Challenging cases in endocrine / neuroendocrine pathology
Case 1
Jorge Pinheiro MD
Challenging cases in endocrine / neuroendocrine pathology: case 1

- 30 month-old male child

- Past history
  - Term pregnancy, watched, uneventful
  - Elective caesarean section without resuscitation.
  - Birth weight: 3100g
  - Neonatal period: uneventful
  - Normal development

- Family history
  - Unremarkable
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- 30 month-old male child
- Main complains
  - Admitted in hospital for right hemiparesis with insidious onset in the last 2 weeks
    - Gait claudication
    - Right to left hand shift
- Physical examination
  - Decreased right muscle strength and tonus
  - Right hyperreflexia
  - Babinsky sign bilaterally
Brain surgery was performed with partial resection of tumor.

In the surgical report…

“Left pterional craniectomy”

“(…) Identification of the carotid, posterior cerebral and choroidal arteries and the oculomotor nerve, being the tumour medial to these structures.”
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Small irregular fragments of tissue, between 0.8 and 0.3cm in largest dimension
Synaptophysin
Chromogranin A
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Our diagnostic proposal:
Giant ectopic suprasellar pituitary neuroendocrine tumour
Follow up

- He was submitted to adjuvant local therapy
- Totalization of resection was performed
- The patient is alive, with no evidence of disease, after 8 years of follow-up
A challenging case because...

1. Pituitary NET in this age group are exceedingly rare
2. Most pediatric pituitary NET are functional
3. A rarely reported ectopic location
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A challenging case because...

1. Pituitary NET in this age group are exceedingly rare

Figure 2 Age-incidence curves for pituitary adenomas, based on a total of 3239 pituitary tumor patients identified from the Family-Cancer Database.

Hemminki (2007): Endocrine-Related Cancer. 14 103–109
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According to most series, only 2-6% of pituitary adenomas occur during childhood and adolescence.

Pituitary adenomas encompass less than 3% of the supratentorial tumors in children and adolescents.

Age incidence curve of pituitary adenomas in pediatric age

Most pediatric pituitary adenomas are functional adenomas

- According most series, only 5-10% of pituitary adenomas are non-functional.

Macroadenomas are not as frequent as in the adult population

Meta-analysis of pituitary adenoma subtypes in reported *surgical* series of paediatric pituitary adenomas

- ACTH-secreting: 7%
- Prolactin-secreting: 36%
- GH-secreting: 12%
- Plurihormonal: 3%
- Non functional: 42%

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Frequency of pituitary adenomas by age.

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Nearly all symptomatic endocrine-inactive macroadenomas have extended beyond the confines of an expanded sella turcica, the most common pattern of extrasellar growth being directly upward into the suprasellar space.
Pituitary blastoma

Bernd W. Scheithauer • Kalman Kovacs • Eva Horvath • D. S. Kim • Robert Y. Osamura • Rhett P. Ketterling • Ricardo V. Lloyd • O. L. Kim

Pituitary blastoma: a pathognomonic feature of germ-line DICER1 mutations

Leanne de Kock • Nelly Sabbaghia John R. Priest • William D. Foulkes
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Pituitary blastoma

Bernd W. Scheithauer · Kalman Kovacs · Eva Horvath · D. S. Kim · Robert Y. Osamura · Rhett P. Ketterling · Ricardo V. Lloyd · O. L. Kim
### Table 1 Literature and case summary

<table>
<thead>
<tr>
<th>Ref</th>
<th>Age/sex</th>
<th>Endocrine function</th>
<th>Tumor size (cm)</th>
<th>Resection</th>
<th>Mitoses/ MIB-1</th>
<th>Recurrence</th>
<th>Adjuvant therapy</th>
<th>Follow-up</th>
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<tbody>
<tr>
<td>[1]</td>
<td>13-month F</td>
<td>Cushing + DI</td>
<td>3.5</td>
<td>ST</td>
<td>Rare/1.5%</td>
<td>NA</td>
<td>NA</td>
<td>Postop DOD</td>
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<tr>
<td>Present case 1</td>
<td>9-month M</td>
<td>Cushing</td>
<td>3 × 2.3 × 1.6</td>
<td>ST</td>
<td>3/15–50% (focal)</td>
<td>No</td>
<td>Polychemo Rx</td>
<td>Alive with disease at 6 mo</td>
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<td>Present case 2</td>
<td>13-month F</td>
<td>None</td>
<td>2.1 × 1.8</td>
<td>ST</td>
<td>16/60%</td>
<td>Yes</td>
<td>Temozolomide</td>
<td>Alive with disease at 84 mo</td>
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<td>Present case 3</td>
<td>24-month F</td>
<td>Cortisol ↑</td>
<td>4</td>
<td>ST</td>
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<td>A&amp;W</td>
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<td>[27]</td>
<td>8-month M</td>
<td>Cushing</td>
<td>12 × 8 × 5</td>
<td>ST</td>
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<td>Unstated</td>
<td>Unstated</td>
<td>Postop DOD</td>
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<tr>
<td>[28]</td>
<td>6-month M</td>
<td>Cushing</td>
<td>Sizeable</td>
<td>GT</td>
<td>Unstated</td>
<td>Unstated</td>
<td>No</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA not applicable, DI diabetes insipidus, DOD dead of disease, ST subtotal, GT gross total
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1. Beginning formation of Rathke’s pouch and infundibular process

2. Neck of Rathke’s pouch constricted by growth of mesoderm

3. Rathke’s pouch “pinched off”

4. Pinched-off segment conforms to neural process, forming pars distalis, pars intermedia, and pars tuberalis

5. Pars tuberalis encircles infundibular stalk (lateral surface view)

6. Mature form

- Infundibular process
- Brain
- Oral ectoderm
- Rathke’s pouch
- Stomodeum
- Mesoderm
- Sphenoid sinus
- Median eminence
- Pars tuberalis
- Infundibulum
- Pars nervosa
- Pars intermedia
- Pars distalis (pars glandularis)
- Cleft
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Ectopic pituitary adenomas (reported locations):

- sphenoid sinus (*)
- clivus (+)
- nasal cavity (#)
- cavernous sinus,
- parasellar region
- sphenoid wing

Hypothetic origin:
neoplastic proliferation of pituitary rests along the embryological path of the pituitary development
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Ectopic pituitary adenomas (reported locations):

- Suprasellar
- Third ventricle

Hypothetic origin: neoplastic proliferation of ectopic suprasellar peri-infundibular pituitary cells.
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Suprasellar peri-infundibular ectopic adenohypophysis in fetal and adult brains

Akira Hori, M.D.

Department of Neuropathology, University of Goettingen, Goettingen, Federal Republic of Germany

Ectopic anterior pituitary cells, identified by histological, electron microscopic, and immunohistochemical methods, were consistently found in the leptomeninges of the suprasellar peri-infundibular region of fetal brains. The cell groups were not in continuity with the pars tuberalis of the adenohypophysis. Suprasellar peri-infundibular ectopic pituitary cells, which showed no neoplastic character, were found in 15 of 20 “normal” adult brains that were similarly examined. This finding sheds new light on the possible origin of intracranial ectopic pituitary adenomas.
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Kleinschmidt-DeMasters BK (1990): J Neurosurgery, 72(1)
## Challenging cases in endocrine/neuroendocrine pathology: case 1

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Age(years)/Gender</th>
<th>Symptoms</th>
<th>Hormone secretion</th>
</tr>
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<tbody>
<tr>
<td>Rothman et al., 1976</td>
<td>15/M</td>
<td>Seizure, headache</td>
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<tr>
<td>Hamada et al., 1990</td>
<td>53/F</td>
<td>Visual disturbance</td>
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<td>Iwai et al., 1990</td>
<td>26/M</td>
<td>Headache, disorientation, choked disc</td>
<td>prolactin</td>
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<tr>
<td>Kleinschmidt-DeMasters, 1990</td>
<td>47/M</td>
<td>Visual disturbance, headache</td>
<td>LH</td>
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<tr>
<td>Matsumura et al., 1990</td>
<td>71/M</td>
<td>Dizziness</td>
<td>ACTH</td>
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<tr>
<td>Tamaki et al., 1991</td>
<td>56/M</td>
<td>Dizziness, N/V, diplopia</td>
<td>prolactin</td>
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<td>Luk et al., 1992</td>
<td>34/F</td>
<td>DI, amenorrhea</td>
<td>prolactin</td>
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<tr>
<td>Lindboe et al., 1993</td>
<td>34/F</td>
<td>Amenorrhea, headache, visual disturbances</td>
<td>ACTH/TSH</td>
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<td>Tal, 1993</td>
<td>32/F</td>
<td>Cushing's syndrome</td>
<td>ACTH</td>
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<tr>
<td>Dyer et al., 1994</td>
<td>20/F</td>
<td>Amenorrhea, galactorrhea</td>
<td>prolactin</td>
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<tr>
<td>Dyer et al., 1994</td>
<td>13/M</td>
<td>Cushing's syndrome</td>
<td>ACTH</td>
</tr>
<tr>
<td>Dyer et al., 1994</td>
<td>14/F</td>
<td>Cushing's syndrome</td>
<td>ACTH</td>
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<tr>
<td>Dyer et al., 1994</td>
<td>22/M</td>
<td>Nelson's syndrome</td>
<td>ACTH</td>
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<tr>
<td>Kohno et al., 1994</td>
<td>33/F</td>
<td>Visual disturbance</td>
<td>No</td>
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<tr>
<td>Tanaka et al., 1994</td>
<td>57/M</td>
<td>Bitemporal hemianopsia</td>
<td>No</td>
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<tr>
<td>Akimoto et al., 1995</td>
<td>68/M</td>
<td>Memory/gait/incontinence</td>
<td>No</td>
</tr>
</tbody>
</table>
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<th>Hormone secretion</th>
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</thead>
<tbody>
<tr>
<td>Takahata et al., 1995</td>
<td>17/F</td>
<td>Cushing's syndrome</td>
<td>ACTH</td>
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<td>Nagatani et al., 1997</td>
<td>61/F</td>
<td>Visual disturbance</td>
<td>Prolactin</td>
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<td>Hou et al., 2002</td>
<td>11/M</td>
<td>Cushing's syndrome</td>
<td>ACTH</td>
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<tr>
<td>Ueda et al, 2003</td>
<td>21/M</td>
<td>Visual disturbance, hyperprolactinemia</td>
<td>Prolactin</td>
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<tr>
<td>Peker et al, 2005</td>
<td>37/F</td>
<td>Menstrual disregulation and visual disturbance</td>
<td>Prolactin</td>
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<td>Dam-Hieu et al, 2007</td>
<td>20/F</td>
<td>Cushing's syndrome</td>
<td>ACTH</td>
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<td>Dam-Hieu et al, 2007</td>
<td>41/F</td>
<td>Cushing's syndrome</td>
<td>ACTH</td>
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<tr>
<td>Guerrero et al, 2007</td>
<td>31/M</td>
<td>Chronic headache, acromegaly</td>
<td>GH</td>
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<td>So et al, 2008</td>
<td>49/M</td>
<td>Headache</td>
<td>No</td>
</tr>
<tr>
<td>Mizutani et al., 2009</td>
<td>52/F</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Kinoshita et al, 2012</td>
<td>59/F</td>
<td>Chronic headache</td>
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<tr>
<td>Fuminari et al, 2015</td>
<td>61/M</td>
<td>Visual disturbance</td>
<td>Prolactin</td>
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<tr>
<td>Wang et al., 2016</td>
<td>46/M</td>
<td>Hyperthyroidism/Visual disturbance</td>
<td>TSH</td>
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<td>Zhou et al. 2017</td>
<td>19/M</td>
<td>Reduced libido/Visual disturbance</td>
<td>Prolactin</td>
</tr>
<tr>
<td>Agely et al., 2019</td>
<td>48/F</td>
<td>Cushing's syndrome</td>
<td>ACTH</td>
</tr>
</tbody>
</table>
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Suprasellar ectopic pituitary adenoma

Hormone Secretion

- ACTH: 34%
- Prolactin: 27%
- None: 27%
- GH: 6%
- TSH: 3%
- FSH/LH: 3%

Gender Distribution:
- Male: 48%
- Female: 52%
Take-home messages

Pediatric pituitary adenomas are uncommon, and in pre-pubertal children exceedingly rare

Not all pituitary adenomas are in the sella turca

- Ectopic pituitary adenomas can occur in the clivus/sphenoidal sinus or in suprasellar location.

Remember the newly described pituitary blastoma