LONDON CANCER ALLIANCE
West and South

LCA Operational Policy

Lateral and Central Skull Base Tumours

June 2014

Delivering world class cancer care for London

Contents

1 Introduction

This operational policy should be read in conjunction with the LCA Brain/CNS Cancer Clinical Guidelines.

Tumours in the lateral and central skull base are rare, affecting fewer than 1 in 40,000 people/year. They form a histologically diverse group and potentially pose significant management problems due to their intimate relationship to the structures running through and within the skull base. These include the arterial and venous supply to the brain, the cranial nerves, brainstem, ear and eye. The majority of tumours have a relatively indolent growth pattern; however, these may still cause significant morbidity and mortality by virtue of their location. Squamous cell carcinoma (SCC) is the most commonly encountered malignant tumour but tumours of a wide variety of histological types can occur. The aggressive tumours include chordoma, chondrosarcoma, high-grade meningioma, adenocarcinoma and adenoid cystic carcinoma. The majority of tumours are, however, benign, the most common being schwannoma, meningioma and paraganglioma (which on rare occasions can be malignant). Schwannomas have a tendency to develop on the 7th nerve in the internal auditory canal and cerebellopontine angle, but are also found on the other cranial nerves, particularly 5, 7 and 10. Meningiomas develop throughout the cranial vault, their presence in the skull base being associated with relatively high morbidity both from the tumour and potentially from its treatment.

Initial symptoms are frequently associated with loss of cranial nerve function, which is often well tolerated or ignored as a result of its gradual onset. The presenting symptoms may therefore be hearing loss, facial weakness or numbness, double vision or visual loss, or difficulties with speech and swallowing.

Investigation should include computerised tomography (CT) and magnetic resonance imaging (MRI) which are complementary in the skull base, and often diagnostic to the extent that biopsy is unnecessary. CT scans give excellent bony details and are helpful in determining the extent of bone involvement as well as defining the relevant bony architecture. MRI allows better distinction of the relationship between the tumour and the brain and associated intracranial oedema. Neurovascular imaging, which may involve CT/MR angiography or formal percutaneous angiography, will be necessary on occasion.

Discussion about management of these tumours should occur in a skull base multidisciplinary team (MDT).

Lymph node involvement at diagnosis is low, and assessment is relevant primarily in those diagnoses with SCC or paraganglioma. Patients with paraganglioma also require assessment through a neuroendocrine MDT to manage the risk of associated secreting and intra-abdominal tumours.

The majority of cases will require long-term management, particularly as initial management is frequently conservative – a decision which requires periodic review.

Recommendation

Lateral and central skull base tumours should be managed by a dedicated skull base MDT.

(Recommendation grade D)

2 Resection of Lateral and Central Skull Base Tumours

Resection of tumours of the lateral skull base is traditionally performed through a variety of open approaches. More centrally placed tumours, involving the petrous apex and clivus, may be approached endoscopically by a suitably qualified team. This is potentially associated with lower morbidity, in particular less risk to hearing and facial nerve function, but there is little evidence to define when this is appropriate.

The majority of patients requiring surgical resection of these tumours will be best served by an open, conservative resection performed by a team with comprehensive skull base expertise that can manage all facets of the patient's care.

The extent of resection is determined by the histology. En bloc resection is usually not possible in the skull base, with the exception of SCC of the temporal bone. In this case, survival is best for patients who have not undergone previous surgery with incomplete resection; therefore, referral at diagnosis to a skull base centre undertaking this surgery regularly (several times a year) is mandatory.

While for some pathologies a priority is to obtain clearance of tumour margins, for the majority of cases the goal of surgery is to minimise tumour related morbidity and mortality without iatrogenic damage. To this end, the patient may be best served by a procedure which leaves some residual disease, preserving function.

2.1 Primarily intradural lateral/central skull base tumours

2.1.1 Cerebellopontine angle tumours

The majority of tumours of the cerebellopontine angle (CPA) are schwannomas (primarily of the 8th nerve), with the most common differential a meningioma. Confident diagnosis is possible on imaging, with biopsy unwarranted. Both are generally slow growing with the potential to remain stable for prolonged periods. Tumours which are not causing brainstem compression should therefore initially be managed with a watch wait rescan policy, to determine the behaviour of the tumour. An exception may be made where patients have significant symptoms which are likely to be relieved by surgery, most commonly vertigo or trigeminal symptoms.

Tumours causing significant brainstem compression should be managed surgically, by a team of ear, nose and throat (ENT) surgeons and neurosurgeons, both with skull base experience (performing >10 cases a year). The goal of surgery is to relieve brainstem compression without inflicting additional morbidity, with complete resection a secondary goal. Residual disease should be monitored and if necessary can be treated with radiation (Gamma Knife or CyberKnife) or further surgery.

Smaller tumours which have demonstrated growth may continue to be observed (as a proportion of them will cease to grow), but treatment with either radiation (Gamma Knife or CyberKnife) or surgery should be discussed.

Patients should be advised that recent evidence suggests that aspirin is associated with reduced tumour growth, and those patients without contraindication may wish to take 75mg aspirin daily. This advice should be offered with the caveat that bleeding into the tumour leading to rapid tumour expansion is a recognised risk.

For the majority of patients with small (<20mm CPA maximum axial diameter) tumour, the risk profile will favour radiation treatment. Exceptions to this include young patients in whom the risk of late radiation

effects may be more relevant. We do not advocate an absolute cut-off minimum age for radiation treatment – the balance shifts increasingly towards surgery as age falls significantly below 40. Cystic tumours may also be unsuitable for radiation treatment and better addressed surgically.

Unilateral vestibular schwannomas in those aged under 25 should be referred to the neurofibromatosis type 2 (NF2) service at Guy's Hospital for multidisciplinary assessment to quantify the risk of this diagnosis, and for initial management. Older patients with multiple central nervous system schwannomas or meningiomas should also be referred for assessment.

CPA schwannoma tumours in all patients under 30 should be sent for genetic analysis and banking in order to allow a diagnosis of mosaic NF2 to be confirmed in the event of a subsequent tumour developing The address for genetic analysis of tumour tissue is:

Professor Gareth Evans
DNA Laboratory, Department of Molecular Genetics
Genetic Medicine
6th Floor, St Mary's Hospital
Oxford Road
Manchester, M13 9WL

2.1.2 Surveillance protocols for CPA tumours

Watch wait rescan:

- First follow-up scan (after initial diagnostic scan): 6–12 months
- Subsequent scans: annually to 3 years
- Then, if stable: biannually to 10 years
- Then: 5-yearly to 20 years.

Post-surgical scan protocol:

- Initial post-operative scan: 3 months
- Rescan: 1 year
- If clear, rescan: 5 years
- If residual disease: monitor as per watch wait rescan protocol.

Post-radiation protocol:

- Initial post-treatment scan: 1 year (6 months if increasing symptoms)
- Subsequent scans: annually to 3 years
- Then, if stable: biannually to 10 years
- Then: 5-yearly to 20 years.

It may well be appropriate to discharge patients from follow-up prior to this, particularly if life expectancy is less than the estimated duration of ongoing growth required for the tumour to reach clinical significance.

2.1.3 Rehabilitation

Hearing loss

Unilateral hearing loss is a common sequel of CPA tumours and their treatment, and patients should be offered rehabilitation with the options of CROS (contra-lateral routing of signal) and bone conducting hearing aids (bone anchored percutaneous (BAHA) or intact skin (BoneBridge/BAHA Attract)).

Vestibular compensation

Ideally, this should be undertaken prior to surgery, but access to dedicated vestibular physiotherapy should be available to post-operative patients, with ongoing follow-up post-discharge.

Facial nerve

A proportion of patients will have a post-operative facial palsy, with incidence increasing with tumour size. Appropriate eye care should be instituted as soon as the palsy is identified; referral to an oculoplastic surgeon with an interest in facial palsy is mandatory for those with dense palsies. Dedicated facial physiotherapy should be available, with follow-up in a multidisciplinary facial nerve clinic with expertise in facial reanimation surgery.

Recommendation

Small CPA tumours should initially be managed conservatively.

Patients with small growing tumours should be offered treatment with radiation or surgery.

Large tumours should be treated by an experienced multidisciplinary surgical team.

Patients should be advised of the potential role of aspirin.

Rehabilitation is an integral part of the management of these patients.

(Recommendation grade D)

2.2 Primarily extradural lateral/central skull base tumours

2.2.1 Chondrosarcoma

Typically arises from the petroclival synchondrosis, extending into the petrous apex, and extradurally into the posterior and possibly middle fossa. Gelatinous tumour may be suitable for debulking and observation, with adjuvant radiotherapy (possibly proton beam) for aggressive or recurrent disease.

Surgical approach is infralabyrinthine or transotic for more significant disease. An endonasal endoscopic approach may be suitable in anatomically favourable cases.

Small tumours may be managed conservatively with serial scanning.

2.2.2 Chordoma

This is a relatively aggressive tumour which requires surgical resection followed by adjuvant radiotherapy. They are relatively rare tumours requiring aggressive surgical management, but they are sited in close proximity to critical structures. Ideally, they should be treated by a team familiar with the pathology.

Small and localised tumours may be treated endoscopically or through open anterior approaches (maxillotomy or mandibulotomy). More extensive tumours may extend into retropharyngeal soft tissues, occipital condyles, cervical vertebrae and neck. An extended far lateral approach facilitating identification and preservation of the carotids, lower cranial nerves, jugular vein and vertebral artery is advised. In these cases, fixation of the craniocervical junction should be considered; however, it is worth noting that the presence of metalwork has a particularly detrimental effect on the delivery of proton beam therapy.

Cases should be referred to the proton beam panel, but if rejected they should be offered intensity-modulated radiotherapy (IMRT) to the tumour bed, adjacent bone and any residual disease.

2.2.3 Paraganglioma

Temporal bone paragangliomas arise within the middle ear cleft (tympanic paraganglioma), jugular bulb (jugular paraganglioma) and vagus associated autonomic ganglia (vagal paraganglioma). Paragangliomas of the carotid body (carotid body tumours) may also extend to the skull base (inferior aspect). Diagnosis is radiological, with both MR and CT imaging of merit.

Tympanic paragangliomas are generally amenable to resection with minimal morbidity, and this is the treatment modality of choice. They are relatively common and frequently isolated lesions.

Patients presenting with jugular, vagal and carotid body paragangliomas below 50 years old should be investigated for multiple and secreting lesions, and referred for genetic analysis. These patients should have blood pressure and plasma metadrenalines assessed in clinic, and MRI head and neck, mediastinum, abdomen and pelvis to exclude synchronous tumours. They should ideally be discussed in a neuroendocrine tumour MDT including genetics, endocrinology, nuclear medicine and skull base surgical input.

Positron emission tomography (PET) may provide prognostic data, with higher standard uptake values likely to be associated with future growth and increased risk of malignancy.

Identification of a mutation increasing the risk of further paraganglioma development (typically succinyl dehydrogenase tumour mutations) mandates long-term surveillance, and vigilance regarding the risk of hypertension associated with secreting tumours.

Treatment may be initially conservative, surgery or radiotherapy (which may be IMRT or Gamma Knife/CyberKnife). Radiotherapy offers good tumour control with minimal morbidity; however, it may not relieve symptoms, and in younger patients should be used with caution.

The risks associated with surgery may be minimised by thorough pre-operative assessment of intracranial arterial and venous anatomy, and by selective tumour embolisation.

2.2.4 Facial and lower cranial nerve schwannoma

Facial and lower cranial nerve schwannomas may have both intradural and extradural components. Intradural tumour may be in the CPA or middle fossa (in the case of 7 nerve schwannoma) and should be managed relatively conservatively where the nerve is still functioning.

The timing of intervention for facial schwannoma is key – conservative management is likely to preserve facial function for the longest period; however, reanimation is more successful when performed earlier in the development of facial palsy. Surgical decompression of the tumour and Gamma Knife or CyberKnife therapy may have a role in preventing symptom and tumour progression respectively. These patients should be managed with the input of specialised facial physiotherapy and with access to all reanimation/rehabilitation options.

Lower cranial nerve schwannomas may have components within the cranial vault, within the bone and extracranially. Functional preservation of the affected and adjacent nerves should be prioritised, and if intervention is warranted conservative surgery to the component causing a mass effect, +/- radiation therapy, is more likely to be appropriate than surgery addressing both intra- and extracranial components (e.g. the petro-occipital trans-sigmoid or POTS procedure).

2.2.5 Greater wing of sphenoid/middle fossa

Meningiomas of the greater wing of the sphenoid and middle fossa may be resected through an orbitozygomatic or extradural middle fossa approach; however, a conservative strategy is often appropriate as growth in this area is frequently not clinically significant.

Recommendation

Chordoma should be treated with surgical resection and adjuvant radiotherapy (consideration of proton beam).

Chondrosarcoma may be managed conservatively or with surgical resection with adjuvant radiotherapy for more aggressive tumours.

Paragangliomas should be managed by a multidisciplinary team with consideration given to the potential for multiple and secreting tumours.

(Recommendation grade D)

3 Radiotherapy and Chemotherapy for Lateral and Central Skull Base Tumours

3.1 Role of radiation therapy

Lateral and central skull base tumours lie in close proximity to the brainstem, and to other structures at risk of damage from radiation (inner ear, retina, optic nerve and chiasm, pituitary gland). This makes irradiation to a radical dose difficult.

Smaller volume tumours and relatively low-grade lesions (schwannoma, meningioma, paraganglioma) may be safely treated with radiation delivered via the Gamma Knife (radiosurgery) or CyberKnife systems, in one to three fractions.

This may be delivered as the primary treatment modality for smaller growing tumours. As the goal of treatment is to prevent tumour growth, it is inappropriate for this treatment to be delivered to tumours which are not demonstrably growing.

Larger tumours (>15cc) are better treated with fractionated IMRT. Surgical debulking may facilitate radiotherapy delivery, by separating tumour from radiosensitive structures (such as chiasm and brainstem).

Temporal bone SCC should be managed by in en bloc resection of the temporal bone tumour, neck dissection and parotidectomy, followed by adjuvant radiotherapy for >T1 and node positive tumours.

Proton therapy is currently under evaluation and may have a role in treating small volume disease, e.g. low-grade tumours at the skull base or close to radiosensitive structures, due to rapid dose fall-off. Sub-volumes may also be potentially treated using protons as a boost to residual tumour masses within a larger photon field as mixed plans.

3.2 Treatment role of nuclear medicine

Paragangliomas may be treated with external beam radiotherapy, MIBG or peptide receptor radionucleotide therapy.

4 Key Points

- Patients should be discussed at a skull base MDT meeting supported by all the necessary expertise. A multidisciplinary approach is paramount.
- Surgery should be performed by teams with appropriate expertise, generally combining ENT and neurosurgery.
- Vestibular schwannoma resection should be undertaken by teams performing 10–20 procedures per annum.
- Vestibular, hearing and facial rehabilitation should be available to all patients who require it.

5 Key References

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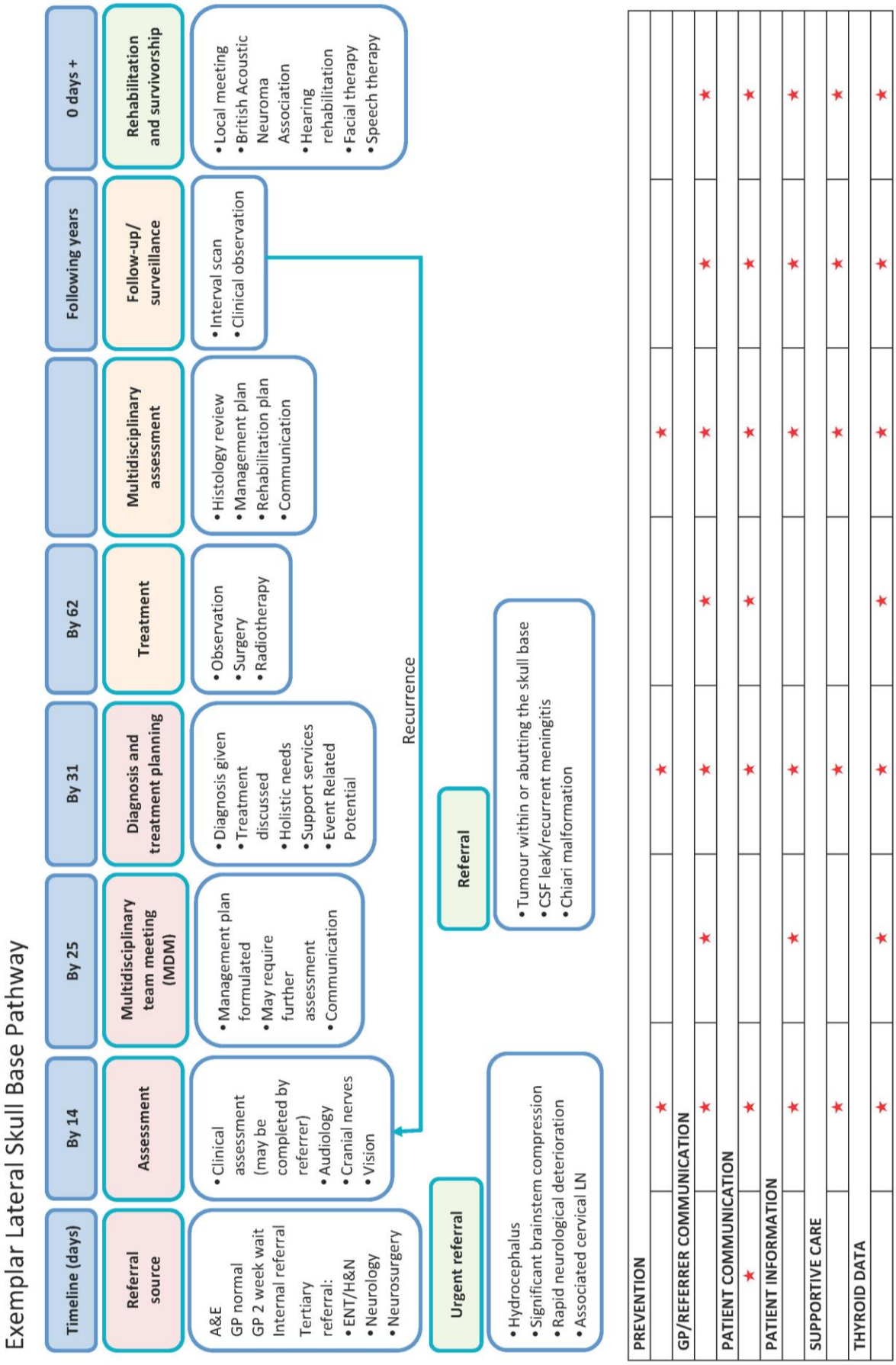
Appendix: Exemplar Lateral and Central Skull Base Tumours Pathway



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London Cancer Alliance

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