PRINCESS MARGARET CANCER CENTRE
CLINICAL PRACTICE GUIDELINES

CENTRAL NERVOUS SYSTEM

LOW GRADE GLIOMAS
CNS Site Group – Low Grade Gliomas

Author: Dr. Norm Laperriere

1. INTRODUCTION .................................................. 3

2. PREVENTION .................................................... 3

3. SCREENING AND EARLY DETECTION .................. 3

4. DIAGNOSIS AND PATHOLOGY .............................. 3

5. MANAGEMENT ................................................... 4

   5.1 MANAGEMENT ALGORITHMS .......................... 4
   5.2 SURGERY .................................................. 4
   5.3 CHEMOTHERAPY .......................................... 5
   5.4 RADIATION THERAPY ................................... 5

6. ONCOLOGY NURSING PRACTICE ....................... 6

7. SUPPORTIVE CARE .......................................... 6

   7.1 PATIENT EDUCATION ..................................... 6
   7.2 PSYCHOSOCIAL CARE ..................................... 6
   7.3 SYMPTOM MANAGEMENT .............................. 6
   7.4 CLINICAL NUTRITION .................................... 7
   7.5 PALLIATIVE CARE .......................................... 7
   7.6 REHABILITATION ........................................... 7

8. FOLLOW-UP CARE ............................................. 7
Low Grade Gliomas

1. Introduction
   • Grade I gliomas: pilocytic astrocytoma (PA), dysembryoplastic neuroepithelial tumor (DNET), pleomorphic xanthoastrocytoma (PXA), ganglioglioma
   • Grade II gliomas: fibrillary astrocytoma, oligodendroglioma, mixed gliomas
   • annual incidence is approx. 1/100,000

This document is intended for use by members of the Central Nervous System site group of the Princess Margaret Hospital/University Health Network.

The guidelines in this document are meant as a guide only, and are not meant to be prescriptive. There exists a multitude of individual factors, prognostic factors and peculiarities in any individual case, and for that reason the ultimate decision as to the management of any individual patient is at the discretion of the staff physician in charge of that particular patient’s care.

2. Prevention
   • genetic counseling for all NF1 carriers

3. Screening and Early Detection
   • baseline MRI brain for all newly diagnosed carriers of NF1

4. Diagnosis and Pathology
   • No TNM staging
   • Typical appearance on CT/MRI: grade I: diffusely enhancing discrete intra-axial mass, grade II: diffusely non-enhancing infiltrative lesions with expansion of involved brain
   • WHO 2007 classification: 2 grades
   • Grade I gliomas: pilocytic astrocytoma (PA), dysembryoplastic neuroepithelial tumor (DNET), pleomorphic xanthoastrocytoma, (PXA), ganglioglioma
     • indolent, potentially curable neoplasms
     • management is expectant, serial single modality followed by periods of observation
     • intervention is based on mass effect, neurologic or impending neurologic loss
     • seizures are managed by anti-convulsant therapy, rarely an indication for intervention otherwise
     • PA often associated with NF1
     • presence of KIAA1549:BRAF fusion present in 50-70% of patients with PA may be associated with novel agents of treatment in the near future
     • pilocytic astrocytomas often associated with NF1 syndrome
   • Grade II: infiltrative astrocytoma, oligodendroglioma, mixed gliomas
     • indolent, incurable neoplasms
     • management is expectant, serial single modality followed by periods of observation
     • seizures are managed by anti-convulsant therapy, rarely an indication for intervention otherwise
     • IDH1 mutation is a good marker for gliomas, present in 50-80% of tumours
     • in tumours containing an oligo component, detection of co-deletion of 1p19Q is expected in 50-70% of cases
• co-deletion of 1p19Q is associated with a favorable prognosis and is an indicator of increased likelihood of response to an alkylating agent
• Ki-67 nuclear antigen and/or MIB-1 indices as indicators of mitotic activity are related to prognosis

5. Management

5.1 Management Algorithms
• occasionally pre-operatively and most often post-operatively once pathology is available, all cases are reviewed at tumour board by a multidisciplinary team (neurosurgery, radiation oncology, neuro-oncology, neuropathology, neuroradiology) for a recommendation on further management

• Grade I gliomas: pilocytic astrocytoma (PA), dysembryoplastic neuroepithelial tumor (DNET), pleomorphic xanthoastrocytoma, (PXA), ganglioglioma
  • indolent, potentially curable neoplasms
  • serial management with surgery, followed by observation or chemotherapy only or chemotherapy followed by focal radiotherapy or radiotherapy only
  • 50% of gangliogliomas may harbor the BRAF-V600E mutation, in which case BRAF agents and n-Myc inhibitors may be utilized as systemic therapy

• Grade II: infiltrative astrocytoma, oligodendroglioma, mixed gliomas
  • standard of care currently a matter of controversy
  • IDH1/2 status is critical
  • these tumours are not surgically curable
  • recent data suggests upfront temozolomide is a reasonable option (await data from recently completed randomized study of upfront temozolomide vs RT)
  • post-surgical options include: observation
    RT alone
    temozolomide alone
  • major prognostic factors include age, seizures, histology (presence of worrisome features, elevated proliferative indices, presence or absence of oligo component), enhancement on MRI, performance status, tumour bulk, neurologic deficit, involvement of eloquent brain (motor strip, internal capsule, brain stem), presence/absence of co-deletion of 1p19Q, presence of IDH1 mutation or wild type
  • decision to proceed with treatment or observation at presentation is related to the constellation of presenting prognostic factors noted above
  • in IDH1 wild type, combined RT & concurrent temozolomide is seriously considered
  • it is at the individual staff’s discretion as to when to recommend treatment
  • treatment almost always includes serial use of surgery, RT, temozolomide in various order

5.2 Surgery
• Grade I gliomas: pilocytic astrocytoma (PA), dysembryoplastic neuroepithelial tumor (DNET), pleomorphic xanthoastrocytoma, (PXA), ganglioglioma
  • tumor location determines resectability of Grade I gliomas
  • tumours located in critical areas of the brain are typically non-resectable and biopsies are usually performed if safely possible or partial resections
  • gross total resection is attempted where possible as this may result in long term control/cure
• resection considered at recurrence if gross total excision possible

• **Grade II: fibrillary astrocytoma, oligodendroglioma, mixed gliomas**
  • tumor location determines resectability of LGGs
  • tumours located in critical areas of the brain are typically non-resectable and biopsies are usually not done for brain stem lesions
  • there are no class 1 data to guide the degree of resection, but most reviews and expert opinion support a maximal safe resection
  • resection considered at recurrence if mass effect an issue

5.3 **Chemotherapy**

• **Grade I gliomas: pilocytic astrocytoma (PA), dysembryoplastic neuroepithelial tumor (DNET), pleomorphic xanthoastrocytoma, (PXA), ganglioglioma**
  • most data with use of chemotherapy for PAs come from the pediatric experience as initial therapy, very little experience in adult setting
  • 50% of gangliogliomas may harbor the BRAF-V600E mutation, in which case BRAF agents and n-Myc inhibitors may be utilized as systemic therapy
  • in adults, chemotherapy most often given at recurrence post-RT
  • typical agents:
    - temozolomide in 5 day/28 day cycle, 150-200 mg/m^2
    - vincristine/carboplatin associated with 65% progression free rate at 3 years
    - weekly vinblastine as salvage associated with 50% response rate

• **Grade II: infiltrative astrocytoma, oligodendroglioma, mixed gliomas**
  • recent data support the use of temozolomide (5 day/28 day cycle, 150-200 mg/m^2) either as an upfront post-surgical approach (particularly in LGGs with co-deletion of 1p19Q) or for post-RT recurrence
  • await data from recently completed randomized study of upfront temozolomide vs RT

5.4 **Radiation Therapy**

• **Grade I gliomas: pilocytic astrocytoma (PA), dysembryoplastic neuroepithelial tumor (DNET), pleomorphic xanthoastrocytoma, (PXA), ganglioglioma**
  • immobilization: thermoplastic U/S frame
  • Imaging: CT, MRI flair, T1 with gadolinium
  • GTV: surgical cavity + flair abnormality
  • care is taken to not include surgical approach areas
  • CTV: 0.5 cm
  • PTV: 0.3-0.5 cm
  • Technique: IMRT
  • Dose: 50 Gy in 25 fractions or 54 Gy in 30 fractions
  • IGRT: daily cone beam CT performed, and all displacements greater than 1 mm are corrected prior to treatment delivery, and for all angular displacements greater than 3 degrees, a repeat set up is undertaken

• **Grade II: infiltrative astrocytoma, oligodendroglioma, mixed gliomas**
  • immobilization: thermoplastic U/S frame
  • Imaging: CT, MRI flair, T1 with gadolinium
  • GTV: surgical cavity + flair abnormality
  • care is taken to not include surgical approach areas
  • CTV: 1.0 cm
• PTV: 0.3-0.5 cm
• Technique: IMRT
• Dose: 50 Gy in 25 fractions or 54 Gy in 30 fractions
• IGRT: daily cone beam CT performed, and all displacements greater than 1 mm are corrected prior to treatment delivery, and for all angular displacements greater than 3 degrees, a repeat set up is undertaken
• Shorter course of irradiation:
  Age > 65-70 with poor performance status.
  Options: 40 Gy/15, CT/MRI based planning to partial brain
  20 Gy/5 or 30 Gy/10 whole brain radiation, clinical set up

6. Oncology Nursing Practice

Refer to general oncology nursing practices

7. Supportive Care

7.1 Patient Education

Driving
• possible restriction

Seizures
• education about seizures
• what to do when a seizure occurs
• how to take seizure medications
• possible side effects of seizure medications
• avoid heights, taking baths or swimming alone

Raised Intracranial Pressure: Steroids
• symptoms of raised intracranial pressure
• side effects of steroids
• titration of steroids for optimal dose

When to call multidisciplinary team
• change in seizure pattern
• new or progressive neurologic loss
• symptoms of raised intracranial pressure

7.2 Psychosocial Care

• assess family finances
• assess for possible disability applications
• assess possible depression/anxiety
• presence or absence of drug program, apply for provincial assistance if necessary
• possible need for assistive devices or services in the home

7.3 Symptom Management

• seizures
• raised intracranial pressure
• neurologic loss
• visual loss
• depression
• psychosis
• anger issues
• poor memory

7.4 Clinical Nutrition
• recommend normal diet as per recommendations of Canadian Cancer Society
• diabetic diet if elevation of blood glucose secondary to steroids

7.5 Palliative Care
• make referral in cases of progressive disease for which there is no further active therapy recommended
• management of uncontrolled symptoms

7.6 Rehabilitation
• in cases of neurologic loss, assess for possible rehabilitation OT/PT
• assess for supportive devices in the home

8. Follow-up Care
• clinical assessment and MRI brain
• 3-4 months initially at first 1-3 visits
• then q 6 monthly for 1-5 years post-treatment
• then q 12 monthly from 5-10 years post-treatment