CURRENT CONCEPTS IN
THE DIAGNOSIS AND TREATMENT OF

Neoplastic Meningitis

AN EDUCATIONAL VIRTUAL LECTURE FOR PHYSICIANS, PHARMACISTS AND REGISTERED NURSES

Activity Workbook

Jointly sponsored by Robert Michael Educational Institute LLC
and Postgraduate Institute for Medicine

Supported by an educational grant from Enzon Pharmaceuticals, Inc.
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Target Audience
This virtual lecture has been designated to meet the educational needs of physicians, pharmacists and registered nurses involved in the care of patients with neoplastic meningitis.

Activity Purpose
This virtual lecture is intended to assist clinicians in understanding how to treat and manage patients with neoplastic meningitis.

Statement of Need
Today, more patients are living longer because of effective treatments for cancer. As a result, more patients are at risk for neoplastic meningitis (NM), which occurs when malignant cells enter the cerebrospinal fluid.\(^1-3\) NM is a devastating and ultimately fatal disease.\(^4\) Although treatment remains palliative, it often affords stabilization and protection against further neurological deterioration.\(^5\) When NM is left undiagnosed or untreated, rapid neurological deterioration can occur.\(^1\) Therefore, healthcare professionals should carefully evaluate patients in order to diagnose NM and plan treatment to maximize its effects while minimizing treatment-associated toxicities.\(^1\)


Educational Objectives
After completing this virtual lecture, the participant should be better able to:

- Describe the epidemiology and pathogenesis of metastatic malignant disease involving the meninges
- Identify signs and symptoms associated with neoplastic meningitis
- Explain methods of diagnosing neoplastic meningitis
- Review existing and emerging treatment options, including intrathecal chemotherapy, systemic chemotherapy and radiation therapy
Marc C. Chamberlain, MD
Professor of Neurology
Department of Neurology
University of Washington
Affiliate Investigator
Fred Hutchinson Cancer Research Center
Seattle, Washington

Marc C. Chamberlain, MD, is Professor of Neurology in the Department of Neurology at the University of Washington and Affiliate Investigator at Fred Hutchinson Cancer Research Center in Seattle, Washington. He is board-certified in both pediatrics and neurology.

After receiving a Bachelor of Arts degree in zoology and a Bachelor of Science degree in biochemistry from the University of California at Berkeley, Dr. Chamberlain earned a medical degree from Columbia University in New York. Subsequently, he completed both an internship and a residency in pediatrics at the Bronx Municipal Hospital Center and a residency in pediatrics at Harbor–UCLA Medical Center in Los Angeles, California. He also completed a fellowship in pediatric neurology at UCLA and an American Cancer Society fellowship.

Dr. Chamberlain is on the editorial boards of CNS Drugs and the American Journal of Cancer and is a reviewer for numerous journals, including Cancer, Journal of Clinical Oncology, Journal of Neuro-Oncology, Neurology, Archives of Neurology, and Lancet Neurology. He has authored more than 160 articles and 22 book chapters and has presented 200 invited lectures.

Over the years, Dr. Chamberlain developed many of the methods in use today to evaluate and manage neoplastic meningitis. Since 1996, his research has focused increasingly on clinical trials in patients with primary brain tumors.
Physician Continuing Education

Accreditation Statement
This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Robert Michael Educational Institute LLC (RMEI) and Postgraduate Institute for Medicine (PIM). PIM is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation
Postgraduate Institute for Medicine designates this educational activity for a maximum of 1 AMA PRA Category 1 Credit™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Pharmacist Continuing Education

Accreditation Statement
Postgraduate Institute for Medicine is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Credit Designation
Postgraduate Institute for Medicine designates this continuing education activity for 1.0 contact hour (0.10 CEU) of the Accreditation Council for Pharmacy Education. (Universal Program Number 809-999-07-047-H01-P)

A statement of credit will be issued only upon receipt of a completed activity Evaluation form and will be mailed to participants within 4 to 6 weeks.

ACPE Release Date: April 25, 2007

Nursing Continuing Education

CNA/ANCC
This educational activity for 1.0 contact hour is provided by Postgraduate Institute for Medicine (PIM).

PIM is an approved provider of continuing nursing education by the Colorado Nurses Association, an accredited approver by the American Nurses Credentialing Center’s Commission on Accreditation.

California Board of Registered Nursing
Postgraduate Institute for Medicine is approved by the California Board of Registered Nursing, Provider Number 13485 for 1.2 contact hours.
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Postgraduate Institute for Medicine (PIM) assesses conflict of interest with its instructors, planners, managers, and other individuals who are in a position to control the content of CME activities. All relevant conflicts of interest that are identified are thoroughly vetted by PIM for fair balance, scientific objectivity of studies utilized in this activity, and patient care recommendations. PIM is committed to providing its learners with high-quality CME activities and related materials that promote improvements or quality in healthcare and not a specific proprietary business interest of a commercial interest.

The following faculty reported a real or apparent conflict of interest:

Dr. Marc C. Chamberlain has asked that we advise participants in this activity that he has an affiliation with Enzon Pharmaceuticals, Inc. and Mundipharma International Limited (Consultant).

The following planners and managers have the following to disclose:

ROBERT MICHAEL EDUCATIONAL INSTITUTE LLC
- Sherri Kramer, MD, has no affiliations with commercial interests to disclose.
- Patricia C. Walter has no affiliations with commercial interests to disclose.
- Marie Bialek, PharmD, has asked that we advise participants in this activity that she has an affiliation with AstraZeneca (Salary) and McNeil Consumer & Specialty Pharmaceuticals (Contractor).

POSTGRADUATE INSTITUTE FOR MEDICINE
- Jan Hixon, RN, has no affiliations with commercial interests to disclose.
- Linda Graham, RN, has no affiliations with commercial interests to disclose.
- Trace Hutchison, PharmD, has no affiliations with commercial interests to disclose.

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Disclaimer
Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without the evaluation of their patient’s conditions and possible contraindications on dangers in use, review of any applicable manufacturer’s product information and comparison with recommendations of other authorities.
Objectives

- Describe the epidemiology and pathogenesis of neoplastic meningitis (NM)
- Identify the signs and symptoms of NM
- Explain methods of diagnosing NM
- Review existing and emerging treatment options for NM
**Background**

- A central nervous system (CNS) metastatic complication in patients with late-stage cancer\(^1,2\)
- Also called leptomeningeal metastasis
  - Carcinomatous meningitis (from solid tumor)\(^2,3\)
  - Lymphomatous meningitis (from systemic lymphoma)\(^2,3\)
  - Leukemic meningitis (from systemic leukemia)
- Malignant cells spread to the leptomeninges and subarachnoid space\(^1\)
- Tumor cells are disseminated within the cerebrospinal fluid (CSF)\(^1\)
- Early diagnosis and treatment are important\(^1\)

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**Incidence of Neoplastic Meningitis**

- NM is diagnosed clinically in 3% to 5% of patients with cancer
- Autopsy studies suggest a higher incidence
  - 4%-15% of solid tumors
  - 5%-15% of leukemia and lymphoma
  - 1%-2% of primary brain tumors

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\(^1\) Gliessner B, Chamberlain MC. Lancet Oncol. 2006;5:443-452.
\(^2\) Jaccard KA. Semin Oncol. 2000;23:312-322.
Risk Factors

- Liquid tumors\(^1\)\(^2\)
  - Raised lactate dehydrogenase; low serum albumin; <60 years of age
  - Involvement of the testis, breast, or bone marrow
  - More than 2 extranodal sites
  - Brain metastases?

- Solid tumors\(^3\)
  - No risk factors identified
  - HER2-positive breast cancer?
  - Brain metastases?

**Pathophysiology: Entry of Cancer Cells into the CSF Compartment**

- Hematogenous dissemination\(^1,2\)
- Centripetal migration from systemic tumors along perineural or perivascular spaces\(^1,2\)
- Direct extension from contiguous tumor deposits\(^1-3\)
  - Epidural- or dural-based disease
  - Brain parenchyma

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**Neoplastic Meningitis in Non-Small Cell Lung Cancer: Brain**

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Neoplastic Meningitis in Non-Small Cell Lung Cancer: Spine

Table: Signs and Symptoms of NM

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>Cognitive defects</td>
</tr>
<tr>
<td>Alteration of mentation</td>
<td>Seizures</td>
</tr>
<tr>
<td>Difficulty walking</td>
<td>Gait disturbances</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Sensory disturbances</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>Papilledema</td>
</tr>
<tr>
<td>Cranial nerves</td>
<td></td>
</tr>
<tr>
<td>Diplopia</td>
<td>Oculomotor paresis III, IV, VI;</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>hypoglossal neuropathy XII</td>
</tr>
<tr>
<td>Visual loss</td>
<td>Trigeminal neuropathy V, diminished</td>
</tr>
<tr>
<td>Facial numbness</td>
<td>facial reflex IX, X; acoustic neuropathy</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>VII; optic neuropathy II</td>
</tr>
<tr>
<td>Spinal</td>
<td></td>
</tr>
<tr>
<td>Focal weakness</td>
<td>Reflex asymmetry</td>
</tr>
<tr>
<td>Paresthesias</td>
<td>Sensory loss</td>
</tr>
<tr>
<td>Back pain</td>
<td>Upper or lower motor neuron weakness</td>
</tr>
<tr>
<td>Radicular pain</td>
<td>Decreased rectal tone</td>
</tr>
<tr>
<td>Bladder and bowel dysfunction</td>
<td>Straight leg raising</td>
</tr>
<tr>
<td></td>
<td>Nuchal rigidity</td>
</tr>
</tbody>
</table>

Adapted from Gliessner B, Chamberlain MC. Lancet Neurol. 2006;5:443-452, with permission.
Etiology of Signs and Symptoms

- Injury to nerves that traverse the subarachnoid space
- Direct tumor invasion of the brain or spinal cord
- Alteration in the local blood supply
- Obstruction of normal CSF flow pathways

Diagnosis of Suspected NM

- Symptoms compatible with NM
- Cranial and spinal MRI
- CSF analysis

Diagnosis can be made by
- Clinical signs and symptoms
- Radiology
- Cytology
- Cytology is persistently negative in ~50% of patients with NM

References:
Findings on CSF Examination

<table>
<thead>
<tr>
<th>CSF Findings</th>
<th>Initial Examination (%)</th>
<th>Total Examinations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opening pressure &gt;150 mm H₂O</td>
<td>30-57</td>
<td>61-72</td>
</tr>
<tr>
<td>White blood cells &gt;4 mm³</td>
<td>57-64</td>
<td>72-79</td>
</tr>
<tr>
<td>Protein &gt;50 mg/dL</td>
<td>73-86</td>
<td>79-91</td>
</tr>
<tr>
<td>Glucose &lt;60 mg/dL</td>
<td>31-55</td>
<td>41-77</td>
</tr>
<tr>
<td>Positive cytology</td>
<td>45-73</td>
<td>77-100</td>
</tr>
</tbody>
</table>

A composite from 5 studies in more than 300 patients.


Sensitivity of CSF Analysis

- False-negative results are common (40% to 60%)
- Prospective evaluation of 39 patients with NM suggests sample size of at least 10.5 mL required to ensure a 3% false-negative rate

CSF Analysis in Liquid Tumors

- Another analytic method is flow cytometry together with 2 to 4 fluorescence markers (FACS)\(^1\)
- Polymerase chain reaction (PCR) amplification of IgH genes is useful for lymphomatous meningitis\(^2\)
  - Each clonal lymphoma cell is characterized by a unique rearranged cell surface heavy chain immunoglobulin (IgH) or T-cell receptor


Use of Magnetic Resonance Imaging

- Gadolinium (Gd)-enhanced MRI imaging is the technique of choice
- Imaging of the entire CNS axis (brain and spine) is required
- T1-weighted with contrast and T2-weighted images with fat suppression

Cranial MRI Findings in NM

<table>
<thead>
<tr>
<th>Neuroimaging Abnormality</th>
<th>Chamberlain, 1990 (N=14) (%</th>
<th>Balm, 1996 (N=126) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenchymal volume loss</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>Focal or diffuse enhancement of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sufi or convexity</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Cisterns</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Tentorium</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Ependymal</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Nodules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subarachnoid</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Parenchymal</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Communicating</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>Obstructive</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Parenchymal metastases</td>
<td>45</td>
<td>24</td>
</tr>
<tr>
<td>Single</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>


Neuroradiographic Differential Diagnosis

- Inflammatory disease
- Infectious disease
- Granulomatous disease (ie, sarcoid)
- Iatrogenic disease (ie, chemical meningitis)
- Stroke (ie, cortical thrombosis, subarachnoid hemorrhage)
- Intracranial surgery
- Low-pressure syndromes
- Trauma

Radioisotope CSF Flow Studies (1)

- CSF flow obstruction is common in NM
  - Approximately one third of patients with solid tumor NM
  - No data on incidence in liquid tumor NM
  - Blocks are most common at base of skull, spinal canal, and over the cerebral convexities

- CSF flow studies are performed in most nuclear medicine departments

- Technique of choice
  - Indium 111-DTPA (only FDA-approved method)
  - 99mTc-Technetium macroaggregated albumin


Radioisotope CSF Flow Studies (2)

- Used as an adjunct to treatment planning
- Enable detection of flow abnormalities in patients considered for treatment
  - Risk for toxicity increases in patients with ventricular outlet obstruction
  - Obstruction of CSF flow prevents drug dissemination

Current Concepts in the Diagnosis and Treatment of Neoplastic Meningitis

**Presentation**

**Indium 111-DTPA CSF Flow Study**

**Treatment of CSF Flow Obstruction**

- Radiation therapy to sites of obstructions
  - One third of CSF obstructions are in the brain
    - 50% resolve after radiotherapy
  - Two thirds of CSF obstructions are in the spine
    - 35% resolve after radiotherapy
- May obviate need for CSF shunting

Treatment Goals

- Maintain neurological quality of life¹
- Stabilize or improve neurological symptoms¹-³
- Extend survival¹-³


Stratification for Treatment

Poor Risk Group
- Low KPS
- Multiple, serious, or major neurological deficits
- Extensive systemic disease with few treatment options
- Bulky CNS disease
- NM-related encephalopathy
- CSF block

Good Risk Group
- High KPS
- No major neurological deficits
- Minimal systemic disease
- Reasonable systemic treatment options
- No CSF block

KPS = Karnofsky Performance Status.
**Treatment Algorithm**

- CNS imaging
  - Bulky disease or symptomatic sites
    - Radiotherapy
  - No bulky disease
    - Supportive care
    - Port placement
    - CSF flow study
      - CSF flow block
      - Radiotherapy to site of block
      - CSF flow study
      - CSF flow block
    - Normal CSF flow
      - Intra-CSF chemotherapy

Adapted from Chamberlain MC. J Clin Oncol. 2005;23:3605-3613, with permission.

**Radiotherapy for NM**

- Palliate symptoms
- Treat bulky disease
- Correct CSF flow abnormalities
- Therapy type
  - Involved-field irradiation
  - Craniospinal irradiation

**Surgery for NM**
- Placement of port for intraventricular therapy
- CSF diversion for patients with symptomatic hydrocephalus
- Meningeal biopsy

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**Treatment Options for NM**
- Regional or intra-CSF chemotherapy
- High-dose systemic chemotherapy
- Craniospinal irradiation

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### Treatment: Intra-CSF Chemotherapy

- Three agents used most often
  - Methotrexate
  - Cytarabine (including the liposomal form)
  - Thiotapec
- Toxicity and complications of treatment
  - Primary toxicity of intra-CSF chemotherapy is transient chemical meningitis
    - May last for 4 to 5 days
    - May be associated with confusion, seizures, fever, stiff neck, photophobia, nausea, vomiting, and headache
  - Device- or port-related complications
    - Failure
    - Infection


### Table: Induction, Consolidation, and Maintenance

<table>
<thead>
<tr>
<th></th>
<th>Induction</th>
<th>Consolidation</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>16-15 mg</td>
<td>2 mg/d x 6 wk</td>
<td>16-15 mg</td>
</tr>
<tr>
<td></td>
<td>x 6 wk</td>
<td></td>
<td>x 6 wk</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>25-100 mg</td>
<td>25 mg/d x 6 wk</td>
<td>25-100 mg</td>
</tr>
<tr>
<td></td>
<td>x 6 wk</td>
<td></td>
<td>x 6 wk</td>
</tr>
<tr>
<td>DepotCyt*</td>
<td>50 mg Q2wd</td>
<td></td>
<td>50 mg Q2wd</td>
</tr>
<tr>
<td></td>
<td>for 2 doses</td>
<td></td>
<td>for 5 doses</td>
</tr>
<tr>
<td>Thiotepa</td>
<td>10 mg</td>
<td>10 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td></td>
<td>x 4 wk</td>
<td></td>
<td>x 4 wk</td>
</tr>
<tr>
<td>Alpha-</td>
<td>1 x 10^6 U</td>
<td>1 x 10^6 U</td>
<td>1 x 10^6 U</td>
</tr>
<tr>
<td>Interferon</td>
<td>x 6 wk</td>
<td></td>
<td>x 6 wk</td>
</tr>
<tr>
<td>Etoposide</td>
<td>5.5 mg/d</td>
<td></td>
<td>5.5 mg/d</td>
</tr>
<tr>
<td></td>
<td>x 6 wk</td>
<td></td>
<td>x 6 wk</td>
</tr>
<tr>
<td>Topotecan</td>
<td>0.4 mg</td>
<td></td>
<td>0.4 mg</td>
</tr>
<tr>
<td></td>
<td>x 6 wk</td>
<td></td>
<td>x 6 wk</td>
</tr>
</tbody>
</table>

*Crioteriy: concomitantly with dexamethasone 4 mg bid PO or IV for 5 days beginning on first day of DepotCyt injection.**

*Indicates: Q1d = daily; Q2wd = every other day; Q2wd = every other week; Q3w = every other month.

**Intra-CSF Chemotherapy**

- **DepoCyt**
  - Clinical or cytologic relapse
    - Methotrexate
      - Supportive care
- Clinical or cytologic relapse
  - Thiopepa
- Clinical or cytologic relapse
  - Interferon or topotecan or etoposide

Adapted from Chamberlain MC. Neurology. 2006;6:179-187, with permission.

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**Randomized Clinical Trial Data (1)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Response</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shapiro et al. J Clin Oncol. 2003;5;34 6 Supply;1528</td>
<td>Solid tumors (n=51) DepoCyt vs MTX</td>
<td>DFS: 35 vs 63 d</td>
<td>DepoCyt vs MTX/Ara-C</td>
</tr>
<tr>
<td></td>
<td>Lymphoma (n=25) DepoCyt vs Ara-C</td>
<td>DFS: 35 vs 63 d</td>
<td></td>
</tr>
<tr>
<td>Bongerd et al. Euro Cancer 2004;40:2728-2733</td>
<td>N=25 Breast cancer IT vs no IT</td>
<td>IT vs no IT</td>
<td>Improvement or stabilization: 50% vs 67%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TTP: 23 vs 24 wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS*: 55 vs 63 d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR: 71% vs 15%</td>
<td></td>
</tr>
</tbody>
</table>

* No significant differences between groups.
† Appropriate systemic chemotherapy and/or radiotherapy given in both arms.
## Randomized Clinical Trial Data (2)

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Response</th>
<th>Toxicity</th>
</tr>
</thead>
</table>
| Glade et al. J Clin Oncol 1999; 17: 3304-3402 | N=61 Solid tumors (eg, breast, SCLC, NSCLC in 52%) | DecoCyt vs MTX | RR: 25% vs MTX,
OS*: 195 vs 78 d, TTP 58 vs 30 d
 | DecoCyt vs MTX | Sensory/motor: 4% vs 10%;
alteration mental status: 5% vs 2%;
headache: 4% vs 2% |
Median survival: 15.8 vs 14.1 wk |
| Hitzler et al. J Clin Oncol 1987; 5: 1605-1612 | N=41 Nonleukemic malignancy (breast, lung, lymphatic in 90%) | IT MTX vs thiotope | Neurological improvements: none
Median survival: 15.8 vs 14.1 wk |
| IT MTX vs thiotope | Serious toxicities similar between groups, mucositis and neurological complications more common in MTX group |

*No significant differences between groups.


### Novel Intra-CSF Chemotherapy

- Etoposide in adults with solid or liquid NM
  - RR of 26% (7/27); reversible arachnoiditis (4/27)
- Topotecan in children and adults with solid or liquid NM
  - RR of 26% (6/23); arachnoiditis DLT (phase I)
  - RR/no change in 16% (5/30); mild toxicity (phase II)
- Mafosfamide in children with brain tumors
  - RR of 42% (11/26) (median follow-up, 26.5 mo)
  - Immediate toxicities manageable

Intra-CSF Biological Agents

- Alpha-interferon
- Rituximab
  - Maximum tolerated dose in one recent, small, Phase I study: 25 mg twice weekly by Ommaya reservoir for a maximum of 9 doses
- Trastuzumab
- Preclinical studies of nonradioactive antibodies or immunonoconjugates


Radioisotopes and Radioimmunoconjugates

- Unconjugated iodine 131
  - Low toxicity with transient improvements (n=31)
- 131I-radiolabeled monoclonal antibodies
  - Case study reported complete response
  - In neuroectodermal tumors, RR was 53%
- I-conjugated antibody to chondroitin proteoglycan sulfate and tenascin
  - CSF or radiographic response achieved; prolonged survival

Supportive Care

- Radiation to symptomatic and bulky sites
- Anticonvulsants for seizure control
- Adequate analgesia
- Antidepressants, anxiolytics
- Corticosteroids (of limited use)
- Antiemetics
- Psychostimulants


Challenges and Complications (1)

- Does intra-CSF chemotherapy contribute to outcome?
- Does site of drug administration matter (ie, intraventricular vs intralumbar)?
- Does positive CSF cytology have clinical relevance?
- Is extent and progression of neurological disease the most relevant outcome measure?
- Can clinicians reliably distinguish between deaths due to NM compared with systemic disease?
Challenges and Complications (2)

- What is the role for intra-CSF chemoprophylaxis aside from ALL?
- Do CSF-negative patients differ from CSF-positive patients?
- What is the role of radioisotope CSF flow studies?
- Is there a preferred intra-CSF drug and schedule?
- What characteristics define a patient for which intra-CSF chemotherapy is reasonable?
- Is there a role for systemic chemotherapy in improving outcomes independent of intra-CSF chemotherapy?

Conclusions

- Intra-CSF chemotherapy is the primary therapy for neoplastic meningitis
- Most patients require a combination of intra-CSF chemotherapy and radiotherapy
- Treatment may prolong survival and improve QOL
  - No significant survival advantages at this time
- Recommend treatment only for a subset of patients
- Further studies are needed to improve outcomes


REFERENCES


