LONDON CANCER
NORTH AND EAST

London Cancer Brain and Spine Pathway Board

Neuro-oncology surgery guidelines

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Contents

1. General principles

1. All patients suspected of having a primary brain tumour should first be screened (history, physical examination, CXR mandatory but often CT chest/abdo/pelvis recommended if metastasis is considered a possibility. PET scan is an alternative) to exclude a primary cancer outside the CNS. If a potential primary tumour elsewhere is identified, histological diagnosis should be attempted from the primary site if possible.

2. Magnetic Resonance Imaging (MRI) is the imaging modality of choice for the assessment of primary tumours of the brain and spine. However it is often practical to obtain a diagnostic CT scan in the first instance in view of the ease of access to CT relative to MR. Furthermore, CT often gives useful information regarding the presence of haemorrhage and calcification, which is better assessed than on MRI.

   Most patients will subsequently have an MRI scan prior to any treatment. MRI should be used for post-treatment follow up at appropriate intervals (sometimes defined in treatment protocols). CT is useful to assess possible VP shunt malfunction or if acute clinical deterioration occurs.

3. The diagnosis of some primary brain tumours can be made without a tissue diagnosis, e.g. functioning pituitary tumours and secreting germ cell tumours. In others a tissue diagnosis is optimal.

4. In certain situations, e.g. pontine gliomas, the risks of biopsy may out-weigh the need, particularly with modern imaging, as the diagnosis is almost certain from imaging. Where a diagnosis is to be accepted and therapy for a brain tumour is to take place without a tissue diagnosis, the reasons for accepting a clinical diagnosis should be documented carefully and agreed by the appropriate multi-disciplinary team.

5. Neurosurgical opinion as to the indications for biopsy and whether debulking is advisable (perhaps after frozen section diagnosis and performed at the same surgical procedure) is next sought.

6. The maximum amount of pathological material should be made available to the neuropathologist. It is recommended that the histology is reported by an experienced neuropathologist, or at least reviewed by such a neuropathologist and a report issued for the notes.

7. For certain brain tumours, neurosurgical debulking is not the first form of definitive therapy: for some pituitary tumours, notably prolactinoma, a carefully controlled trial of a dopamine against may be recommended first line therapy. For germ cell tumours, chemotherapy is often first employed. For cerebral lymphoma, chemotherapy is first-line therapy. Such therapies can shrink the tumours and obviate the need for surgery.

8. For all brain tumours, the presence of obstructive hydrocephalus, caused by the tumour, may require shunting or another CSF diversion such as third ventriculostomy prior to cancer directed therapy.

9. For multiple brain metastases, the correct therapy is usually whole brain radiotherapy. For single or small numbers of deposits, there is frequently a need for a neurosurgical opinion regarding surgical resection or stereotactic radiosurgery.

10. The use of potent anti-inflammatory steroids, usually dexamethasone, is very common in the therapy of all types of brain tumour and causes reduction in the oedema that is almost always present which adds to the rise in intracranial pressure.

    Patients on steroids must be monitored for the side effects of these drugs, such as routine monitoring for diabetes, thrush and gastrointestinal inflammation (for which protection by the prescription of ranitidine, omeprazole, sucralfate etc) is advisable, and their continuing need for steroids appraised regularly.

11. The use of anti-convulsants in neuro-oncology is sometimes indicated. In patients who have presented with fits this is essential. It may be indicated in patients who have not fitted where the clinician feels that the risk of seizures is high enough to justify treatment. Levels are monitored in the serum where appropriate.

12. Clinicians will defer to DVLA guidelines concerning ability to drive.

13. The therapy of brain tumours involves high risk medical treatments (surgical, radiotherapeutic and drug) and the need for carefully documented counselling of patients, and their relatives, of the perceived needs, benefits and risks of such therapy is essential. For surgical and oncological procedures, this will require a signed consent form.

14. The follow-up of patients with brain tumours will usually take place in routine outpatient clinic at which time the results of therapy are monitored and the continuing need for medications and the new needs of the patient are assessed. It is important that the GP is kept up to date by correspondence of the present situation and other local services (e.g. physiotherapy and rehabilitation, terminal care etc) may need to be involved.

15. Patients should be referred to the palliative care team when the prognosis is poor or they are having problems coming to terms with their diagnosis, distressing symptoms or psychological problems.

16. Emergency surgical intervention may be required to alleviate immediately life-threatening mass effect or hydrocephalus.

2. The diagnostic pathway

Patients present in a variety of ways. Patients are referred by their general practitioner (GP) or self-refer to one of a number of specialties including neurology, acute services (such as acute medicine), ophthalmology, endocrinology, radiology or orthopaedics.

The establishment of an accurate diagnosis to inform management decisions is a key element in the care pathway for patients with brain and other central nervous system (CNS) tumours. This usually involves neuroradiological imaging and histopathological evaluation following biopsy or tumour resection.

Other laboratory tests, such as for germ cell tumour markers, occasionally have a role in specific situations. Molecular analysis will increasingly be used alongside histopathological evaluation to characterise CNS tumours, providing information about prognosis and therapeutic response, and thereby facilitating patient stratification.

2.1. First line investigations

MRI is the investigation of choice. CT may miss small tumours and is sub-optimal in the posterior fossa and spine.

Radiological imaging (computed tomography [CT] or magnetic resonance imaging [MRI], is essential in the diagnosis of CNS tumours, and it is the first point at which a suspected diagnosis of a CNS tumour is made that prompts entry into the appropriate MDM.

2.2. Second line investigations

The NSMDT should determine whether or not further imaging is necessary prior to surgery. Second line imaging will usually be carried out at the neurosurgical centre.

Functional MR with or without tractography is indicated where concern exists regarding a tumour's relationship to functional cortex or white matter. There is a role for cerebral angiography in the assessment of vascular tumours. Occasionally, pre-operative embolisation by an interventional radiologist will be appropriate. This should be agreed by the NSMDT and will be appropriate for some large meningiomas. The NSMDT will decide whether further investigation such as neuro-psychological assessment, EEG, tumour markers, endocrine assessment, further body/brain imaging or additional spinal imaging in the presence of intracranial tumours that may seed through the CSF.

3. Histopathology

All suspected tumours identified on imaging should be considered for biopsy and or resection. The decision to refer for biopsy will be made by the NSMDT.

3.1. Intraoperative neuropathology

1. Prior to performing a biopsy / resection the neurosurgeon will consider whether an intraoperative neuropathological assessment is required.

   It should be noted that intraoperative assessment should be used to guide intra-operative management.

   The concordance rate between the intraoperative diagnosis and the final diagnosis is generally high, but it is important to bear in mind that the intraoperative diagnosis is a provisional diagnosis, which may need revision after the paraffin sections and immunohistochemical assessment has become available.

2. The neuropathologist will decide whether a frozen section, smear or both is most appropriate. Frozen sections are not performed on cases of known or suspected tuberculosis. Frozen sections and smears are not performed on cases of known or suspected prion disease.

3.2. Non-intraoperative neuropathology

1. Specimens must be sent in formalin, in a container substantially larger than the specimen, to the histopathology laboratory.

2. Every case is examined by a consultant neuropathologist who participates in the British Neuropathological Society's External Quality Assessment scheme, and participates in the Royal College of Pathologists' Continuing Professional Development programme.

4. The treatment pathway

4.1. Intracranial tumours

Patients with CNS tumours need a multidisciplinary approach to their care throughout their illness and follow-up, with continuing input from a variety of rehabilitation and support services. The patient pathway must be structured to ensure that access to appropriate services is always safe, easy and equitable. At all stages of the patient pathway, there may be a need to involve AHPs and supportive and palliative care services to address the patient's needs.

4.2. Intrinsic primary cerebral tumours

Patients are predominantly adults with malignant lesions. When referred, they will be discussed with and where necessary transferred to the Neurosurgical unit for further investigation and management. The role of neurosurgery is to confirm diagnosis, maximise survival and where possible alleviate symptoms. This usually entails an open or stereotactic/image guided biopsy and/or craniotomy and debulking. Image guidance should be used in the vast majority of craniotomies for tumours, for accurate lesion localisation. The use of intraoperative technologies such as iMR or ultrasound guided navigation may also be used. Once the diagnosis has been confirmed by a neuropathologist the patient will be referred back to the referring clinician with advice for further management. In most cases this will mean referral to oncology. In a few cases, tissue diagnosis may not be required where the diagnosis is clear from the imaging.

With certain exceptions neurosurgeons generally provide the best outcome for their patients if they remove as much tumour as possible, keeping neurosurgical morbidity to a minimum, and ensuring that an accurate diagnosis has been made. Decisions regarding how aggressive a surgical approach should be are complex and depend on the tumour situation in the brain, the age and performance status of the patient.

The surgical options include a stereotactic or open biopsy, a debulking or major resection procedure – this last carries with it an expectation of removing at least 90% of the total tumour bulk. In cases where resection is considered in patients with tumours adjacent to or involving eloquent brain regions, awake craniotomy with cortical and sub-cortical mapping may be appropriate. The use of fluorescence techniques (eg 5-ALA) to identify residual tumour after resection is a management option currently being evaluated in several clinical trials and should generally be used in this context.

4.3. High grade gliomas

The goals of primary surgery are to obtain the diagnosis, alleviate symptoms related to any increased intracranial pressure and to reduce the need for corticosteroids. Extensive surgery is beneficial to the patient's survival, providing attention to surgical morbidity is observed. In some patients histology may not be available, eg brain stem tumours. Treatment in these circumstances must be discussed by the NSMDT. Following debulking surgery for high grade glioma, implantation of carmustine impregnated wafers is an option for adjunctive therapy, either at primary surgery (with intra-operative pathological confirmation), at subsequent surgery after the diagnosis has been confirmed or for recurrent tumours. Implantation of wafers improves median life expectancy by 8-10 weeks but also increases operative morbidity. Surgery will generally be followed by radiotherapy and/or chemotherapy.

4.4. Low grade gliomas

For non-infiltrative low grade gliomas including pilocytic astrocytoma, pleomorphic xanthoastrocytoma, subependymal giant cell astrocytoma and subependymoma, primary surgery may be curative in some cases. Post-operative therapy is often withheld, but careful MR based follow-up is essential.

Despite a common impression that these tumours are benign, the majority of the infiltrative low grade gliomas will progress ultimately – usually despite surgery and radiotherapy. As early intervention does not cure, there is controversy as to the optimal time to deliver therapy.

Presumed low grade glioma involving non-eloquent brain regions should be considered for surgical resection: although this is not curative, evidence suggests a survival benefit in patients where a resection is performed. Surgical resection may also be considered to control intractable seizures. After resection, adjuvant therapy is generally not offered unless there is histological evidence of high grade change in the resected tumour.

Radiotherapy at presentation (usually preceded by a biopsy to confirm the diagnosis) has been shown to extend time to progression but does not extend overall survival. It is a treatment option that can be considered for patients who cannot undergo resection and in those with difficult to control seizures, although radiotherapy is often deferred until the time of tumour progression or transformation.

In those patients who are not appropriate or do not wish to consider intervention, radiological surveillance with MRI scans (usually at 6 monthly intervals) is performed with intervention (resection or biopsy with or without radiotherapy) at the time of tumour progression. Biopsy may be performed at presentation to confirm the diagnosis although surveillance is most commonly undertaken on the basis of a radiological diagnosis alone. After diagnosis, consideration should be given to an early rescan (eg 2-3 months) if radiological surveillance is to be performed without a biopsy to ensure there is no early and rapid progression.

There is no conclusive evidence from clinical trials that primary or adjuvant chemotherapy is of benefit.

4.5. Oligodendroglioma

In general these tumours behave and are treated as for other gliomas although they are more chemosensitive. 1p19q testing is valuable for indication of prognosis and, occasionally, for diagnostic purposes.

4.6. Ependymoma

Any patient with a suspected or proven ependymoma should undergo whole neuraxis MRI to detect CSF seeding. Maximal resection of the tumour should be the aim as this improves survival and can be curative. Post-operative adjuvant therapy is often indicated as per radiotherapy guidelines.

4.7. Meningioma

Where treatment is indicated, surgical resection is generally the option of choice. However, small, non-progressive or asymptomatic tumours may be managed with radiological surveillance and often do not progress. Stereotactic radiosurgery is an alternative option in patients who are not suitable

for or who decline surgery. Post-operative radiotherapy may be indicated for some tumours, particularly when histology shows atypical or malignant features, as per the radiotherapy guidelines. Patients with recurrent tumour or post-operative residual tumour may be candidates for stereotactic radiosurgery, repeat surgical excision or radiological surveillance as decided by the MDT.

4.8. Primary central nervous system lymphomas

A biopsy is usually required to confirm the diagnosis. Debulking surgery is not indicated unless the tumour mass effect is immediately life-threatening. Further investigation and management will be by the haemato-oncology team. Patients with a suspected lymphoma must have careful management of any steroid treatment which can reduce the ability to obtain a histological diagnosis and may need to be withheld or stopped prior to surgery if possible.

4.9. Brain metastases

Surgical biopsy or resection is sometimes necessary to confirm the histological diagnosis when no obvious primary tumour site is apparent. However, histology should usually be obtained from any extracranial sites first if possible.

For patients with known cancer and brain metastasis, referral should be made with full up-to-date staging of the cancer and a prognostic evaluation by an appropriate oncologist. Patients with an expected prognosis of greater than six months and stable or absent systemic disease may be candidates for more aggressive management. Surgical resection of up to three metastases in non-eloquent brain regions may be beneficial in these circumstances and should be followed by adjuvant therapy to gain benefit. Stereotactic radiosurgery is an alternative in any patient with controlled systemic disease. This is often performed after whole brain radiotherapy has been used but in selected cases (e.g. relatively radioresistant mets such as renal cancer or melanoma), radiosurgery may be used prior to whole brain radiotherapy. However, most patients will be treated with palliative whole brain radiotherapy alone in the first instance.

4.10. Pineal region tumours

Imaging should include MRI of the whole neuraxis to exclude CSF seeding. Search for a primary neoplasm may be indicated if metastasis is a possible diagnosis. Surgery will generally not be undertaken unless immediately life-saving until blood or preferably CSF β-hCG and AFP have been performed. If these are high then the diagnosis is a germ cell tumour which should be managed non-surgically (excepting occasional intervention for hydrocephalus). If tumour markers are not raised, the surgical approach will be guided by the tumour's appearance and position and the presence or absence of hydrocephalus. Options include endoscopic third ventriculostomy with or without biopsy through the ventricle, VP shunt, image guided or stereotactic needle biopsy (the trajectory should take into account overlying deep cerebral drainage and is often performed via a low frontal burr hole) and surgical resection. Stereotactic radiosurgery is a treatment option for some tumours in this region. Post-operative adjuvant therapy may be offered depending upon the diagnosis.

4.11. Intradural extramedullary spinal tumours

These include meningiomas and neurofibromas and are usually best managed by surgery. Cyberknife is occasionally used for such tumours.

4.12. Intramedullary spinal cord tumours

These tumours will require laminectomy for access. Astrocytomas will usually lend themselves to biopsy only and occasionally debulking. The mainstay of treatment will then be radiotherapy. Ependymomas may be removable using microsurgical techniques. Appropriate spinal cord monitoring should be employed when operating upon intrinsic and sometimes extrinsic cord lesions. Patients with this condition usually require craniospinal MRI as the tumour may disseminate via cerebrospinal fluid pathways. All patients will be assessed for the need for radiotherapy.

4.13. Follow-up

The follow-up required varies between tumour types and will involve a combined approach to symptom management and disease surveillance. The main reasons for clinical assessment and imaging follow-up are to:

- manage any continuing problems, such as epilepsy, resulting from the disease or initial treatment
- diagnose recurrence when symptoms change and refer for appropriate management
- provide access to appropriate information, support and rehabilitation
- provide symptomatic and palliative care
- Provide information to patients on new treatments and opportunities to participate in research studies.

4.14. Imaging follow up

Imaging is an integral part of follow-up for patients with brain tumours. Frequency of follow up imaging will depend on the histology and site of the original tumour and previous treatment. Ideally it should be reserved for patients in whom the result of the scan will alter management.

Where imaging is indicated, pre and post contrast MRI is the imaging modality of choice unless contra-indicated, when CT can be used as an alternative.

The frequency of scans and the period of surveillance should then be determined by the MDT. MR spectroscopy and/or PET CT scans can be used when uncertainty exists regarding changes on surveillance scans to distinguish progression from pseudo-progression/radiation necrosis. Occasionally biopsy will be required to confirm the nature of such changes.

All follow up patients with continuing or new problems related to their treatment or disease progression will be discussed at the CN MDT. Depending upon the circumstances, recurrence may be managed by repeat biopsy, resection or debulking, radiotherapy, chemotherapy, stereotactic radiosurgery or palliation. Repeat debulking of progressing high grade glioma can be considered in patients with relatively localised, unilateral tumours in non-eloquent brain regions, usually where previous debulking was performed greater than six months previously.