15 month-old female with a cystic brain lesion

Magdalena Dumin, MD
Pediatric Endocrinology Fellow
University of Chicago
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Chief Complaint

- 15 month-old female admitted to PICU for concern for seizure and found to have a cystic focus on brain MRI consistent with Rathke cleft cyst.

- Endocrine consulted for hypopituitarism evaluation.
History of Present Illness

11/5:
- Multiple episodes of emesis and elevated temperature to 99F
- Seen at OSH ER and discharged home

11/7:
- Noted to have eye rolling and deviation, BL upper extremity stiffening, head shaking
- OSH ED:
  - Na 133, bicarb 15, AG 22, BG 66, AST 56, ALT 33
  - UA: SG 1.015, neg glc, ketones 150 mg/dL
  - CBC: WBC 7.7, 69% segs
Transferred to Comer PICU

LP: 0 WBC, 1 RBC, glc 64, protein 10, no cells or organisms, no growth.

CMP: Na 138, bicarb 21, AG 13, BG 103, AST 34, ALT 23

Blood cx negative

Enterovirus and HSV PCR negative

Urine tox screen negative

Neurology consulted

11/9: EEG without epileptic abnormalities
HPI cont’d

11/10:

MRI:

- T2 hyperintense, T1 hypointense cystic appearing focus between anterior and posterior pituitary lobes, 8 mm x 7 mm x 4 mm. Differential diagnosis most likely consistent with Rathke cleft cyst. Craniopharyngioma, cystic pituitary adenoma, and arachnoid cyst unlikely.

- There may be BL congenital malrotation of the hippocampal formations. Repeat MRI at 2-3 yo recommended.

- Endocrine consulted.
History

Past Medical History:
- FT infant.
- Previously healthy.

Developmental History:
- Age-appropriate.
- Trips frequently.

Allergies: none

Medications: none

Family History:
- Parents with asthma in childhood, resolved.
- Mother: PCOS.
- MGM: breast CA, ovarian cysts, hyperthyroidism.
- PGM: hyperthyroidism.
- Great-PGM: T2DM

Social History:
- Lives with parents and dog.
- No daycare.
Review of Systems

- Constitutional: neg for chills, diaphoresis, activity/appetite change, fatigue, weight change. + mild fever.
- HENT: neg for congestion, rhinorrhea, hearing changes.
- Eyes: + esotropia.
- Resp: neg for SOB. + cough.
- CV: neg for chest pain, palpiations.
- GI: neg for abd pain. + vomiting, diarrhea, constipation.
- Endocrine: neg for heat/cold intolerance, polydipsia.
- GU: neg for polyuria.
- Musc: neg for edema. + frequent tripping.
- Skin: neg for rash, dry skin. + cyanosis.
- Neuro: neg for tremors, weakness. + seizure.
- Heme: neg for easy bruising/bleeding.
- Psych/Beh: neg for sleep disturbance, irritability.
Physical Exam

- T 36°C, BP 73/41, HR 110, Length 78 cm (54%), Wt 11.6 kg (93%), BSA 0.5 m²
- Constitutional: active, well-developed.
- HENT: AF closed, no midline defects, MMM, OP clear
- Eyes: EOM intact, PERRLA
- Neck: normal ROM, supple, no adenopathy, thyroid nonpalpable
- CV: RRR, no murmur, 2+ pulses
- Resp: CTAB, no distress/retractions
- GI: S/NT/ND, normal bowel sounds
- GU: Tanner 1 for PH and breasts, no AH
- Musc: normal ROM, no edema
- Neuro: alert, normal muscle tone, 2+ DTRs
- Skin: no rash, cyanosis, pallor
Next steps in evaluation?
Rathke cleft cyst

- Pituitary gland:
  - Rathke pouch -> anterior lobe
  - Neuroectoderm -> posterior lobe
- Remnant of the Rathke pouch
- Well-defined, non-enhancing midline cyst within sella
- Asymptomatic vs symptomatic
  - Uncommon in childhood and adolescence
  - Compression -> visual disturbance, headache, endocrine defects

Rathke cleft cyst. Radiopaedia.org.
Rathke Cleft Cyst

- Preoperative hypopituitarism: 38-81%
  - GH deficiency: 4-66%
  - Corticotroph dysfunction: 6-46%
  - Hypothyroidism: 39%
  - Hyperprolactinemia: 18-39%
  - DI: 0-25%
- Gonadotropin deficiency versus central precocious puberty

Differential Diagnosis

- Craniopharyngioma
- Cystic pituitary adenoma
- Arachnoid cyst
- Epidermoid cyst
- Teratoma

Rathke cleft cyst. Radiopaedia.org.
Labs

- Adrenal:
  - ACTH 19.3 pg/mL
  - Cortisol 20.9 mcg/dL

- Thyroid:
  - FT4 1.37 ng/dL
  - TSH 3.32 mcU/mL

- Growth:
  - IGF-1 71 ng/mL
  - IGF-BP3 4.1 ug/mL

- Gonadotropins:
  - FSH 2.4 mIU/mL
  - LH <0.1 mIU/mL

- Estradiol <10 pg/mL

- Prolactin 16.75 ng/mL

- Reference Ranges:
  - ACTH 6-48 pg/mL
  - IGF-1 56-144 ng/mL
  - IGF-BP3 0.8-3.0 ug/mL
  - FSH 1.0-4.2 mIU/mL
  - LH 0.02-0.3 mIU/mL
  - Estradiol <15 pg/mL
  - Prolactin 3-24 ng/mL
Clinical Questions

- What are the risk factors for hypopituitarism in patients with RCC?
- What are the clinical outcomes of patients with incidental RCC?
- What are the endocrine indications for surgery in patients with RCC?
Risk factors for pituitary dysfunction

Table 3. Changes in Pituitary Dysfunction from Before to After Surgical Treatment

| Pituitary hormone | At presentation (N=15) (%) | Postoperative state | | | |
|-------------------|-----------------------------|---------------------|-----------------|-----------------|-----------------|-----------------|
|                   | Improved (%) †              | Persistent (%) †    | New onset (%)   |
| GH deficiency     | 3 (20.0)*                   | 0 (0.0)             | 3 (100.0)       | 4 (26.7)         |
| TSH deficiency    | 6 (40.0)*                   | 0 (0.0)             | 6 (100.0)       | 2 (13.3)         |
| ACTH deficiency   | 7 (46.7)*                   | 3 (42.9)            | 4 (57.1)        | 5 (33.3)         |
| LH/FSH deficiency | 2 (13.4)                    | 0 (0.0)             | 2 (100.0)       | 4 (26.7)         |
| Hyperprolactinemia| 3 (20.0)                    | 3 (100.0)           | 0 (0.0)         | 0 (0.0)          |
| Diabetes insipidus| 6 (40.0)                    | 0 (0.0)             | 6 (100.0)       | 3 (20.0)         |

*These are suggestive hormone insufficiency, not confirmed hormone provocation test.
†The results are on the basis of counts at presentation.

Table 5. Factors Reflecting Pituitary Dysfunction in Patients with Rathke’s Cleft Cysts

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P value</td>
<td>R²</td>
</tr>
<tr>
<td>Symptom &amp; Sings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>0.136</td>
<td>0.149</td>
</tr>
<tr>
<td>Visual disturbance</td>
<td>0.021</td>
<td>0.168</td>
</tr>
<tr>
<td>General weakness</td>
<td>0.010</td>
<td>0.311</td>
</tr>
<tr>
<td>Brain MRI findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyst size</td>
<td>0.282</td>
<td>0.145</td>
</tr>
<tr>
<td>Cyst shape</td>
<td>0.696</td>
<td>0.001</td>
</tr>
<tr>
<td>Cyst location</td>
<td>0.002</td>
<td>0.240</td>
</tr>
<tr>
<td>T1-weighted</td>
<td>0.282</td>
<td>0.082</td>
</tr>
<tr>
<td>T2-weighted</td>
<td>0.012</td>
<td>0.202</td>
</tr>
</tbody>
</table>
Clinical outcomes and management

Table 4. Differences in the incidence of peculiar MR signal patterns according to groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Signal intensity patterns of RCCs, n (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cystic MR pattern (T1-hypo/T2-hyper)</td>
<td>Noncystic MR pattern (other than T1-hypo/T2-hyper)</td>
</tr>
<tr>
<td>I</td>
<td>19 (73.1)</td>
<td>7 (26.9)</td>
</tr>
<tr>
<td>II</td>
<td>2 (25.0)</td>
<td>6 (75.0)</td>
</tr>
</tbody>
</table>

MR, magnetic resonance; RCC, Rathke's cleft cyst; group I, the patients with RCCs in whom concomitant endocrine disorders were identified; group II, the patients without concomitant endocrine disorders.

Table 3. Signal intensity characteristics of RCCs on T1- and T2-weighted MR images according to groups

<table>
<thead>
<tr>
<th>Group</th>
<th>T2-weighted image</th>
<th>T1-weighted image, n (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hypointense</td>
<td>Isointense</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>I</td>
<td>1 (3.8)</td>
<td>3 (11.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Isointense</td>
<td>0 (0)</td>
<td>1 (3.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hyperintense</td>
<td>19 (73.0)</td>
<td>2 (7.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>II</td>
<td>1 (12.5)</td>
<td>4 (50)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Isointense</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hyperintense</td>
<td>2 (25.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

RCC, Rathke's cleft cyst; MR, magnetic resonance; group I, the patients with RCCs in whom concomitant endocrine disorders were identified; group II, the patients without concomitant endocrine disorders.

The P-value was expressed as the ^a statistical significance of the hypointense signal and the hyper- or iso-intense signal on the T1-weighted image and the ^b statistical significance of the hyperintense signal and the iso- or hypointense signal on the T2-weighted image according to the groups. Statistical analysis was performed using Fisher exact test.

Clinical outcomes cont’d

Table 5. Comparison of the clinical parameters and outcomes between the patients with endocrine disorders and the matched controls before and 1 year after the treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>CPP</th>
<th>Control</th>
<th>P-value</th>
<th>GHD</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male/female, n (%)</td>
<td>12 (4/8)</td>
<td>20 (6/14)</td>
<td>NS</td>
<td>7 (3/4)</td>
<td>14 (6/8)</td>
<td>NS</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>8.4±2.2</td>
<td>8.9±0.8</td>
<td>NS</td>
<td>10.3±3.2</td>
<td>10.2±2.7</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>134.7±15.6</td>
<td>137.0±6.8</td>
<td>NS</td>
<td>123.9±15.6</td>
<td>123.8±14.7</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>37.4±1.5</td>
<td>38.1±9.1</td>
<td>NS</td>
<td>27.1±10.6</td>
<td>25.9±11.3</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>20.1±2.6</td>
<td>20.0±3.2</td>
<td>NS</td>
<td>17.1±3.9</td>
<td>16.3±3.5</td>
<td>NS</td>
</tr>
<tr>
<td>Tanner stage V/VI/III</td>
<td>0/8/4</td>
<td>0/15/5</td>
<td>NS</td>
<td>5/2/0</td>
<td>10/5/0</td>
<td>NS</td>
</tr>
<tr>
<td>BA (yr)</td>
<td>10.8±2.4</td>
<td>10.9±0.8</td>
<td>NS</td>
<td>7.6±2.8</td>
<td>8.1±3.0</td>
<td>NS</td>
</tr>
<tr>
<td>BA-CA (yr)</td>
<td>2.4±1.0</td>
<td>2.1±0.7</td>
<td>NS</td>
<td>−2.8±1.1</td>
<td>−2.1±0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Height SDS</td>
<td>1.3±1.0</td>
<td>1.1±0.9</td>
<td>NS</td>
<td>−2.4±0.3</td>
<td>−2.4±0.4</td>
<td>NS</td>
</tr>
<tr>
<td>Weight SDS</td>
<td>1.4±0.7</td>
<td>1.2±1.0</td>
<td>NS</td>
<td>−1.8±1.4</td>
<td>−2.0±0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Basal LH (mIU/mL)</td>
<td>2.1±1.7</td>
<td>1.0±0.8</td>
<td>0.048</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Peak LH (mIU/mL)</td>
<td>15.9±13.2</td>
<td>12.1±9.9</td>
<td>NS</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Peak FSH (mIU/mL)</td>
<td>20.3±1.2</td>
<td>17.1±4.2</td>
<td>NS</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Peak GH (ng/mL)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>5.8±2.8</td>
<td>4.8±2.8</td>
<td>NS</td>
</tr>
<tr>
<td>GH dose (IU/kg/wk)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>0.7±0.1</td>
<td>0.7±0.1</td>
<td>NS</td>
</tr>
<tr>
<td>1 Year after treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>9.4±2.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9.9±0.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NS</td>
<td>11.2±3.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.2±2.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NS</td>
</tr>
<tr>
<td>BA-CA (yr)</td>
<td>1.8±0.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.3±0.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NS</td>
<td>−2.4±1.6</td>
<td>−2.0±0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Height SDS</td>
<td>1.1±1.0</td>
<td>1.1±0.9</td>
<td>NS</td>
<td>−1.9±0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>−1.8±0.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NS</td>
</tr>
<tr>
<td>Weight SDS</td>
<td>1.2±0.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.2±1.1</td>
<td>NS</td>
<td>−1.8±1.3</td>
<td>−1.6±0.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NS</td>
</tr>
<tr>
<td>Basal LH (mIU/mL)</td>
<td>0.7±0.8&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.8±0.4</td>
<td>NS</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>HV (cm/yr)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>8.0±2.4</td>
<td>8.9±2.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation unless otherwise indicated. CPP, central precocious puberty; GHD, growth hormone deficiency; NS, not significant; BMI, body mass index; BA, bone age; CA, chronological age; SDS, standard deviation score; LH, luteinizing hormone; FSH, follicular stimulating hormone; GH, growth hormone; HV, height velocity.

<sup>a</sup>P < 0.05 compared with the same parameter at the time of diagnosis.

### Clinical outcomes

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (y)/sex</th>
<th>Presentation</th>
<th>Cyst location</th>
<th>Hormonal deficits</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15/M</td>
<td>Headache, endocrinopathy</td>
<td>Sellar</td>
<td>↓ GH, IGF-1</td>
<td>NEC</td>
</tr>
<tr>
<td>2</td>
<td>12/F</td>
<td>Headache</td>
<td>Suprasellar</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>12/F</td>
<td>Headache</td>
<td>Suprasellar</td>
<td>None</td>
<td>↓ Cortisol, DI</td>
</tr>
<tr>
<td>4</td>
<td>13/M</td>
<td>Headache, endocrinopathy</td>
<td>Sellar/ suprasellar</td>
<td>↓ Cortisol</td>
<td>Residual cyst, decreased in size</td>
</tr>
<tr>
<td>5</td>
<td>16/F</td>
<td>Headache, amenorrhea, galactorrhea, endocrinopathy</td>
<td>Sellar</td>
<td>↑ Prolactin</td>
<td>NEC</td>
</tr>
<tr>
<td>6</td>
<td>17/M</td>
<td>Headache, dizziness</td>
<td>Sellar</td>
<td>None</td>
<td>NEC</td>
</tr>
<tr>
<td>7</td>
<td>2/F</td>
<td>Meningitis, visual loss, endocrinopathy</td>
<td>Sellar/ suprasellar</td>
<td>↓ Thyroid, ↓ cortisol</td>
<td>NEC</td>
</tr>
<tr>
<td>8</td>
<td>10/F</td>
<td>Weight gain, short stature, endocrinopathy</td>
<td>Sellar</td>
<td>↓ GH</td>
<td>NEC</td>
</tr>
<tr>
<td>9</td>
<td>14/F</td>
<td>Headache, seizure</td>
<td>Sellar/ suprasellar</td>
<td>None</td>
<td>NEC</td>
</tr>
<tr>
<td>10</td>
<td>15/M</td>
<td>Incidental finding, endocrinopathy</td>
<td>Sellar/ suprasellar</td>
<td>↓ GH, ↑ prolactin</td>
<td>NEC</td>
</tr>
</tbody>
</table>

*GH, growth hormone; IGF-1, insulin-like growth factor 1; NEC, no evidence of cyst; HRT, hormone replacement therapy; DI, diabetes insipidus; DDAVP, 1-deamino-8-D-arginine vasopressin; NA, not available.

Back to our patient…

- Discharged on 11/12 without AED.
- Parents instructed to monitor symptoms of thyroid or adrenal dysfunction, poor growth, polydipsia or polyuria.
- Follow up with Ophthalmology for esotropia in 4-6 weeks.
- Follow up with Neurology in 2 months.
- Repeat MRI and follow up with Neurosurgery in 3 months.
Conclusions

- Any child with RCC presenting with generalized weakness should undergo pituitary function evaluation and consideration of surgical treatment.

- RCC with endocrinopathy tends to show a hypointense T1 and hyperintense T2 signal on MRI.

- Presence of RCC does not impact treatment with hormone supplementation in the case of GHD or CPP.

- Patients with hyperprolactinemia are potential candidates for surgical therapy for RCC, as are patients who report headache and visual disturbance. However, most anterior pituitary deficits do not improve, and new deficits may develop.


Indications for surgery

Assessment of pre- and postoperative endocrine function in 94 patients with Rathke’s cleft cyst

Natsuko Oyama, Shigeyuki Tahara, Kenichi Oyama, Yudo Ishii and Akira Teramoto

Department of Neurosurgery, Nippon Medical School, Tokyo 113-8603, Japan
Analysis of the correlation between pre-and postoperative anterior pituitary hormone loading tests (Wilcoxon test).