Adenomas of the Pituitary Gland: Size Matters

Experience of a Neuropathology Referral Center

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Pituitary Gland Adenomas
Pituitary Gland Adenomas

- Adenomas constitute 10-15% of all intracranial neoplasms.
- The vast majority are sporadic
- They are clonal but no specific chromosomal alterations are characteristic
- They may produce anterior pituitary hormones, resulting in elevated serum levels and endocrinopathies (functional adenoma)
- In cases of non-functional adenomas, mass effects and hypopituitarism predominate
Pituitary Gland Adenomas

- They are classified according to:
  - Functional classification
    - Endocrine hyperfunction
    - Clinically nonfunctional
    - Functional status indetermined
  - Size
    - Microadenoma: ≤10mm
    - Macroadenoma: >10mm
    - Giant adenomas; >40mm
  - Growth pattern
    - Expansive
    - Invasive
Pituitary Gland Adenomas

- They are classified according to:
  - Histology
    - Adenoma (Benign)
    - Atypical Adenoma
      - Cytological Atypia
      - Invasion
      - Ki-67 index >3%
      - Nuclear staining for p53
      - No metastasis
  - Carcinoma
    - Atypical characteristics
    - Metastasis
Objective

Our aim was to assess the **prognostic value** of histologic and non-histologic characteristics of Pituitary Gland Adenomas (PGA) in our population, specially in terms of tumor recurrence.
Methods

- Patients submitted to surgery for PGA, over a 10 year period (2006-2015), were retrospectively identified.
- Clinical, imagiologic and histologic data were reviewed, based on clinical records and histologic slide revision.
Methods

**Parameters** assessed included:
- Epidemiologic patient data
- Presence of blood mediators (functional adenoma)
- Tumor size on Magnetic Resonance Imaging (MRI)
- Evidence of invasion on MRI
- Histologic type (morphologic and immunohistochemical analysis)
- Cytological atypia
- Mitotic rate
- Presence of residual disease on follow-up MRI
- Patient follow-up period
- Tumor relapse
- Subsequent need of surgery
Methods

- Logistic regression model was used to estimate the relative risk of tumor relapse and need for subsequent surgery.
Results

- Among the 188 PGA identified, **165 cases** were evaluated.
- Sex: 86 male/79 female
- **Tumor size**
  - Max: 49 mm
  - Min: 4 mm
  - Average: 21 mm
- Microadenomas (≤10mm): 30
- Macroadenomas:
  - 10 – 20 mm: 54
  - 20 – 40 mm: 76
  - >40mm: 5
- Presence of invasion on MRI: 50
Results

<table>
<thead>
<tr>
<th>Residual Tumor (follow-up MIR)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross total resection</td>
<td>62</td>
</tr>
<tr>
<td>Residual tumor</td>
<td>103</td>
</tr>
</tbody>
</table>
Results

Histology

- **Cytological atypia**: 10 cases
- **No** cases with characteristics for **carcinoma** were identified
Results

- Average follow-up period was 39 months.
  - (min: 3 months / max: 80 months)

<table>
<thead>
<tr>
<th>Tumor Relapse</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No Relapse</td>
<td>146</td>
</tr>
<tr>
<td>Relapse</td>
<td>19</td>
</tr>
</tbody>
</table>
Results

- Presence of **invasion** and **tumor relapse** were significantly associated with **larger tumors** when compared with smaller ones (p<0,001 and p=0,015 respectively).

- **Tumor size** proved to be an independent prognostic factor in predicting tumor relapse (Odds Ratio=2,53, 95% confidence interval=1,09-5,82).
Problems

- No immunohistochemistry for Ki-67 (MIB-1 proliferative index) or p53 was applied to any of our samples
  - It is not a current procedure at our institution:
    - Lack of evidence in scientific literature
    - Unproven cost-benefit
  - The presence of atypia and mitosis is always stated in the report
    - Definition of “Atypical adenoma”??
- Most samples received are partial representations of the tumor mass.
- Representation bias: tertiary neuropathology referral center.
Conclusions

- Our findings corroborate the results published in scientific literature.

- Presence of **cytological atypia and invasion on MRI** are related with residual tumor and relapse, but **tumor size** was the most important factor in predicting the outcome of our patients.
Conclusions

- Although invasiveness is usually related with MIB-1 index >3%, behavior in pituitary adenomas can not be predicted based solely on histologic features.

- There are still conflicting results and recommendations about the utility for immunohistochemistry assessment of MIB-1 and p53 – they do not correlate significantly with invasiveness or progression in many studies.
KI-67 (MIB-1 index), although controversial, is repeatedly referred as means of evaluating tumor aggressiveness.

Should we try to evaluate it in our population?
References


