22 month old female with polyuria and polydipsia

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Chief Complaint

- 22 month old female with history of neuroblastoma who presented to oncology for follow up with polyuria and polydipsia of 4-5 weeks’ duration.
- Advised follow up in endocrine clinic for concern of diabetes insipidus.
History of Present Illness

- 7/11/2014: presented to local oncologist with polyuria and polydipsia, labs were drawn.
- Parents began documenting water intake and diapers:
  - 7/12: 44 oz water in (2.6 L/m2), 40 oz urine output (2.4 L/m2)
  - 7/13: 53.5 oz water in (3.1 L/m2), 35 oz urine output (2.1 L/m2)
- Presented to pediatric endocrine clinic on 7/14.
• Initially started asking for more water and became reattached to her bottle
• Drinks 6-10 8 oz water bottles daily, ~60-80 oz water per day, including 1-3 times nightly
• Has ~10 wet diapers per 24 hour period, weighing 4-16 oz
• No symptoms of dehydration
• Additional “clinginess” and behavioral problems reported
• No water between 1900 and 0500 for few nights prior to visit
• **Heme/Onc History:**
  - Diagnosed with stage 4, *MYC-N* amplified, high-risk neuroblastoma with liver mets in 11/2012.
  - Induction chemotherapy with cyclophosphamide, topotecan, cisplatin, etoposide, doxorubicin, vincristine in 12/2012.
  - R adrenalectomy and multiple liver biopsies in 4/2013.
  - Autologous SCT in 5/2013, conditioning with carboplatin, etoposide, melphalan.
  - Radiation therapy to liver and R adrenal post-operative bed in 7/2013.
  - Completed all therapy in 1/2014.
  - Most recent MIBG showed no avid tumor in 2/2014.
More History…

- **Medical History:**
  - Hypertension, now resolved, and mild-mod SNHL with hearing aids resulting from chemotherapy
  - C. difficile infection in 3/2014

- **Surgical History:**
  - CVC insertion in 12/2012

- **Allergies:**
  - Restlessness with dexamethasone
  - Skin rash with tegaderm and chloraprep

- **Medications:**
  - MVI
  - Nystatin topical for diaper dermatitis
• **Developmental History:**
  • Speech delay, in ST
  • Frequent falls and balance issues with walking

• **Family History:**
  • MGM with hypertension
  • Cervical and breast cancers in extended family members

• **Social History:**
  • Lives with parents, 10 yo brother, 3 yo sister.
  • Mother is a teacher, and father works in RV industry and construction.
  • No daycare.
Review of Systems

- Constitutional: neg for fever, chills, diaphoresis, activity/appetite change, fatigue, weight change.
- HENT: neg for congestion, rhinorrhea. + hearing loss.
- Eyes: neg for pain /discharge. + photophobia.
- Resp: + cough, choking.
- CV: neg for chest pain, palpitations, leg swelling.
- GI: neg for vomiting, abd pain, bloody stool. + diarrhea.
- Endocrine: neg for cold/heat intolerance. + polydipsia, polyuria.
- GU: neg for hematuria, dysuria. + increased frequency of urination.
- Musc: + gait problem.
- Skin: neg for rash. + pallor.
- Neuro: neg for tremors, seizures, syncope, weakness. + speech difficulty.
- Heme: + easy bruising/bleeding.
- Psych/Beh: neg for sleep disturbance. + hyperactivity, behavioral problems.
Physical Exam

- T 37.1C, BP 84/58, HR 120, Ht 82.5 cm (10%), Wt 11.2 kg (51%), BSA 0.51 m²
- Constitutional: active, persistently drinking from water bottle
- HENT: MMM, clear OP
- Eyes: EOM intact, PERRLA
- Neck: normal ROM, supple, no adenopathy, thyroid nonpalpable
- CV: RRR, no murmur, 2+ pulses
- Resp: CTAB, no distress/retraction
- GI: S/NT/ND, normal bowel sounds
- GU: Tanner 1 for PH and breasts, no AH
- Musc: normal ROM, no edema
- Neuro: alert, responsive, 2+ DTRs
- Skin: no rash, cyanosis, pallor
Initial assessment and further workup?
Polyuria

• Defined as urine production > 2 L/m²/24h
• Results from water diuresis
  • Primary polydipsia
  • Diabetes insipidus, central vs nephrogenic
• Also from solute diuresis
  • Organic solutes (glucose, urea)
  • Inorganic solutes

<table>
<thead>
<tr>
<th>Test</th>
<th>7/11/2014</th>
<th>7/14/2014</th>
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</thead>
<tbody>
<tr>
<td>Na (RR 134-149 mEq/L)</td>
<td>140</td>
<td>140</td>
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<tr>
<td>K (RR 3.5-5 mEq/L)</td>
<td>4.0</td>
<td>3.5</td>
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<tr>
<td>BUN (RR 7-20 mg/dL)</td>
<td>6</td>
<td>9</td>
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<tr>
<td>Cr (RR 0.2-0.5 mg/dL)</td>
<td>0.2</td>
<td>0.3</td>
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<tr>
<td>Glucose (RR 60-109 mg/dL)</td>
<td>90</td>
<td>99</td>
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<td>Ca (RR 8.4-10.2 mg/dL)</td>
<td>10.9</td>
<td>10.3</td>
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<tr>
<td>Albumin (RR 3.5-5.0 g/dL)</td>
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<tr>
<td>Serum osmolality (RR 289-308 mOsm/kg)</td>
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<tr>
<td>Urine osmolality (RR 500-800 mOsm/kg)</td>
<td>61</td>
<td>119</td>
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<tr>
<td>Urine specific gravity (RR 1.016-1.022)</td>
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<tr>
<td>Urine Na (RR &gt;20 mEq/L)</td>
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<td>35</td>
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</table>
Next steps…

• Admitted to PICU on 7/16 for water deprivation test
  • 8 hour test
  • Hourly vitals, weight, serum and urine Na, serum and urine osm, urine SG
  • ADH and BMP at hours 0 and 8

• Other criteria:
  • Terminate if >5% weight loss or tachycardia
  • If serum osm <300 (Na <145), urine osm <600, continue until signs of hypovolemia
  • If urine osm >1000 or >600 and stable (<30 mosm change for 2 time points), stop test = NORMAL
  • If serum osm >300 and urine osm <600 = DI. Give pitressin.
## Results

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<tr>
<th>Hour</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<tbody>
<tr>
<td>ADH (pg/mL)</td>
<td>&lt;0.5</td>
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<td>1.1</td>
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<tr>
<td>Serum Na (RR 134-149 mEq/L)</td>
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<td>137</td>
<td>138</td>
<td>139</td>
<td>137</td>
<td>138</td>
<td>137</td>
<td>137</td>
<td>141</td>
</tr>
<tr>
<td>Urine Na (RR &gt;20 mEq/L)</td>
<td>90</td>
<td>118</td>
<td>147</td>
<td>166</td>
<td>162</td>
<td>171</td>
<td>188</td>
<td>189</td>
<td>196</td>
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<tr>
<td>SG (RR 1.016-1.022)</td>
<td>1.011</td>
<td>1.013</td>
<td>1.014</td>
<td>1.018</td>
<td>1.020</td>
<td>1.022</td>
<td>1.015</td>
<td>1.021</td>
<td>1.021</td>
</tr>
<tr>
<td>Serum osm (RR 289-308 mOsm/kg)</td>
<td>285</td>
<td>284</td>
<td>282</td>
<td>285</td>
<td>286</td>
<td>288</td>
<td>285</td>
<td>286</td>
<td>295</td>
</tr>
<tr>
<td>Urine osm (RR 500-800 mOsm/kg)</td>
<td>428</td>
<td>501</td>
<td>591</td>
<td>712</td>
<td>766</td>
<td>747</td>
<td>733</td>
<td>792</td>
<td>827</td>
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<tr>
<td>HR</td>
<td>114</td>
<td>120</td>
<td>104</td>
<td>97</td>
<td>110</td>
<td>108</td>
<td>110</td>
<td>125</td>
<td>111</td>
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<tr>
<td>Wt (kg)</td>
<td>10.835</td>
<td>11</td>
<td>10.6</td>
<td>10.85</td>
<td>10.8</td>
<td>10.63</td>
<td>10.6</td>
<td>10.685</td>
<td></td>
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<tr>
<td>UOP (mL)</td>
<td>0</td>
<td>28</td>
<td>25</td>
<td>9</td>
<td>12</td>
<td>9</td>
<td>9</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>
Upon discharge...

- Parents advised to:
  - Return to sippy cup as opposed to bottle
  - Decrease each bottle of water by 1 oz every 5 days until back to regular drinking habits
  - Watch for symptoms of dehydration
  - Follow up in endocrine clinic in 1 month

- Advised Heme/Onc service to obtain pituitary cuts if ordering brain MRI
Clinical Questions

1. What mechanisms are responsible for the different etiologies of acquired central DI, particularly in pediatric cancer patients?

2. What is the method of proper diagnosis of DI?

3. Has primary polydipsia been reported in children in this age group? How is it treated?
# Etiologies of CDI

<table>
<thead>
<tr>
<th>ETIOLOGY</th>
<th>CHILDREN</th>
<th>ADULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary brain tumor: craniopharyngioma, glioma, neoplasm, leukemia, lymphoma, meningioma</td>
<td>50%</td>
<td>30%</td>
</tr>
<tr>
<td>Idiopathic (isolated or familial)</td>
<td>29%</td>
<td>25%</td>
</tr>
<tr>
<td>Head trauma</td>
<td>2%</td>
<td>17%</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>—</td>
<td>9%</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>—</td>
<td>8%</td>
</tr>
<tr>
<td>Intracranial hemorrhage and hypoxia, postpartum pituitary necrosis (Sheehan syndrome), aneurysm, thrombosis, sickle cell crisis</td>
<td>—</td>
<td>6%</td>
</tr>
<tr>
<td>Infection: tuberculosis, meningitis, encephalitis, intracranial abscess, syphilis</td>
<td>2%</td>
<td>—</td>
</tr>
<tr>
<td>Histiocytosis X</td>
<td>16%</td>
<td>—</td>
</tr>
<tr>
<td>Granulomatosis, sarcoidosis, alcohol, phenytoin, clonidine</td>
<td>—</td>
<td>5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cause</th>
<th>No. of patients (%)</th>
<th>Sex (F/M)</th>
<th>Other symptoms (# patients)</th>
<th>Age at presentation</th>
<th>Endocrine deficiencies at last visit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Idiopathic</strong></td>
<td>41 (52)</td>
<td>23/18</td>
<td></td>
<td>6.4 (0.1-14.9)</td>
<td></td>
</tr>
<tr>
<td>• Pit stalk thickening</td>
<td>18 (23)</td>
<td>8/10</td>
<td>Growth retardation (7), HA (3), fatigue (3)</td>
<td>7.3 (4.5-11.8)</td>
<td>GH (9); GH + TSH (3); GH + FSH or LH (3); GH, TSH, + FSH or LH (2)</td>
</tr>
<tr>
<td>• Normal pit stalk</td>
<td>19 (24)</td>
<td>12/7</td>
<td>Growth retardation (1), HA (1), fatigue (1)</td>
<td>5.0 (0.5-14.9)</td>
<td>GH (2)</td>
</tr>
<tr>
<td>• CNS malformation</td>
<td>4 (5)</td>
<td>3/1</td>
<td></td>
<td>3.9 (0.1-6.8)</td>
<td>GH (1)</td>
</tr>
<tr>
<td><strong>LCH</strong></td>
<td>12 (15)</td>
<td>7/5</td>
<td></td>
<td>3.4 (1.1-19.6)</td>
<td>GH (6); GH + TSH (1); GH + FSH or LH (1); panhypopit (1)</td>
</tr>
<tr>
<td><strong>Intracranial tumor</strong></td>
<td>18 (23)</td>
<td>6/12</td>
<td></td>
<td>8.5 (5.8-13.8)</td>
<td></td>
</tr>
<tr>
<td>• Germinoma</td>
<td>6 (8)</td>
<td>3/3</td>
<td>Growth retardation (3), visual defect (2)</td>
<td>10.1 (7.3-13.8)</td>
<td>GH + TSH (1); GH + ACTH (1); GH, TSH, + FSH or LH (2); GH, TSH, + ACTH (2)</td>
</tr>
<tr>
<td>• Craniopharyngioma</td>
<td>6 (8)</td>
<td>2/4</td>
<td>Visual defect (3), HA (3), growth retardation (2)</td>
<td>7.5 (5.8-12.0)</td>
<td>Panhypopit (4); GH, TSH, + ACTH (1); GH, ACTH, + FSH or LH (1)</td>
</tr>
<tr>
<td>• Post-resection</td>
<td>6 (8)</td>
<td>1/5</td>
<td></td>
<td>9.4 (5.8-17.3)</td>
<td>Panhypopit (3); GH, TSH, + ACTH (1); GH, ACTH, + FSH or LH (1)</td>
</tr>
</tbody>
</table>

Mechanisms of Acquired CDI

• Idiopathic:
  • Autoimmune disease and the AVP cell autoantibody
  • Lack of posterior pituitary hyperintense signal (PPHS)
  • Pituitary stalk thickening in 50-60%
  • Anterior pituitary deficits

• Langerhans cell histiocytosis
  • Pituitary stalk thickening in 50-70%
  • Presence of AVP cell autoantibody

Mechanisms cont’d.

- Primary brain tumor:
  - Germinoma:
    - Suprasellar and neurohypophyseal tumors arise from posterior pituitary to infundibulum
    - Pituitary stalk thickening in 78-100%
    - Presence of AVP cell autoantibody
  - Craniopharyngioma:
    - Suprasellar lesion arising from Rathke’s pouch
    - Compression of pituitary stalk

- Metastasis:
  - Occur in post pituitary lobe
    - Direct arterious vascularization of post pituitary
    - Microinfarcts and hemorrhages
    - Spread from contiguous bony sites to greater area of adjacent dura
    - Meningeal seeding
    - Leukemic infiltration of posterior lobe, pit stalk, or peripituitary gland

Diagnosis of Diabetes Insipidus

1. Water Deprivation Test
2. Hypertonic Saline Infusion
3. Desmopressin “Trial”

Water Deprivation Protocol

Time of start of test ______ hr

Initial body weight ________ kg

1. Place IV hep lock 30 minutes prior to start of test
2. Make patient NPO
3. Measure all parameters at hour 0
4. Measure all other parameters hourly as left blank in the chart below

<table>
<thead>
<tr>
<th>Interval Minutes</th>
<th>Body Weight</th>
<th>Vital Signs</th>
<th>Serum</th>
<th>Plasma</th>
<th>Urine</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Na</td>
<td>OSM</td>
<td>BUN</td>
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<td></td>
<td></td>
<td></td>
<td>VP</td>
<td>Na</td>
<td>OSM</td>
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<tr>
<td>-30</td>
<td>Place IV hep lock</td>
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<td>0</td>
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<td>60</td>
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<td>420</td>
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<td>480</td>
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5. At any time during the test:
   Notify Endocrinology service if >5% body weight lost or tachycardia present, will consider terminating
   If serum osm <300 (Na <145), urine osm <600, continue test until vital signs demonstrate hypovolemia
   If urine osm >1000, or >600 and stable (<30 mosm change for 2 time points), stop test = NORMAL
   If serum osm >300 and urine osm <600 = DIABETES INSIPIDUS. Give pitressin 0.5 units (1 u/m2, BSA 0.51) subq and measure:

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<td>60</td>
<td>X</td>
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</tbody>
</table>

- If there is less than a twofold increase in urine osmolality after vasopressin administration, the patient probably has nephrogenic diabetes insipidus.
Primary Polydipsia

- 3yo female admitted for Achilles tendon surgery
- 10yo male with Langerhans cell histiocytosis
- 12yo male with an intrasellar epidermoid cyst
Back to our patient…

- Seen in clinic on 8/26
  - Initially halved intake but then increased to original volumes
  - Temper tantrums when denied water
  - Recommended to see neuropsychiatrist

- Our recommendations
  - Continue to decrease fluid intake by 1 oz per bottle every 5 days
  - Follow up in 3 months
Works Cited

- Sperling MA. Pediatric Endocrinology 2008;3498-349.