Solitary Metastases to the Brain

Problems
Options
Guidelines
Case series
Discussion
Problems posed by solitary mets to brain

- Focal encephalopathy
  - Communications
  - Dexterity
  - Mobility
  - Cognition; behaviour; mood

- Diagnosis
- Mass effect +/- Intracranial hypertension
- Seizures
- Discomfort
- Death

Disability <-> Dependency
Prognosis in patients presenting with brain metastasis from an undiagnosed primary tumor

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342 patients with computed tomography–diagnosed brain metastases were treated at a single institution.

Survival was not statistically different between patients with an undiagnosed primary (UDP) lesion and those with a diagnosed primary (DP) tumor (6 and 4.5 months, respectively; p = 0.097). In the UDP group (122 patients [36%]), survival was not affected by the eventual identification of the primary disease (p = 0.905).

The median survival for the entire population was 5.2 months, with 1-, 2-, and 3-year survival rates of 25, 11, and 4%, respectively. Prognostic factors for the overall population included treatment (p < 0.0001), an age less than 65 years (p = 0.004), discharge status (p < 0.001), absence of systemic metastasis (p = 0.036), and asymptomatic cerebral metastasis (p = 0.05).

Conclusions. Treatment modality was the most significant independent variable affecting survival inpatients with brain metastases. Eventually identification of a primary tumor does not affect overall survival; therefore, delaying therapeutic intervention in pursuit of a primary diagnosis may not be appropriate. Data in this study failed to demonstrate a statistically significant difference in survival between patients with UDP and those with DP lesions, on first presenting with brain metastases.
Treatment options

- Local ...... Surgery; radiation
- Systemic ...... Chemo; steroids
- Disease specific ... +/- chemo
- Non-specific ..... Usually
- Adaptive ...... Needed
- Supportive ...... Variable
Solitary Metastatic Brain Tumours

Surgery or radiosurgery (if inoperable and < 4 cm. lesion) is recommended if $K \geq 70$, age < 65 years, absent or stable (controlled) primary disease and no other systemic disease

$K =$ Karnofsky Score
# Karnofsky

100% - normal, no complaints, no signs of disease
90% - capable of normal activity, few symptoms or signs of disease
80% - normal activity with some difficulty, some symptoms or signs
70% - caring for self, not capable of normal activity or work
60% - requiring some help, can take care of most personal requirements
50% - requires help often, requires frequent medical care
40% - disabled, requires special care and help
30% - severely disabled, hospital admission indicated but no risk of death
20% - very ill, urgently requiring admission, requires supportive measures or treatment
10% - moribund, rapidly progressive fatal disease processes
0% - death.
Radiation therapy
Gamma knife
Brain tumour biopsy
Management of single brain metastases: a clinical practice guideline.


SCOPE

DISEASE/CONDITION(S)

Confirmed cancer and a single brain metastasis
GUIDELINE OBJECTIVE(S)

• To evaluate if patients with confirmed single brain metastases should have surgical resection
• To evaluate if patients with single brain metastases undergoing surgical resection should receive adjuvant whole brain radiation therapy (WBRT)
• To evaluate the role of stereotactic radiosurgery in the management of patients with single brain metastases

TARGET POPULATION

Adults with confirmed cancer and a single brain metastasis

Note: This practice guideline does not apply to patients with metastatic lymphoma, small cell lung cancer, germ cell tumour, leukemia, or sarcoma.
INTERVENTIONS AND PRACTICES CONSIDERED

Management/Treatment
1. Whole brain radiation therapy (WBRT) versus WBRT plus surgery
2. Surgery plus WBRT versus surgery alone
3. WBRT with or without stereotactic radiosurgery (SRS)
4. SRS versus surgical resection
5. SRS with or without WBRT

MAJOR OUTCOMES CONSIDERED

• Survival
• Quality of life
• Local control of disease
• Adverse effects
Inclusion Criteria
Articles were selected for inclusion in this systematic review if they were fully published reports or published abstracts of:

1. Meta-analyses, systematic reviews and randomized controlled trials (RCTs) addressing specific guideline questions. If none of those study types were available, non-randomized prospective studies and retrospective reviews were eligible for inclusion.

2. Outcomes of interest were survival, local control of disease, quality of life, and adverse effects. Studies had to report data on at least one of these outcomes to be eligible for inclusion.

Exclusion Criteria
1. Letters and editorials were not considered.
2. Papers published in a language other than English were not considered.
3. Articles regarding patients with metastatic lymphoma, small cell lung cancer, germ cell tumour, leukemia, and sarcoma were excluded.
4. Studies including patients with multiple brain metastases in which results for patients with single brain metastases were not reported separately were excluded.
NUMBER OF SOURCE DOCUMENTS

5 randomized controlled trials, 3 prospective case series, 7 retrospective reviews, and 1 meta-analysis were reviewed.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Surgical excision should be considered for patients with good performance status, minimal or no evidence of extracranial disease, and a surgically accessible single brain metastasis amenable to complete excision. Since treatment in this disease is considered palliative, invasive local treatments must be individualized. Patients with lesions requiring emergency decompression due to intracranial hypertension were excluded from the randomized control trials but should be considered to be surgical candidates.

Postoperative whole brain radiotherapy (WBRT) should be considered to reduce the risk of tumour recurrence for patients who have undergone resection of a single brain metastasis. The optimal dose and fractionation schedule for whole brain radiation therapy is 3,000 cGy in 10 fractions or 2,000 cGy in five fractions.

Stereotactic radiosurgery (SRS) boost should be considered following WBRT for patients with single metastases. There is insufficient evidence to recommend SRS alone as single modality therapy.
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

• Two randomized controlled trials (RCTs) have shown that surgical excision followed by whole brain radiotherapy (WBRT) significantly improves survival compared with radiation alone. In one RCT, that survival benefit was greatest in patients with controlled extracranial disease. A third RCT, which included patients with poorer prognostic characteristics, did not demonstrate any significant benefit for the addition of surgery compared with radiation alone. A pooled analysis of reported data from the three trials showed no significant overall survival advantage for the surgery plus radiation therapy group; however, significant heterogeneity was detected between study results.

• One RCT of surgery plus WBRT compared with surgery alone demonstrated a significant reduction in the incidence of recurrent brain metastases favouring WBRT, although an overall survival advantage or prolonged maintenance of functional independence was not detected.

• One RCT comparing WBRT with SRS to WBRT alone reported a significant survival benefit for patients with single brain metastases who received WBRT with SRS boost.

• No RCTs were found that compared SRS to surgical resection. Preliminary evidence suggests that stereotactic radiosurgery provides similar median survivals to surgical resection in highly selected patients.
POTENTIAL HARMS

In the trials by Patchell et al and Mintz et al, surgical mortality, defined as death within 30 days following surgery, did not differ significantly from 30-day mortality in the whole brain radiotherapy (WBRT)-alone groups.

In the trial by Vecht et al, 30-day mortality was nine percent in the combined treatment group and zero percent in the WBRT-alone group; however, death within two months did not differ between groups.

Thirty-day morbidity was eight percent in the surgery plus WBRT group and 17 percent in the WBRT-alone group in one trial and did not differ between groups in another trial. Postoperative complications in the trial by Vecht et al included respiratory problems in four patients, intracerebral hemorrhage in one patient, infectious disease in three patients, and other complications in nine patients. Postoperative morbidity affected 13 patients, and those complications were serious in four patients. Complications of radiotherapy, including nausea, vomiting, and headache, did not differ between treatment groups (10 patients in the surgery plus WBRT group versus 9 patients in the WBRT-alone group). No significant difference in adverse effects was detected between groups in the Cochrane meta-analysis (overall risk [OR] 1.25 [95% confidence interval [CI] 0.68 to 2.66, p=0.39]).
Conclusions. The results of the evidence-based analysis demonstrated that there was insufficient information to establish standards of care. Data from the literature does, however, support a guideline stating that surgical resection accompanied by whole brain radiation therapy is associated with the best survival rate. Additional lower-quality evidence supports an option for management with radiosurgery.
Comfort  Safety  Ability  Productivity

<table>
<thead>
<tr>
<th>Monitor</th>
<th>Biopsy</th>
<th>Remove</th>
<th>Radiate</th>
<th>Chemo</th>
<th>Support</th>
</tr>
</thead>
</table>

**Gains**
- Labelling
- Cure
- Control
- Prevent
- Improve
- Restore
- Preserve
- Delay
- Enable
- Palliate

**Losses**
- Life
- Independence
- Autonomy
- Cognition
- Communication
- Comfort
- Income

**Costs**
- Pain
- Temporary loss of control
- Stress
- Fatigue
- Scar
- Occ ICU with ETT

**Risks**
- Bleeding
- Infection
- Incomplete removal
- Stroke
- Seizure
- MI
- DVT
- Resp illness

Comfort | Safety | Ability | Productivity
Gain, Loss, Cost, Risk
My own series of 36 solitary brain met cases treated surgically

- Ages 18 – 79: lung, breast, colon, kidney, melanoma, thyroid, endometrial, uncertain
- M/F = 19/17
- Karnofsky: 50 - 90
- Primary identified pre-op: 19/17
- Biopsy without removal: 6/36
- Craniotomy for removal: 30/36
- Supratentorial/infratentorial = 20/16
- Post op radiation: 32/36
Goals

• Confirm diagnosis: .................. 17/36

• Restore/improve function: ............... 27/36
  – Communication .................... 11/36
  – Cognition ..........................  6/36
  – Mobility............................. 17/36
  – Dexterity/ADL’s............... 15/36

• Prevent loss of function: ............... 9/36

• Relieve dangerous mass effect: ......... 8/36

• Prolong survival: .................... 26/36
Gains

• Confirm diagnosis: ..................17/17
• Improve function: ..................14/27
  – 9 same
  – 4 worse
• Prevent loss of function: ..........8/9
• Relieve dangerous mass effect...8/8
• Prolong survival....................?
• Possible cures: ....................5/36 @ 1 yr
Losses

<table>
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<tr>
<th>Condition</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Decline in function</td>
<td>4/36</td>
</tr>
<tr>
<td>Death in 30 days</td>
<td>1/36</td>
</tr>
<tr>
<td>Sepsis</td>
<td>5/36</td>
</tr>
<tr>
<td>DVT</td>
<td>4/36</td>
</tr>
<tr>
<td>DVT &amp; PE</td>
<td>1/36</td>
</tr>
<tr>
<td>Craniotomy infection</td>
<td>1/36</td>
</tr>
</tbody>
</table>

% Risks from these #’s:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>3%</td>
</tr>
<tr>
<td>Function loss</td>
<td>12%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>15%</td>
</tr>
<tr>
<td>DVT</td>
<td>12%</td>
</tr>
<tr>
<td>PE</td>
<td>3%</td>
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