Brain Metastasis and Leptomeningeal Carcinomatosis

Anthony Simon RN, AGACNP-BC, AOCNS
Objectives

• To be able to localize 3 symptoms, and their respective locations in the brain
• Name and understand the primary prognostic indicator for patients with brain metastasis and leptomeningeal disease
• Understand what differentiates the treatment goals for a patient with good prognosis vs a poor prognosis patient
• Name approaches to each form of treatment- Surgery, Radiation, and chemotherapy
Introduction

- Brain metastasis and leptomeningeal disease are lethal
- Untreated brain metastasis from solid tumors has a prognosis of 1-2 months
- Once diagnosed leptomeningeal disease has a prognosis of 2 weeks–2 months
The Lobes of the Brain

- **Frontal Lobe**: Thinking, planning, problem solving, emotions, behavioural control, decision making.
- **Parietal Lobe**: Perception, object classification, spelling, knowledge of numbers, visuospatial processing.
- **Occipital Lobe**: Vision, visual processing, colour identification.
- **Temporal Lobe**: Memory, understanding language, facial recognition, hearing, vision, speech, emotion.
- **Cerebellum**: Gross and fine motor skills, hand-eye coordination, balance.
- **Brain Stem**: Regulates body temperature, heart rate, swallowing, breathing.
Brain Metastasis

• Brain metastasis is the most common intracranial tumor in adults
• In systemic malignancy brain metastasis occurs in 10-30% of adults, and 6-10% of children
• Incidences increasing
  – Improved imaging with MRI
  – Improve control of extracranial disease
The Tentorium Cerebelli

Supratentorial (cerebrum)

Tentorium

Infratentorial (cerebellum)
Common Malignancies Responsible for Brain Metastasis

• Adults
  – Lung
  – Breast
  – Kidney
  – Colorectal
  – Melanoma

• Children
  – Sarcomas
  – Germ Cell tumors
  – Neuroblastoma
Distant Metastasis

Primary Tumor

Local Metastasis
Clinical Manifestations

• Headache
  – 40-50% of patients
  – Early morning headache
• Focal neurologic dysfunction
  – 20-40% pf patients
  – Hemiparesis most common
• Cognitive dysfunction
  – 30-35% of patients
• Seizures
• Stroke
• Others
Imaging

• Magnetic resonance imaging with contrast
• More sensitive than non contrast MRI or CT scan
Prognostic Indicators

- Performance status
- Age younger than 65
- Control of extracranial disease
- Underlying cancer histology and genealogy
# Karnofsky Performance Scale

<table>
<thead>
<tr>
<th>General category</th>
<th>%</th>
<th>Specific criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Able to carry on normal activity</td>
<td>100</td>
<td>Normal general status - No complaint - No evidence of disease</td>
</tr>
<tr>
<td>• No special care needed</td>
<td>90</td>
<td>Able to carry on normal activity - Minor sign of symptoms of disease.</td>
</tr>
<tr>
<td>• Normal activity with effort, some signs or symptoms of disease.</td>
<td>80</td>
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<td>• Unable to work</td>
<td>70</td>
<td>Able to care for self, unable to carry on normal activity or do work</td>
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<td>• Able to live at home and care for most personal needs</td>
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<td>Requires occasional assistance from others, frequent medical care</td>
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<td>• Various amount of assistance needed</td>
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<td>30</td>
<td>Severely disabled, hospitalization indicated, death not imminent</td>
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<td>• Disease may be rapidly progressing</td>
<td>20</td>
<td>Very sick, hospitalization necessary, active supportive treatment necessary</td>
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<tr>
<td>• Terminal states</td>
<td>10</td>
<td>Moribund</td>
</tr>
<tr>
<td>• Dead</td>
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Treatments

• Surgery
• Radiation
• Chemotherapy
Surgery

• There is a single metastatic lesion
• Large symptom producing tumors
• Or if there is an uncertain diagnosis, excisional biopsy is considered
Eloquent Areas of the Brain
Radiation Therapy

• Many who undergo surgery get local radiation therapy to the surgical bed
• For those with a limited number of small brain metastasis, they may have stereotactic radiosurgery alone
• Whole brain radiation therapy
Chemotherapy

• Chemotherapy is based on the primary site of cancer
  – Breast
  – Lung
  – Melanoma
Surveillance

- Imaging
  - 1 month after initial therapy, and then every 2-3 months after
  - Up to 50% progress within the first 6 months to one year
Recurrence

• Pseudo-progression

• Recurrence
  – Additional surgery a possible option
  – Additional radiation therapy is unlikely
  – Chemotherapy
Leptomeningeal Disease

• Malignant cancer cells in the CSF
• Rare and devastating complication of advanced cancer
• Diagnosed in approximately 5% of patients with metastatic cancer
• Most common cancers to result in leptomeningeal disease—breast, lung, melanoma, GI cancers
• Primary brain tumors may also lead to the leptomeningeal disease—high-grade astrocytomas, oligodendroglioma, medulloblastoma, pineoblastoma
• The development may be influenced by treatment
Pathophysiology/review
Cerebrospinal fluid

Flow of Cerebrospinal Fluid

1. CSF is secreted by choroid plexus in each lateral ventricle.
2. CSF flows through interventricular foramina into third ventricle.
3. Choroid plexus in third ventricle adds more CSF.
4. CSF flows down cerebral aqueduct to fourth ventricle.
5. Choroid plexus in fourth ventricle adds more CSF.
6. CSF flows out two lateral apertures and one median aperture.
7. CSF fills subarachnoid space and bathes external surfaces of brain and spinal cord.
8. At arachnoid villi, CSF is reabsorbed into venous blood of dural venous sinuses.

Arachnoid villus
Superior sagittal sinus
Arachnoid mater
Subarachnoid space
Dura mater
Choroid plexus
Third ventricle
Cerebral aqueduct
Lateral aperture
Fourth ventricle
Median aperture
Central canal of spinal cord
Subarachnoid space of spinal cord
Pathogenesis
Clinical Manifestations

- Mass effect
- Cranial nerves and spinal root dysfunction
- Invasion of the brain parenchyma
- Disruption of the blood brain barrier
Signs and symptoms

• Any neurological symptom may be related to LM
• Symptoms present acutely and progress within days to weeks
• Multifocal neurological signs and symptoms
• Be aware of those that present with a single symptom
Diagnostics

- Brain MRI
- CSF analysis through lumbar puncture
Leptomeningeal contrast enhancement
Leptomeningeal Contrast Enhancement
Treatment Goals

• Stabilizing or improving neurological function
• Prolonging survival
• Palliation of symptoms
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Poor Risk Patients

- Patients with multiple serious/fixed neurological deficits
- Extensive systemic disease even with active treatment
- Focus is largely on palliation of symptoms
Treatments

• Radiation therapy
• Analgesics for pain
• Corticosteroids
• Anticonvulsants
• VP shunting
• SSRIs
Good Risk Patients

• Those without fixed neurological deficits
• Minimal systemic disease
• Cancer with reasonable treatment options
• Goal is direct tumor control
Treatments

- Surgery
- Radiation
- Chemotherapy
Surgery

• Treatment of increased intracranial pressure
  – For signs of increased intracranial pressure initially treat with steroids
  – VP shunting
Radiation Therapy

• Used to treat bulkier symptomatic areas of disease
• Appears to be more effective at relieving symptoms when compared to chemotherapy
• Standard radiation dose for leptomeningeal disease includes 30-36 Gy, in 3 Gy daily fractions
• Major adverse effects during or after focal radiation therapy unusual
• With large extension radiation fields common adverse effects include myelosuppression, mucositis, esophagitis, leukoencephalopathy
Intrathecal chemotherapy

• Mainstay of treatment with leptomeningeal metastasis
• It may be delivered via lumbar puncture versus Ommaya reservoir
• Methotrexate is the chemotherapy most often used for the leptomeningeal disease
Systemic Chemotherapy

• There are several therapeutic chemotherapy agents provide therapeutic concentration within the CSF when given at appropriate doses

• Advantages
  – Surgery risks
  – Obstruction normal CSF flow
  – Increased availability of cytotoxic agents
  – Uniform drug distribution
Common Systemic Chemotherapy Agents

• High-dose methotrexate with leucovorin rescue
• High-dose cytarabine
• Capecitabine
• Tyrosine kinase inhibitors such as erlotinib
• Anaplastic lymphoma kinase inhibitors such as Crizotinib
Investigational Therapies

• IT etoposide
• Intrathecal trastuzumab
• Intrathecal rituximab
Prognosis

• Despite aggressive therapy even good risk patients with leptomeningeal disease have limited survival
• Average survival with aggressive treatment is 3-4 months
• Tumor histology and molecular subtype may influence prognosis
• Performance status and control of systemic disease are important factors
QUIZ

• Questions to ask yourself
  – What lobe of the brain is this lesion in?
  – Would you resect the tumor?
  – What part of the brain would receive radiation?
  – Name 2 symptoms the patient may experience with a metastatic lesion in this area.
References


