Incidence, Symptomatology and Mortality of Spontaneous Intracerebral Hemorrhage in Oncologic Patients Presenting to the Emergency Department

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Disclosure of Commercial Relationships

• Adriana H. Wechsler, MD

• NO FINANCIAL COI TO DISCLOSE
Etiology of spontaneous intracerebral hemorrhage (sICH)

- **Hypertension** (most common)
- **Amyloid angiopathy** (rising incidence with aging population)
- Hemorrhagic ischemic stroke
- Aneurysm
- Arteriovenous malformation
- Venous angioma
- Dural venous sinus thrombosis
- Vasculitis
- Medications, e.g. oral anticoagulants
- Coagulopathy

- Hypertension and amyloid angiopathy combined account for 78-88% of cases of sICH in the general population
Incidence & Mortality of sICH - General Population

- By admission to US hospitals
  - 21 per 100 K person-years (1998-2008: 63,000)
  - 34% in-hospital mortality (1984-2008)
    - Rincon, Neurocrit Care, 2013
  - One month case fatality ratio 35%; one year case fatality ratio 59%
    -- Sacco, Stroke 2009

- From pooled worldwide studies
  - 25 per 100 K person-years
  - 40% median case fatality at 1 month
    -- van Asch, Lancet Neurology, 2010

- Of those who survive, only 12-39% achieve functional independence
sICH: Not just Fatal, Rapidly Fatal

- Of those who die, half do so within the first 48 hours
- Rapid hematoma expansion occurs within the first 4 hours

-Quereshi, Lancet Neurology, 2009
Incidence and Mortality of Spontaneous Intracerebral Hemorrhage in Patients with Cancer Presenting to the Emergency Department

Hyperacute Hematoma Expansion
What about the cancer patient???
Increasing the risk of sICH in patients with cancer

- Thrombocytopenia due to anti-neoplastic therapy
- Prior brain or head & neck irradiation
- Pro-thrombotic anti-neoplastic agents: e.g. Avastin
- Thrombocytopenia due to hematologic malignancy
- Anti-coagulation for VTE disease (very common in cancer)
- Brain malignancies
- Brain metastases
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MD Anderson Emergency Department

- 650 bed hospital
- 27,000 ED visits per year
- 73 patients/day
- 98% with cancer
- 51% admission rate
- 43% of inpatients thru ED
What about the patient with cancer?

- Retrospective cohort study
- 10-year period 2006-2016
- ICD-9 and ICD-10 codes

- 678 (0.33%) of all ED visits
- 0.79% of unique patients
Which Cancers? Which Symptoms? What Risk Factors?

• Melanoma, choriocarcinoma, thyroid cancer, RCC adrenal cell cancer most common metastases to bleed in the brain
  • Manybur, Neurology, 1977; Wakai, Neursurg, 1982

• Other primary tumors, such as lung, breast are less likely to cause sICH
  • Gerber, J Clin Oncol, 2006; Srivastava, J Thoac Oncol, 2009
Percentage of sICH by cancer type
Incidence and Mortality of Spontaneous Intracerebral Hemorrhage in Patients with Cancer Presenting to the Emergency Department

Incidence of sICH in ED by cancer type

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Number of patients</th>
<th>ICH (Incidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>77925 (100.0%)</td>
<td>614 (0.79%)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>7231 (8.78%)</td>
<td>131 (1.81%)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>2272 (2.76 %)</td>
<td>72 (3.17%)</td>
</tr>
<tr>
<td>Brain and spinal cord</td>
<td>2343 (2.85 %)</td>
<td>76 (3.24%)</td>
</tr>
<tr>
<td>Lung</td>
<td>7941 (9.64 %)</td>
<td>61 (0.77%)</td>
</tr>
<tr>
<td>Breast</td>
<td>9039 (10.98 %)</td>
<td>51 (0.56%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>13621 (16.54%)</td>
<td>47 (0.35%)</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>7415 (9.00 %)</td>
<td>43 (0.58%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>5541 (6.73%)</td>
<td>24 (0.43%)</td>
</tr>
<tr>
<td>Gynecological</td>
<td>5035 (6.11%)</td>
<td>19 (0.38%)</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>5823 (7.07%)</td>
<td>27 (0.46%)</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2877 (3.49%)</td>
<td>13 (0.45%)</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
<td>1792 (2.18%)</td>
<td>12 (0.67%)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1192 (1.45%)</td>
<td>9 (0.76%)</td>
</tr>
<tr>
<td>Other cancer types</td>
<td>5803 (7.05%)</td>
<td>29 (0.50%)</td>
</tr>
</tbody>
</table>

Three most common overall:
1. Brain & spinal cord
2. Melanoma
3. Leukemia

Most common solid tumors:
1. Melanoma
2. Lung
3. Thyroid
4. Breast
Most common complaints to our Cancer Center

- Fever: 15.9%
- Abdominal pain: 13.2%
- Pain: 11.6%
- Shortness of breath: 7.6%
- Multiple complaints: 6.5%
- Nausea/vomiting: 5%
- Weakness/fatigue: 5%
- Chest pain: 3.6%
- Back pain: 3.5%
- Headache: 3.1%
- Altered mental status: 0%

- Courtesy of Dr. Terry Rice
sICH: Presenting Symptoms

- Syncope: 1.1%
- Speech problems: 1.8%
- Vision problems: 2.8%
- Seizure: 7%
- Weakness / Fatigue: 7.2%
- Nausea / vomiting: 14.2%
- AMS / confusion: 19.4%
- Headache: 25.9%
Mortality in patients presenting to the ED with sICH

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>7 days mortality</th>
<th>14 days mortality</th>
<th>30 days mortality</th>
<th>One year mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>73 (11.89 %)</td>
<td>101 (16.45%)</td>
<td>149 (24.27%)</td>
<td>389 (63.36%)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>25 (19.08%)</td>
<td>33 (25.19%)</td>
<td>46 (35.11%)</td>
<td>86 (65.65%)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>8 (11.11%)</td>
<td>8 (11.11%)</td>
<td>18 (25%)</td>
<td>57 (79.17%)</td>
</tr>
<tr>
<td>Brain and spinal cord</td>
<td>5 (6.58%)</td>
<td>6 (7.89%)</td>
<td>11 (14.47%)</td>
<td>39 (51.32%)</td>
</tr>
<tr>
<td>Lung</td>
<td>5 (8.2%)</td>
<td>10 (16.39%)</td>
<td>13 (21.31%)</td>
<td>48 (78.69%)</td>
</tr>
<tr>
<td>Breast</td>
<td>6 (11.76%)</td>
<td>9 (17.65%)</td>
<td>13 (25.49%)</td>
<td>28 (54.9%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>7 (14.89%)</td>
<td>10 (21.28%)</td>
<td>12 (25.53%)</td>
<td>30 (63.83%)</td>
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<td>7 (16.28%)</td>
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<tr>
<td>Lymphoma</td>
<td>1 (4.17%)</td>
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<td>3 (12.5%)</td>
<td>16 (66.67%)</td>
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<td>Gynecological</td>
<td>0 (0.0%)</td>
<td>2 (10.53%)</td>
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<td>Head and Neck</td>
<td>2 (7.41%)</td>
<td>4 (14.81%)</td>
<td>5 (18.52%)</td>
<td>15 (55.56%)</td>
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<td>Sarcoma</td>
<td>1 (7.69%)</td>
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<td>2 (15.38%)</td>
<td>8 (61.54%)</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
<td>4 (33.33%)</td>
<td>6 (50%)</td>
<td>8 (66.67%)</td>
<td>9 (75%)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0 (0.0%)</td>
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<td>1(11.11%)</td>
<td>5 (55.56%)</td>
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<td>Other cancer types</td>
<td>4 (13.79%)</td>
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<td>5 (17.24%)</td>
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sICH-related mortality in solid versus liquid tumors
one month p<0.001; one year p=0.377

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Why this study?

• It is assumed that cancer patients have a higher incidence and higher mortality from ICH due to their increased risk factors: namely, coagulopathy, thrombocytopenia, brain metastases and prior brain radiation

• Nihilistic approach: Over 68% of patients with ICH dying within one month had been made DNR, cause of death was withdrawal of care

• Are these assumptions correct?

• How aggressive should we be in managing these patients; how can we rapidly identify them

• The first fours following a bleed, the emergency department hours, are the golden hours to intervene in limiting hematoma expansion
Spontaneous ICH in General Population: DEADLY

- One month case fatality ratio is 34.6% - Sacco, Stroke, 2009
- One year case fatality ratio is 59% - Sacco, Stroke, 2009

Spontaneous ICH in Cancer Population: Initially LESS DEADLY

- 7 day mortality 12%
- 30 day mortality 24.7%
What can we conclude?

- Spontaneous ICH is a rare presentation, even in cancer patients. (.33%)
- Suspicion for ICH should be highest in patients with CNS tumors, melanoma and leukemia (solid tumors: melanoma, lung, thyroid, breast)
- The mortality at 1 month is not higher in cancer patients; more than three quarters live beyond the first month (except for liquid tumors)
- The mortality at 1 year may be higher than in the general population, but it cannot necessarily be attributed to the sICH
- Quantifying the incidence & mortality by cancer type can help guide diagnostic and therapeutic efforts when sICH is suspected.
Limitations

• All-cause mortality vs. case fatality
• Incidence vs. prevalence
• Denominator is not entire cancer population at risk
• Comparison studies: differing methodologies, populations, time frames
• Are we missing bleeds that were asymptomatic? or where diagnostic imaging was not obtained due to low suspicion by the clinician?

Further Study

• Are there predictive risk factors aside from symptoms
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