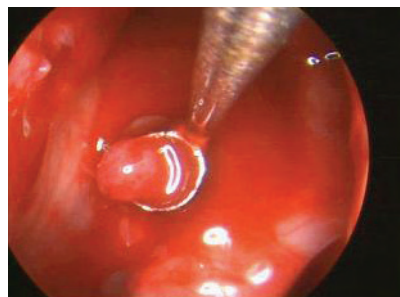


Figure 4 Endoscopic transsphenoidal view of removal of pituitary adenoma.

anopia and 8% a unilateral quadrantanopia in Ebersold's series.⁴ The capsule of a pituitary adenoma compresses but does not invade the optic chiasm facilitating postoperative visual recovery (Figure 1). Of 289 patients reported by Mortini with impairments of fields or acuity, over 90% improved following surgery with 40.5% returning to normal at early follow-up.⁵ Vision improved in 74.6% of Ebersold's patients at a median follow up of 73.4 months.⁴ In Dekkers' cases, assessment at three months postoperatively showed 30% of patients had normalisation of visual fields and a further 60% had improved. Thereafter 36% showed further improvement in visual fields in the interval between three months and one year.⁶ Data appear less favourable when assessing the prevalence of field defects in a population of previously operated adenoma patients. 162 patients (84%) out of 192 revision surgery patients had a residual visual defect.⁷

Skull base endoscopy for pituitary adenoma has gained rapid acceptance. This modification of the transsphenoidal route was developed by Jho in the USA and Cappabianca in Europe.^{8,9} Direct transnasal access to the sphenoid sinus is achieved without a submucosal tunnel. The endoscope provides a wider angle of view than that afforded by the microscope (Figure 4). No differences in neurological outcome are yet evident between transsphenoidal microsurgery and an endoscopic approach but the enhanced view of the optic apparatus possible with the endoscope suggests that outcome might improve for more adherent and inaccessible lesions. Intra-operative MRI is likely to be a useful adjunct to achieving maximal resection in centres with this facility.¹⁰

Non-surgical treatment is successful in selected cases of macroadenoma with visual impairment, notably in prolactinoma where dopamine agonists

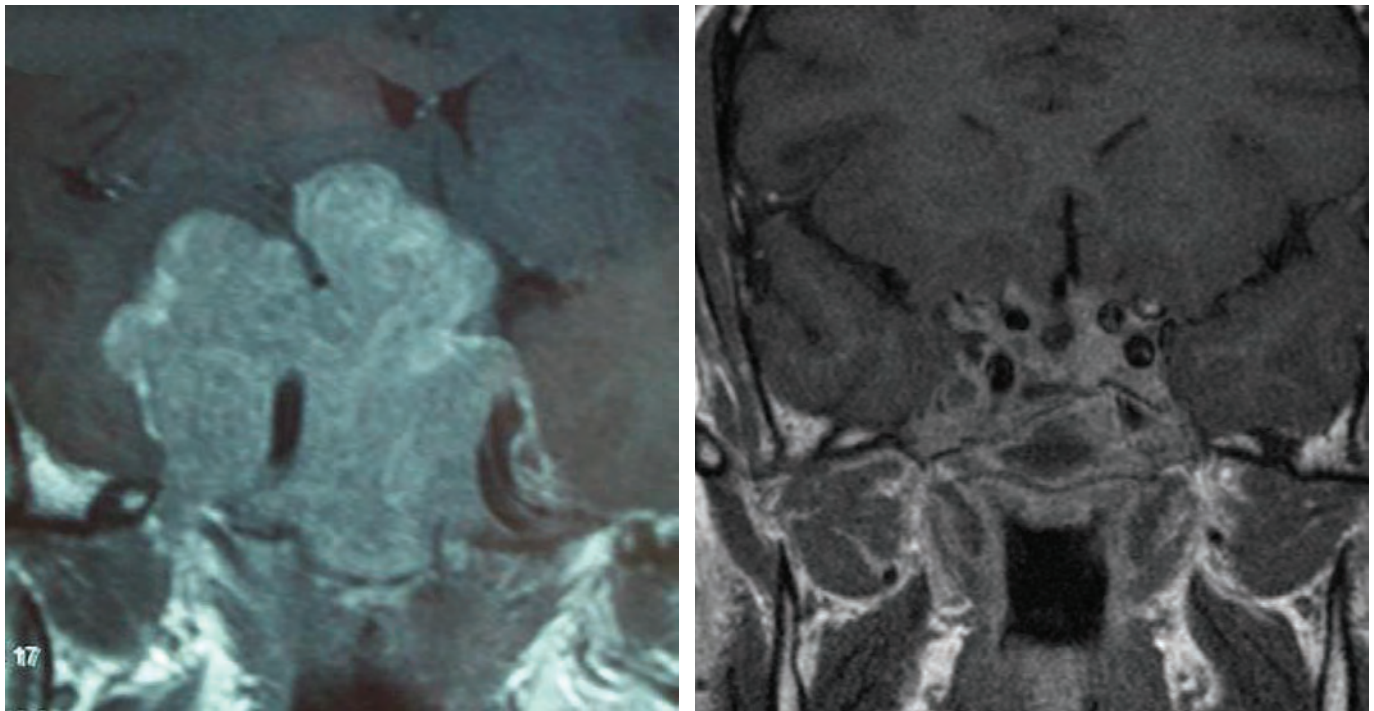


Figure 5a left: Coronal MRI T1+Contrast. Prolactinoma at presentation with a dense bitemporal hemianopia and prolactin level of 950 000 mIU/L. Figure 5b right: Same lesion after 7 months of treatment with Cabergoline.

(e.g. Cabergoline) produce visual improvement in addition to radiological shrinkage in 70% of cases (Figure 5).¹¹ Medical therapy is the treatment of choice in prolactinoma even with large tumours and those producing significant visual symptoms. Surgery can be reserved for drug-resistant cases or for cases of spontaneous cerebrospinal fluid rhinorrhoea which is an occasional complication of this treatment.

Surgical removal remains the mainstay of therapy for non-functioning macroadenomas. The somatostatin analogue Octreotide produced visual improvement in a series of non-prolactinoma patients but the significant side effects of these drugs make surgery much more successful by comparison.¹²

Conventional 3-D conformal radiotherapy

(RT) is effective at reducing the recurrence rate after surgery. Breen reported that 87.5% of tumours were controlled at 10 years.¹³ This is at the expense of complications, most notably a high incidence of new pituitary hormone deficits which increases over time.¹⁴ A 2.5% incidence of second brain tumours at 20 years has been reported.¹⁵ Optic neuropathy following radiotherapy is rare and is related to the dose received by the optic apparatus.¹⁶

Stereotactic radiosurgery (SRS) provides an alternative to conventional RT. The radiation dose is administered via a multi-field source such as the Gamma Knife, or a shaped beam LINAC system. Both modalities aim to deliver a very high dose to a highly conformal field reducing collateral damage. Advantages over

conventional RT include the theoretical possibility that the higher radiation dose might improve control of growth rate and the potential to spare normal functioning pituitary gland from subsequent hypopituitarism. Seventy-eight cases of residual or recurrent adenoma treated with SRS using the gamma knife were described by Petrovich.¹⁷ Only 4% of 52 patients with normal pre-treatment hormone function developed hypopituitarism, but follow-up was limited to a mean of 41 months. Reduction or stability of tumour volume was achieved in all the non-functioning adenomas.

For tumours that lie in very close proximity to the optic apparatus, SRS may cause radiation-induced visual impairment. To minimise the injury to such “organs at risk” a hypo-fractionat-

Table 2: Summary of management of pituitary apoplexy

Clinical features	Acute onset neurological symptoms and signs e.g. bitemporal field defect, possible diplopia or ptosis in a patient with haemorrhage or necrosis in a surgically proven pituitary adenoma. ⁴¹ Hypopituitarism present in 74%. ²²
Investigations	
Radiology	CT Brain. Expanded sella with haemorrhage. Possible associated SAH MRI Brain. More sensitive for diagnosis than CT. ²⁰
Endocrine assessment	Cortisol measurement prior to commencing Hydrocortisone - 9am measurement if possible. Subsequent short synacthen test or ITT, TSH; Free T4; LH; FSH; prolactin; IGF-1; testosterone / oestradiol. ²⁰
Visual assessment	Visual acuity; Clinical field assessment; Humphrey visual fields if well enough.
Treatment	Resuscitation: Correct hypotension and hypoxia; i.v. steroid therapy; other endocrine replacement where indicated.
	Consider transphenoidal surgery in presence of significant or progressive visual failure with or without visual motor deficit. Emergency surgery rarely required.
	Consider conservative management in moderate visual impairment if stable or improving, or when symptoms limited to visual motor deficits.
Late management	Endocrine re-assessment after the acute phase + hormone replacement where indicated
	MRI at 3 months in all cases. Some tumours may involute. ²⁰
	Consider late surgery in conservatively managed cases with residual symptoms or tumour; possible role for radiotherapy.

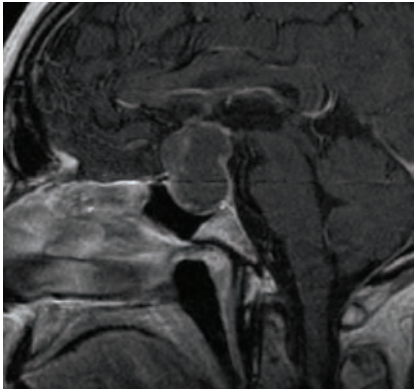


Figure 6: Sagittal T1W MRI + contrast. Pituitary Apoplexy presenting with sudden onset of bitemporal field defect, impaired acuity and partial right third nerve palsy.

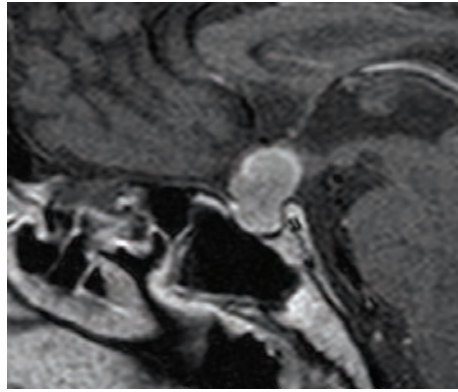


Figure 7: Sagittal T1W MRI + contrast. Rathke's cleft cyst.

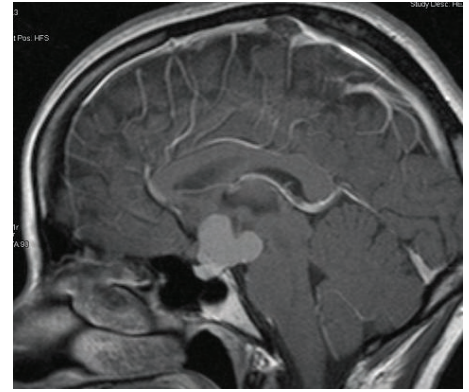


Figure 8: Sagittal T1W MRI + contrast. Craniopharyngioma.

ed regime of stereotactic radiotherapy using a re-locatable frame is gaining credence.

Best current practice is to optimise surgical resection with a view to avoiding adjuvant radiotherapy. Postoperative MRI and endocrine assessment is then performed to plan treatment of any residual tumour and to detect asymptomatic recurrence during long-term follow-up in the multi-disciplinary clinic.

Pituitary apoplexy (Figure 6 and Table 2) is a rare but clinically important subgroup of pituitary adenoma, comprising 2.9% of McFadzean's series.¹⁸ Pituitary apoplexy is a syndrome of haemorrhage or infarction within a pituitary adenoma and usually presents acutely, although a subacute presentation is sometimes seen and the diagnosis may be made in retrospect. The symptoms overlap with those of subarachnoid haemorrhage, which may be present in severe cases.¹⁹ At presentation the responsible pituitary adenoma is unsuspected in the majority of patients. Precipitating factors such as major illness, surgery, conditions that impair or acutely enhance blood flow to the gland, dynamic endocrine testing and coagulation abnormalities have been noted in 40% of patients.^{20,21}

Surgery should always be considered since

field defects and diplopia are both disabling conditions and swift relief of elevated intracapsular pressure should minimise them. However, authors differ in their emphasis on surgical management. Semple et al. recommend emergency surgery when there is deteriorating vision, sudden onset of blindness, or diminished level of consciousness.²² Surgery within the first week may yield better outcomes than surgery at a later time point.^{23,24} Other authors report successful non-surgical treatment in selected cases.^{20,25} Indeed, visual motor deficits have a favourable outcome, whether treated conservatively or with surgery.²² As with elective adenomas, patients rendered blind by the condition do poorly even with an operation.²² In the absence of any clinical trials, this author recommends urgent decompression in a patient with significant or progressive visual impairment with or without a visual motor deficit.

Rathke's cleft cyst (Figure 7) is a common abnormality arising from remnants of the craniopharyngeal duct. It is non-neoplastic but cystic enlargement can occur, causing visual and endocrine symptoms.²⁶ As with adenoma, the cyst compresses the visual apparatus without invasion or adherence, and surgical removal, usually via a transsphenoidal route, is associated

with a favourable visual outcome. El-Mahdy found that visual acuity recovered in 66.6% of eyes and field defects recovered in 68% of eyes.²⁶ Belleci reported complete recovery of vision in seven patients. Favourable results are also seen in simple or arachnoid cysts of the pituitary region.²⁷

Craniopharyngioma (Figure 8) is an epithelial tumour derived from Rathke's pouch epithelium. Presentation with impaired visual acuity, frequently in association with features of hypopituitarism, is common.²⁸ Although non-malignant, the lesion has an intimate relationship with surrounding structures. The surgical approach is governed by the radiological appearances. Cyst drainage may be appropriate but is often associated with symptom recurrence and disease progression. Total, or subtotal resection, may be achieved by a transsphenoidal route but frequently a transcranial exposure is required.

In most series, microsurgical removal produces improvements in vision, but the morbidity in the post-operative cohort remains significant. Children tend to have a worse visual prognosis than adults. 39% of Abrams surgical series of 31 children had visual symptoms at presentation. 10% had acuity of less than 20/200 prior to

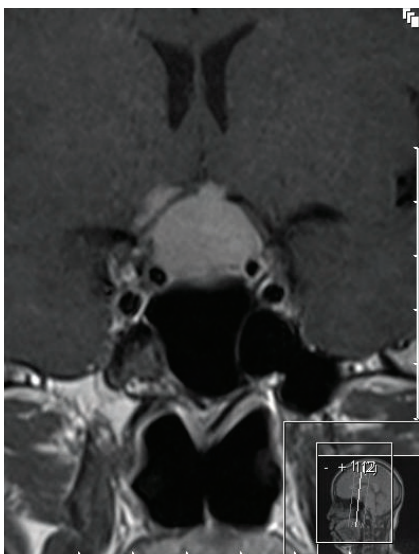


Figure 9: Coronal T1W MRI + contrast. Tuberculum sellae meningioma.

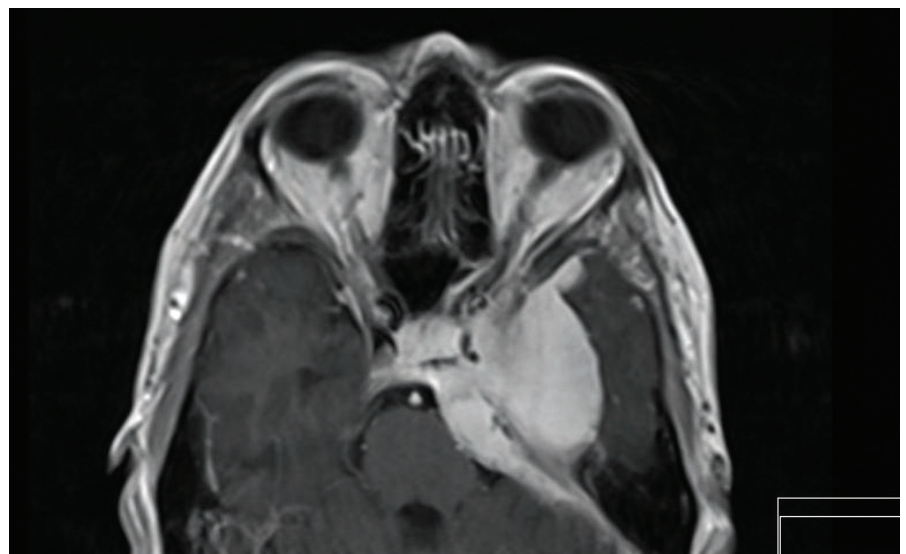


Figure 10: Axial T1W MRI + contrast. Extensive cavernous sinus meningioma with middle fossa and posterior fossa extension. 20y of left-sided visual failure, proptosis and intermittent left sided facial numbness.

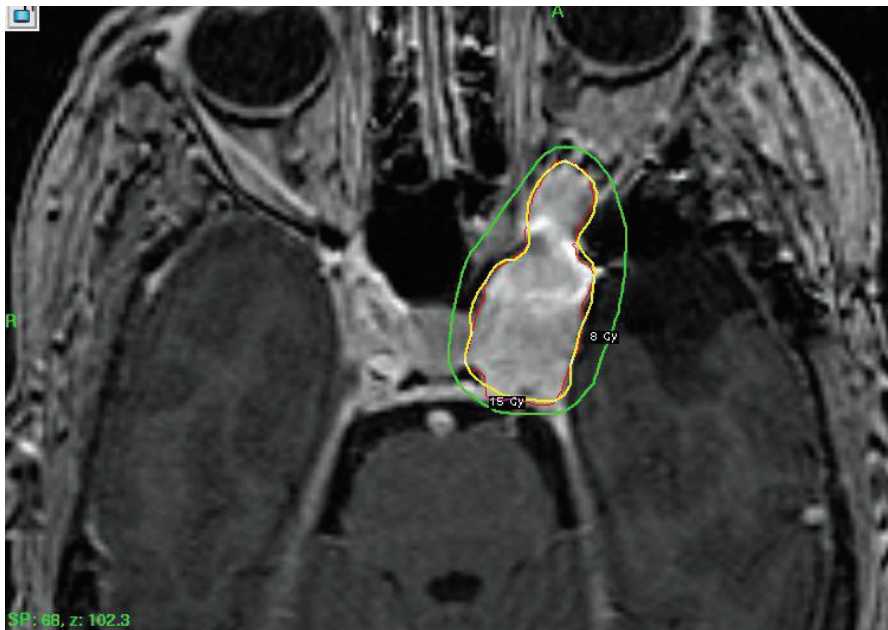


Figure 11: Radiosurgical plan for Gamma Knife treatment of cavernous sinus meningioma.

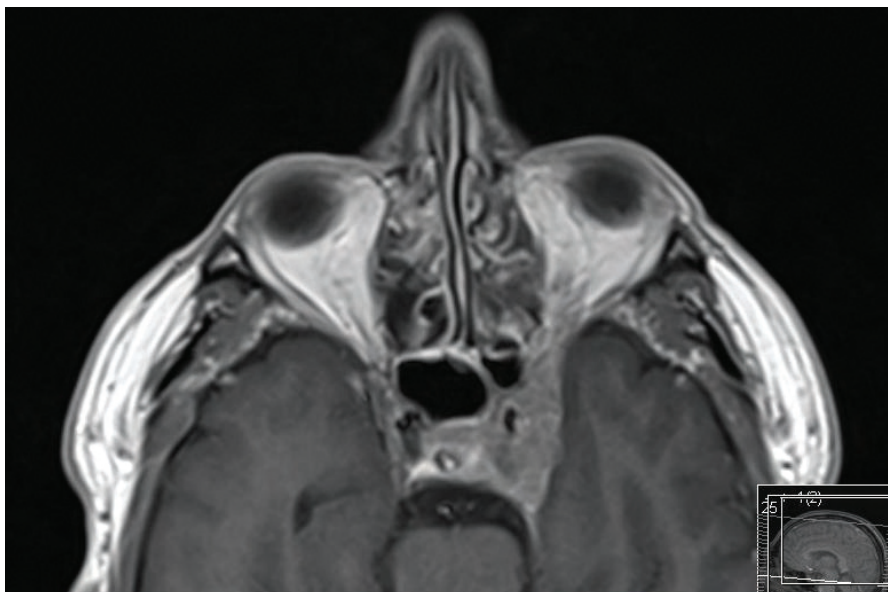


Figure 12: T1W MRI + contrast. Proptosis and left cavernous sinus lung metastasis with intraorbital extension.

surgery and this group increased to 26% following surgery, when 81% of eyes showed evidence of optic atrophy.²⁹ In a series of adults and children, 93% of patients had impairment of visual fields at presentation with post-operative improvement in 87%.²⁸ Yasargil noted visual improvement in 60% of cases.³⁰ Associated endocrine deficits are common at presentation and rarely improve after surgery. In addition, hyperphagia and weight gain due to hypothalamic dysfunction occur in 44% of cases and short-term memory impairment occurs in 5.8% of patients.²⁸ Radiotherapy is commonly used as an adjuvant therapy when residual disease is present.

Meningioma (Figure 9) of the suprasellar region commonly presents with impaired visual acuity, external ocular movement dysfunction,

ptosis and sometimes, pituitary dysfunction. The arachnoid plane around the optic nerves is often breached by tumour with direct involvement of the pial network of neural blood vessels. In advanced cases the optic nerves may be completely encased by tumour.³¹ Microsurgical removal therefore presents significant risk to the vascularity of the nerves, and removal only produced improvement in visual acuity in 18% of Margalit's series. Visual acuity deteriorated in 20% and remained stable in 62% of cases.³¹ Care is required in selecting the operative approach for sellar region meningiomas; good access to the plane between the optic apparatus and the tumour is imperative and this usually requires a subfrontal or pterional craniotomy. Extradural optic nerve decompression has been pro-

posed to optimise visual outcome.³² Although total resection is the main objective of surgery, sub-total resection may be the best that can be achieved for extensive tumours. Stereotactic radiosurgery or radiotherapy is an appropriate postoperative treatment option in patients with residual or recurrent disease.

The cavernous sinus region

The pattern of neurological symptoms from tumours of the cavernous sinus (CS) is different to those confined to the midline. Diplopia or ptosis may result from impairment of oculomotor, trochlear or abducent nerve function, and sensory loss in the upper two divisions of the trigeminal nerve territory can occur. The mandibular nerve is usually spared because of its inferior course via the foramen ovale. Facial pain, sometimes diagnosed as trigeminal neuralgia, can be a feature. Diplopia is a disabling condition that precludes driving and impacts significantly on quality of life (Table 1).

Pituitary adenomas often show extensive radiological CS involvement with little or no CS neurological deficit. The prolactinoma in Figure 5a produced a dense bitemporal hemianopia but no other cranial nerve symptoms. Yokoyama described 10 similar patients with no CS neurological symptoms.³³ This type of CS involvement does not predict an adverse prognosis for the tumour, and the most likely explanation for this pattern of growth may be weakness of the medial CS wall, rather than increased tumour aggressiveness.³³

Cavernous sinus meningiomas have a high incidence of CS neurological deficits (figure 10). 23.5% of nerves III, IV and VI showed a deficit in 39 preoperative patients reported by O'Sullivan et al.³⁴ Associated visual failure and proptosis is common; 57% of Litre's series had reduced acuity and 30% had exophthalmos.³⁵ 39% of cases had impaired visual acuity in Abdel Aziz's series.³⁶

Microsurgery to this region has been pioneered by Dolenc, using extensive extradural drilling to achieve exposure of the neurovascular contents.³⁷ Despite this, neurological outcome from surgery remains very disappointing, chiefly because of the intimate association of the cranial nerves with the tumour.^{38,39} Seven out of 10 patients with normal preoperative oculomotor function developed a significant new permanent deficit, and only 2 of the 17 patients with preoperative dysfunction improved.³⁴

Conservative management in the first instance is therefore a preferable option for CS meningiomas with minimal symptoms. Skull base meningiomas as a group are generally more benign in behaviour than their convexity counterparts,⁴⁰ and serial scanning can be performed whilst monitoring symptoms. This is also an attractive location for the use of SRS or SRT (Figure 11). Meningiomas treated in this way show good rates of tumour control with minimal neurovascular morbidity albeit without extended follow-up to date.^{35,36}

Metastases to the skull base may present in

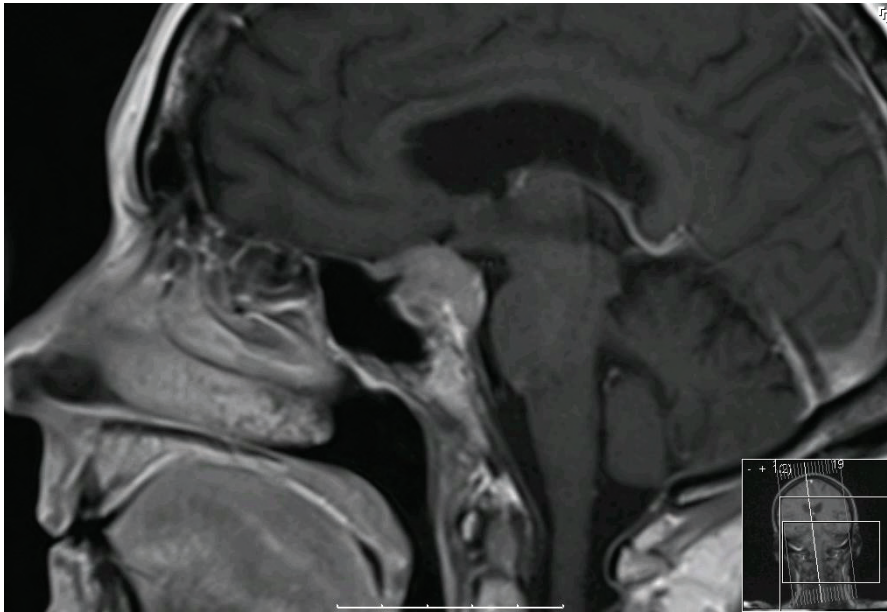


Figure 13: Sagittal T1W MRI + contrast. Sellar region metastasis; multiple myeloma.

the sellar and cavernous sinus regions (Figures 12 and 13). Symptom progression with multiple cranial nerve deficits is often rapid. Stereotactic radiosurgery may be an appropriate treatment option in such patients.

Summary

Decision making for parasellar tumours of all types requires careful clinical, radiological and endocrine assessment. This is effectively undertaken in the context of the pituitary or skull base MDT where the required skills are available.

Surgery is an important treatment modality for parasellar tumours, especially for pituitary adenomas, where the visual prognosis following surgery is usually good. Craniopharyngioma can be cured by surgery but is associated with a guarded visual prognosis. Meningiomas exhibit complex relationships with the cranial nerves, therefore observation or incomplete resection with adjuvant treatments including SRS or SRT may be favoured. ♦

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