LONG-TERM RISK OF MELANOMA-RELATED MORTALITY IN PATIENTS WITH UVEAL MELANOMA TREATED WITH PROTON BEAM THERAPY

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BACKGROUND

Long-term mortality data over 25 years are only available for patients with uveal melanoma who have undergone enucleation.
Jensen, 1982
- Cumulative mortality rate at 25 years after treatment was 60% (N=302)
- Metastases 23 years after treatment

Kujala, 2003
- Cumulative mortality rate at 25 years after treatment was 49% (N=289)
- Metastases 34 years after diagnosis
For conservative therapy, mortality data are only available through 12 years after treatment for patients in the COMS study

- I-125 radiotherapy
  - COMS, 2006
    ✓Cumulative mortality rate at 12 years after treatment was 21% (N=657)
• The purpose of this study was to determine long-term mortality in a large series of 3128 patients with uveal melanoma treated with proton therapy over a 30 year period
• We also evaluated patient and tumor characteristics in a small group of patients who survived more than 2 years after the development of metastasis
METHODS

Vital status was ascertained

• active surveillance
  – active patient follow-up at MEEI

• Social Security Death Index (SSDI)
  – free online service that uses data provided by Social Security Administration
METHODS

Cause of death was ascertained

• active surveillance
• National Death Index (NDI)
  – federal repository that houses data from death certificates provided by state bureaus
METHODS

Kaplan-Meier method was used to calculate cumulative rates of melanoma-related mortality
RESULTS

• Overall, 1472 deaths had occurred by the end of observation period.
• 623 (42.3%) of these deaths were due to melanoma metastasis.
Cumulative rates of deaths from melanoma

<table>
<thead>
<tr>
<th>Year post-rx</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>24.6 (22.4-25.9)</td>
</tr>
<tr>
<td>20</td>
<td>25.9 (23.6-27.4)</td>
</tr>
<tr>
<td>25</td>
<td>26.6 (24.1-28.2)</td>
</tr>
</tbody>
</table>

melanoma-related deaths

year after PBI
Longer-term survival after metastasis

Classified patients with “longer-term” survival after metastasis as

- those who lived more than two years after diagnosis of metastasis (n=43; 7.7%)
  - 12 patients (2.1%) lived more than 5 years after diagnosis of metastasis
  - longest survival time was 11.2 years
Comparison of Longer-term Survivors, by Site of Metastasis

<table>
<thead>
<tr>
<th>Site</th>
<th>&gt;2 yrs</th>
<th>P= .001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic</td>
<td>32/505 (6.3%)</td>
<td></td>
</tr>
<tr>
<td>Extra-hepatic</td>
<td>11/43 (24.4%)</td>
<td></td>
</tr>
</tbody>
</table>

- Only 6% of patients diagnosed with hepatic metastasis survived more than 2 years after diagnosis of metastasis
- In comparison, 24% of patients with extra-hepatic metastasis survived more than 2 years after diagnosis of metastasis
Comparison of Longer-term Survivors, by Site of Metastasis

<table>
<thead>
<tr>
<th>Site</th>
<th>&gt;5 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic</td>
<td>8/32</td>
</tr>
<tr>
<td>Extra-hepatic</td>
<td>4/11</td>
</tr>
</tbody>
</table>

• Of the 32 patients with hepatic metastasis surviving > 2 years, one-quarter survived more than 5 years after diagnosis compared to over one-third of the 11 patients with extra-hepatic metastasis.
Time to Metastasis Diagnosis

Median survival from malignant melanoma diagnosis to metastasis diagnosis

- Longer term survivors (> 2 yrs): 5 yrs
- Shorter term survivors (≤ 2 yrs): 3.4 yrs

P=.10
We compared tumor and patient characteristics known to predict mortality in patients surviving more than 2 years after metastasis diagnosis to patients with shorter survival.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>&gt; 2 yrs</th>
<th>&lt;= 2 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy Pigment (%)</td>
<td>53.5</td>
<td>49.2</td>
</tr>
<tr>
<td>Ciliary Body (%)</td>
<td>46.3</td>
<td>39.5</td>
</tr>
<tr>
<td>LTD (median, mm)</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>
Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>&gt;2 yrs</th>
<th>&lt;= 2 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms Dx (%)</td>
<td>93.0</td>
<td>84.1</td>
</tr>
<tr>
<td>Age (median, y)</td>
<td>56</td>
<td>62**</td>
</tr>
<tr>
<td>Light iris (%)</td>
<td>34.9</td>
<td>44.4</td>
</tr>
</tbody>
</table>

** P=.009
Treatment for Metastasis

Regarding treatment, more success has been demonstrated with surgery, which is often used when extra-hepatic metastasis develops.
CONCLUSIONS

• Cumulative mortality rate at 25 years after proton therapy is 27% compared to 50%-60% reported after enucleation
  – Most likely due to larger tumors treated by enucleation
CONCLUSIONS

• Patients continue to be at risk of death from melanoma more than 20 years after treatment
  – last observed death in this series was 22 years after treatment
CONCLUSIONS

• Younger age may be associated with longer-term survival after diagnosis of metastasis

• Diagnosis of metastasis in non-hepatic sites are associated with longer-term survival