55th annual diagnostic slide session
Case 2014-4

Submitted by
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I have no disclosures
Clinical history – Dec 2012

• 39 year-old female suffered a seizure while doing Christmas shopping
Intraoperative diagnosis

- Malignant neoplasm with rhabdoid features
Differential diagnosis?
FISH

• EGFR
  – Overall NOT amplified (ratio = 1.53)
  – Amplified in FEW cells

• P16
  – 11.7% homozygous deletion

• 1p and 19q
  – No deletions
Molecular anatomic pathology testing

- *IDH1* and *IDH2*
  - NOT identified
- *MGMT* promoter methylation
  - NOT identified
Final diagnosis – Dec 2012

• Glioblastoma, WHO grade IV
  – Rhabdoid/epithelioid morphology
• E-GBM: superficial, supratentorial tumors, monomorphic cells

• R-GBM: rhabdoid cells in an otherwise “classic” GBM
Results

• 8 E-GBM and 2 R-GBM

• R-GBMs show focal loss of INI and show monosomy 22

• E-GBMs do not
Epithelioid GBMs Show a High Percentage of BRAF V600E Mutation

Bette Kay Kleinschmidt-DeMasters, MD,†‡ Dara L. Aisner, MD, PhD,* Diane K. Birks, MS,†§ and Nicholas K. Foreman, MD§
## RESULTS

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Cases</th>
<th>BRAF V600E</th>
<th>INI IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-GBM</td>
<td>13</td>
<td>7/13</td>
<td>No loss</td>
</tr>
<tr>
<td>GC-GBM</td>
<td>9</td>
<td>0/9</td>
<td>Not done</td>
</tr>
<tr>
<td>R-GBM</td>
<td>2</td>
<td>0/2</td>
<td>Focal loss</td>
</tr>
</tbody>
</table>
E-GBM histology
6 patients
- Median age: 7.6 years
- 3/6 (50%) harbored *BRAF* V600E mutation
Final diagnosis

- POSITIVE for BRAF V600E mutation
- Epithelioid glioblastoma, WHO grade IV
Clinical course

- 1/13
  - Temozolomide and radiation therapy
- 3/13 – First recurrence
  - Cyberknife treatment to new temporal lobe lesion
- 6/13 – Second recurrence
  - Multifocal enhancing disease progression.
  - Patient begins Avastin therapy
- 11/13 – Maximally symptomatic
  - Discussions for hospice care
December 2013

• Patient is finally approved for vemurafenib (Zelboraf), a BRAF inhibitor.
December 2013

• Within two weeks, she reports resolution of headaches, improvement of speech and memory.
• She celebrates Christmas with her husband and two kids.
Complete clinical regression of a BRAF V600E-mutant pediatric glioblastoma multiforme after BRAF inhibitor therapy

Giles W Robinson¹, Brent A Orr² and Amar Gajjar¹
Conclusion

• Epithelioid GBM with *BRAF* V600E mutation in an adult that responded dramatically to a BRAF inhibitor (vemurafenib)
Thank you!