Pituitary Stalk Interruption Syndrome

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Case:

- NP, 42 year old female, from Dominican Republic.
- Initially seen in Endocrine clinic for “premature menopause”.
- She did not have regular pubertal development
- She had minimal breast growth, and no hair growth in the pubic area or in the axillary area.
- Recalls only one menstrual period at age 17.
• She was treated in DR with hormonal therapy for 6 months, got only spotting, no regular period, so stopped taking it.

• She has never been pregnant or sexually active.

• She moved to USA in 2013, established care with PCP.

• She was found to have hypothyroidism, so was started Levothyroxine 50 mcg took it for 2 months and stopped.
• Since she moved to the States, she has lost about 20 pounds because of decreased appetite.

• She reports that for few months prior to presentation, she started feeling dizzy, without inducing factors.

• She denies palpitations, tremors, constipation, diarrhea, sweating, heat or cold intolerance, difficulty breathing, swallowing, galactorrhea, headache, polyuria or polydipsia.
• She has no similar history in her family including her fraternal twin sister.

• She denied previous hospitalizations or surgeries.
Physical Exam:

- Height 4’11”, weight 87 lb, BMI 17.5

- BP 97/63, heart rate 71/min.

- She looks younger than her estimated age.

- No classic Turner's features (webbing of the neck or cubitus valgus)

- No Cushing features.
• Neck: Thyroid was palpated, not enlarged, no nodules appreciated.

• Skin: No rash was noted.
  She had no hair in the axilla or in pubic area.

• Breast: Development Tanner stage II.
  No secretions from nipples were noted.

• Genitourinary: external genitalia pre-pubescent.

• Neurologic: normal, visual field intact.
<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH</td>
<td>0.5 mIU/ml</td>
</tr>
<tr>
<td>LH</td>
<td>1.2 mIU/ml</td>
</tr>
<tr>
<td>PROLACTIN</td>
<td>10.4 ng/ml</td>
</tr>
<tr>
<td>ESTRADIOL</td>
<td>&lt; 20 pg/ml</td>
</tr>
<tr>
<td>CORTISOL</td>
<td>2 mcg/dl</td>
</tr>
<tr>
<td>ACTH</td>
<td>18 pg/ml</td>
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<tr>
<td>TSH</td>
<td>10.33 uIU/ml</td>
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<tr>
<td>FT4</td>
<td>0.41 ng/dl</td>
</tr>
<tr>
<td>IGF1</td>
<td>-3.7 SD</td>
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<tr>
<td>Na</td>
<td>137 mmol/l</td>
</tr>
<tr>
<td>Cortisol after ACTH stim</td>
<td>0 min 1.6 mcg/dl</td>
</tr>
</tbody>
</table>
- **DXA:** L1-L4: T-Score -4.3
  Femoral neck: T-Score -2.7

- **Bone age:** adult with closure of all physes

- **MRI brain:** Posterior pituitary ectopia with a partially empty sella, absence of the pituitary stalk and small adenohypophysis.
**Treatment:**

She was treated with hydrocortisone followed by Levothyroxine and birth control pills.
Pituitary stalk interruption syndrome (PSIS) is a rare disease with an estimated incidence rate of 0.5/100,000 births. (1)

- Gets more frequently recognized these years due to the fact that MRI is routinely performed in patients suspected of pituitary diseases.
• PSIS is characterized by a typical triad in pituitary imaging: (2)

1- Absent or thin pituitary stalk (PS)
2- Ectopic posterior pituitary
3- Anterior pituitary hypoplasia.
• Pituitary stalk interruption syndrome, first described as transection of PS in 1987 by Fujisawa et al. (3)

• Age at diagnosis is 25 (22-28). (4)
The common presentations of the disease:

1- Short stature.
2- Absent or delayed pubertal development.
3- Other symptoms associated with anterior pituitary hormone deficiencies.
**Manifestations:**

- Short stature associated with growth hormone deficiency is the most common presentation in children with PSIS. (4)

- 40–100% of them may at the same time have other anterior pituitary hormone deficiencies. (4)

- The function of posterior pituitary is generally intact, but there are case reports of patients with PSIS diagnosed with diabetes insipidus (DI). (4)
• Prevalence of:
  1. Isolated deficiency in growth hormone (GH) 100%, gonadotrophins 97.2%, corticotrophin 88.2% and thyrotrophin 70.3%
  2. Hyperprolactinemia 24.3%

• The lack of portal blood supply during the differentiation and proliferation of lactotroph cells might explain the relatively low ratio of hyperprolactinemia.
• Deficiency of:
GH was 100%; ACTH, 77.6%; TSH, 43.1%; LH/FSH, 94.2%; combined pituitary hormone, 93.1%; Prolactin, 1.7%

• Hypofunction of posterior pituitary 1.7%
It was noted that patients with invisible PS on MRI tended to have multiple anterior pituitary hormone deficiencies, whereas visibility of the PS was related to isolated GH deficiency. (4,5)
In a detailed review of clinical presentations and hormonal status in patients with PSIS, it was found that multiple anterior pituitary hormone deficiencies were more common in adult population than previously reported in children.
On MRI:

1. Anterior pituitary hypoplasia in 98.3%.
2. Pituitary stalk absence in 98.3%.
3. Pituitary stalk thinning in 1.7%.
4. Ectopic neurohypophysis in 91.4%.
5. Neurohypophysis invisibility in 8.6%.

- In 60.4% the ectopic neurohypophysis, is located at the infundibular recess. (6)
Etiology:

- The pathogenesis of the condition has not been fully understood yet.

- At first, it was thought that perinatal injury to the PS was the primary cause. Due to the high frequency of perinatal events in PSIS patients.

- But the existence of family history and associated malformations in a large proportion of patients suggest that the high frequency of perinatal events is a consequence rather than the cause. (4)
Other studies revealed that mutations of certain genes involved in the development of pituitary might be the true cause, which led to increased incidence of adverse events during birth.

To date, only few gene mutations have been identified in <5% of patients with PSIS, including LHX4, OTX2, HESX1, SOX3, GLI2 and PROKR2.(4)
A Chinese study consistent with previous studies, found significantly more male than female patients in the PSIS group suggesting that it may have an X-linked inheritance. (6)
Etiology:

- It could be acquired by the aberrant embryonic development of pituitary. (4)

This process requires:

- Co-ordination of complex structural and cellular differentiation, during which neurohypophysis begins to fuse with adenohypophysis (Rathke’s pouch, ectodermal).
- Normally during the formation of mature pituitary, diverticulum descends and gives rise to the posterior lobe right behind the anterior pituitary.

- In the meanwhile PS comes into shape and brings about the hypothalamic-pituitary vessels with it.
When the neural migration is interrupted in PSIS, the angiogenesis of hypophyseal portal circulation is disturbed as well, leading to the hypoplasia of anterior pituitary and anterior pituitary hormone deficiencies.
Conclusion:

- We present a rare case of pituitary stalk interruption with multiple anterior hormone deficiencies. The presentation of PSIS is variable, and the degree of hypopituitarism seems to correlate with the visibility of a pituitary stalk on imaging. This is consistent with the imaging finding in our case.
References:


Thank you