Insulin-like growth factor 2 in paediatric gliomas: expression, intracellular localization and association with clinical outcome

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Background

- The insulin-like growth factors (IGFs) system are known to play an important role in both normal and neoplastic growth.
- IGF2 overexpression has been identified in several cancers and was significantly related to the initiation and progression of cancers.
- Gliomas are the most frequent solid tumours in paediatric patients.

Aim

To characterize the expression and intracellular localization of IGF-2 in a large cohort of paediatric gliomas, and its association with clinical outcome.

Methods

- Design: Prospective study of gliomas from paediatric patients that underwent surgery in our Hospital between August 2007 and April 2018.
- Gliomas were classified as low (LGG) and high grade (HGG) according to "2016 WHO classification of central nervous system tumours".

Immunohistochemistry (IHC): IGF-2 intracellular expression and localization

- Using IGF2 antibody (Abcam Ab9574) in fixed tumour samples.
- Evaluated independently by two pathologists under optic microscope.
- The results were classified according to IGF2 labeling in:
  - Negative
  - Positive: Cytoplasmatic
  - Cytoplasmatic/nuclear

Quantitation PCR (qPCR): IGF2 gene expression

- In those tumours where fresh sample were available.
- Follow-up since surgery until August 2019.
- Clinical outcome: - Dead
  - Alive: Without tumour
  - With tumour

Total gliomas studied by IHC

<table>
<thead>
<tr>
<th>Sex (F/M)</th>
<th>Low grade n=82</th>
<th>High grade n=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>F: 42 / M: 57</td>
<td>8.24 ± 4.87 years (0.37 – 18.32)</td>
<td>4.66 ± 2.21 years (0.27 – 11.81)</td>
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<tr>
<td>Supratentorial n=48</td>
<td>Infratentorial n=46</td>
<td>Intramedullary n=5</td>
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<tr>
<td>Alive without tumour n=32</td>
<td>Alive with tumour n=35</td>
<td>Dead n=17</td>
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Total gliomas studied by qPCR

<table>
<thead>
<tr>
<th>Sex (F/M)</th>
<th>Low grade n=37</th>
<th>High grade n=9</th>
</tr>
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<tbody>
<tr>
<td>F: 20 / M: 26</td>
<td>9.03 ± 4.82 years (0.87 – 18.32)</td>
<td>5.05 ± 1.43 years (1.65 – 7.22)</td>
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<tr>
<td>Supratentorial n=22</td>
<td>Infratentorial n=23</td>
<td>Intramedullary n=1</td>
</tr>
<tr>
<td>Alive without tumour n=21</td>
<td>Alive with tumour n=14</td>
<td>Dead n=6</td>
</tr>
</tbody>
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Staining | n | LGG | HGG |
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Negative</td>
<td>11</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Citoplasmatic</td>
<td>21</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td>Citoplasmatic and nuclear</td>
<td>66</td>
<td>55</td>
<td>11</td>
</tr>
</tbody>
</table>

No association was found between IGF-2 expression and subcellular localization with tumour grade, neither with clinical outcome.

Results

Conclusions:

- We are reporting the second tumour type presenting nuclear IGF2 intracellular localization and the first in the paediatric patients.
- In contrast with results found in other tumours, IGF-2 intracellular localization performed by IHC does not correlate with clinical outcome in paediatric gliomas. However, the association between initial elevated IGF-2 mRNA levels with clinical outcome in low grade gliomas suggest a role for IGF2 in the biological behavior of these tumours.