Sheehan’s Syndrome-The Most Common Cause of Panhypopituitarism at Moderate Altitude: A Sub-Himalayan Study

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Abstract

Background: Panhypopituitarism is a rare disorder with varied clinical presentation having various etiologies. Sheehan’s syndrome (SS) is decreasing in frequency worldwide and is a rare cause of panhypopituitarism in developed nations.

Methodology: A retrospective study done between May 2011 and May 2015 in tertiary care hospital. We reviewed the records of patients with hypopituitarism. Clinical features, hormonal profile and radiological investigations noted.

Results: Total 14 patients of panhypopituitarism included with average duration of symptoms 1.93± 1.96 years. four (28.57%) were males and ten (71.43%) were females with mean age of diagnosis 37.78± 13.68 years. Sheehan’s syndrome (SS) was the most common cause of panhypopituitarism in 57.14%(8 patients), followed by post surgery in 14.28% (2 patients). 80% of women had SS with a mean duration of symptoms 2.39±1.54 years.

Conclusion: Sheehan’s syndrome is not uncommon in developing countries, High degree of clinical suspicion is desired as clinical features are most often subtle.

Editorial Viewpoint

• Sheehan’s syndrome is the most common cause of panhypopituitarism in developing countries.
• Diagnosis can be missed due to varied clinical presentations.
• Lifelong treatment is needed.

Introduction

Hypopituitarism is the partial or total loss of anterior pituitary hormone secretion. The deficiency of all anterior pituitary hormones is termed as panhypopituitarism, and less than all is termed often termed as partial hypopituitarism.¹ ² Due to lack of data on hypopituitarism in India, the exact prevalence of hypopituitarism in India is not known. However, Kochupillai et al estimated total prevalence of pituitary disorder to 4 million in 2000.³

Panhypopituitarism is a rare disorder with varied clinical presentation having various etiologies. It may present as an acute illness or have an obscure presentation with a progressive hormonal deficiency. Degree and speed of loss of hormone, age of onset and cause of hypopituitarism affect the clinical manifestations of hypopituitarism. Pituitary tumors and postoperative and post radiotherapy states are the most common cause in adults in developed nations.¹ Sheehan’s syndrome (SS) is decreasing in frequency worldwide and is a rare cause of panhypopituitarism in developed nations owing to advance in obstetric care.¹ Long-standing pituitary damage is associated with increased mortality primarily due to increased cardiovascular and cerebrovascular mortality.⁴

Material and Methods

This retrospective study was conducted at a tertiary care hospital, having no endocrinologist service, in sub-Himalayan region at an altitude of 7,200 feet between May 2011 and May 2015. We reviewed the records of patients admitted with the diagnosis of hypopituitarism. Presenting features, age at diagnosis, time to diagnose, clinical and laboratory data, number of pituitary hormone deficiencies and MRI of the sella.

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were recorded and analyzed. Basal hormone estimations in fasting state between 08.00 and 09.00 am of Adrenocorticotropic hormone (ACTH), serum cortisol, thyroid stimulating hormone (TSH), free thyroxine (fT4), gonadotropins [luteinizing hormone(LH), follicle stimulating hormone(FSH)] and prolactin were done using chemiluminescent immunoassay. Growth hormone assay was not done because of financial constrains. Low dose 1µg ACTH (short Synacthen test) was done in three patients having fasting serum cortisol levels >5 µg/dl. Contrast enhanced magnetic resonance imaging (MRI) of pituitary was done in all. Diagnostic criteria of SS were (a) history of PPH or lactation failure and/or amenorrhea following last child birth; (b) more than one anterior pituitary hormone deficiency; and (c) empty sella on magnetic resonance imaging.5

Table 1: Clinical profile of patients with panhypopituitarism

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age</th>
<th>Sex</th>
<th>Symptoms duration</th>
<th>Symptoms</th>
<th>PPH$</th>
<th>LF#</th>
<th>Examination</th>
<th>BP</th>
<th>MRI</th>
<th>Diagnosis</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>M</td>
<td>3 mo</td>
<td>Empirical ATT for meningitis, with recurrent fever/headache</td>
<td>-</td>
<td>-</td>
<td>normal</td>
<td>70/30</td>
<td>LH'</td>
<td>LH</td>
<td>HR</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>F</td>
<td>2 yr 6 mo</td>
<td>Scanty menstruation, milky secretion from breast, tiredness, fatigue</td>
<td>No</td>
<td>No</td>
<td>Galactorrhea, delayed DTR, contraction of visual field</td>
<td>110/86</td>
<td>MA°</td>
<td>MA</td>
<td>Cabergoline and then surgery</td>
</tr>
<tr>
<td>3</td>
<td>27</td>
<td>F</td>
<td>5 yrs</td>
<td>Amenorrhea, tiredness</td>
<td>Yes</td>
<td>Yes</td>
<td>WNL</td>
<td>80/56</td>
<td>Empty sella</td>
<td>SS†</td>
<td>HR</td>
</tr>
<tr>
<td>4</td>
<td>21</td>
<td>F</td>
<td>2 yrs</td>
<td>h/o surgery for astrocytoma 5 yrs back. Amenorrhea, excessive tiredness and altered sensorium for 15 days</td>
<td>No</td>
<td>No</td>
<td>Obesity, absence of axillary, pubic hair, delayed DTR, optic atrophy</td>
<td>70/54</td>
<td>Empty sella</td>
<td>Gliosis and no recurrence of primary tumor</td>
<td>Post-cranial radiotherapy hypopituitarism HR</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
<td>M</td>
<td>1 yr</td>
<td>Tiredness, easy fatigability, loss of libido</td>
<td>-</td>
<td>-</td>
<td>WNL</td>
<td>112/70</td>
<td>Empty sella</td>
<td>Post-head injury pituitary damage</td>
<td>HR</td>
</tr>
<tr>
<td>6</td>
<td>28</td>
<td>F</td>
<td>4 yrs</td>
<td>Amenorrhea, weakness, postural dizziness</td>
<td>+</td>
<td>+</td>
<td>Delayed DTR</td>
<td>110/70</td>
<td>Empty sella</td>
<td>SS</td>
<td>HR</td>
</tr>
<tr>
<td>7</td>
<td>46</td>
<td>F</td>
<td>21</td>
<td>Amenorrhea, generalised weakness, tiredness, decreased appetite</td>
<td>+</td>
<td>+</td>
<td>Breast atrophy, scanty pubic, axillary hair, delayed DTR</td>
<td>90/60</td>
<td>Empty sella</td>
<td>SS</td>
<td>HR</td>
</tr>
<tr>
<td>8</td>
<td>26</td>
<td>F</td>
<td>6</td>
<td>Amenorrhea, weakness, swelling, change in voice</td>
<td>+</td>
<td>+</td>
<td>Pallor, facial puffiness, delayed DTR, hoarseness, Slowness</td>
<td>92/60</td>
<td>Empty sella</td>
<td>SS</td>
<td>HR</td>
</tr>
<tr>
<td>9</td>
<td>32</td>
<td>M</td>
<td>3 days</td>
<td>h/o surgery for pituitary tumor 2y back, fever and altered sensorium</td>
<td>-</td>
<td>-</td>
<td>GCS8/15, acromegaly features, obesity, delayed DTR</td>
<td>88/58</td>
<td>No recurrence of tumor</td>
<td>Post-pituitary surgery</td>
<td>HR</td>
</tr>
<tr>
<td>10</td>
<td>56</td>
<td>M</td>
<td>7 days</td>
<td>h/o pituitary surgery 10 yrs, fever and altered sensorium</td>
<td>-</td>
<td>-</td>
<td>GCS 10/15</td>
<td>74/54</td>
<td>Gliosis</td>
<td>Post-pituitary replacement</td>
<td>Hormonal replacement</td>
</tr>
<tr>
<td>11</td>
<td>59</td>
<td>F</td>
<td>10 yrs</td>
<td>Amenorrhea, generalised weakness, tiredness</td>
<td>+</td>
<td>+</td>
<td>Breast atrophy</td>
<td>90/60</td>
<td>Empty sella</td>
<td>SS</td>
<td>HR</td>
</tr>
<tr>
<td>12</td>
<td>41</td>
<td>F</td>
<td>3</td>
<td>Easy fatigability, body aches</td>
<td>+</td>
<td>+</td>
<td>Delayed DTR</td>
<td>102/78</td>
<td>Empty sella</td>
<td>SS</td>
<td>HR</td>
</tr>
<tr>
<td>13</td>
<td>35</td>
<td>F</td>
<td>5</td>
<td>Amenorrhea, generalised weakness, tiredness</td>
<td>+</td>
<td>+</td>
<td>WNL</td>
<td>120/76</td>
<td>Empty sella</td>
<td>SS</td>
<td>HR</td>
</tr>
<tr>
<td>14</td>
<td>28</td>
<td>F</td>
<td>1</td>
<td>Amenorrhea, tiredness</td>
<td>+</td>
<td>+</td>
<td>Delayed DTR</td>
<td>84/60</td>
<td>Empty sella</td>
<td>SS</td>
<td>HR</td>
</tr>
</tbody>
</table>


Results

Total fourteen patients of panhypopituitarism were diagnosed in the previous three years with average duration of symptoms 1.93± 1.96 years. Clinical profile of the patients has been tabulated in Table 1. Of fourteen patients, four (28.57%) were males and ten (71.43%) were females with mean age of diagnosis 37.78± 13.68 years (age range...
of them from >9000 feet altitude) and low socioeconomic background. Post-partum hemorrhage was present in all patients and 62.5% were home conducted deliveries. All patients had history of lactation failure and amenorrhea after the inciting delivery. Generalized weakness and easy fatigability was the commonest symptom at presentation with a mean duration of symptoms 2.39±1.54 years. The time between the previous obstetric event and diagnosis of Sheehan’s Syndrome was 1 to 21 years with a mean of 6.12±6.39 years. All eight (100%) female with SS had empty sella on MRI.

All patients were treated with oral hydrocortisone, levothyroxine. Except for two females (age>45), all were treated with oral contraceptive pills and one male was treated with testosterone. On follow-up (1-2 years after diagnosis) all were symptomatically and biochemically better. Growth hormone was not given because of cost, availability and storage problem.

Discussion

In this small retrospective study, we presented data of fourteen patients regarding spectrum of panhypopituitarism admitted at a tertiary care hospital having no service of endocrinologist. SS was the commonest cause of panhypopituitarism accounted for 57.14% followed by post-pituitary surgery for another 14.28%, whereas pituitary adenoma accounted only for 7.14% of all cases. Two largest published series of adult hypopituitarism from India by Gundgurthi et al and Chatterjee et al have shown pituitary adenoma followed by Sheehan’s Syndrome as the commonest cause of hypopituitarism in India. This study further supports the poor recognition of hypopituitarism other than those due to primary sellar tumors in clinical practice, hypopituitarism were diagnosed after admission in all fourteen patients in this study.

Advances in obstetric care in developed nations have led to rarity of SS as a cause of hypopituitarism. However, SS continues to be the most common cause of hypopituitarism in underdeveloped or developing countries. Though, there is scanty data on SS from India, a recent epidemiological study by Zargar et al from Kashmir valley has estimated the prevalence about 3 percent. Sheehan’s Syndrome most often evolves slowly and the diagnosis of SS delayed for several years after the inciting delivery. In various studies, the average time to make the diagnosis of SS after previous obstetric event was 13 to 16.35 years. However,
our study supported the shorter interval (average 6.0 years) between the previous obstetric event and diagnosis of SS. Unlike various previous studies in which patients with SS exhibit variable degree of hypopituitarism, this study support a recently published studies by Sert et al and Dokmetas et al in which all 28 and 20 patients of SS exhibit panhypopituitarism at the time of diagnosis. The diagnosis of SS in this study was based on PPH, lactation failure, amenorrhea after the last delivery and presence of empty sella on MRI imaging. The slow and progressive loss of pituitary hormones and vague or nonspecific symptoms in the initial years after inciting events probably explain the delay in the diagnosis of SS.

**Conclusion**

Sheehan’s syndrome is not uncommon in developing countries and mostly remained unrecognized due to lack of awareness among primary care physicians coupled with non-availability of endocrine specialized investigations. High degree of clinical suspicion is of paramount importance, as clinical features are most often subtle and many years may pass before diagnosis is suspected. History of post-partum hemorrhage, failure of lactation and amenorrhea are important clues for the early diagnosis. Timely replacement of deficient hormones is required lifelong with the primary goals of treatment centered on restoration of normal activities and better quality of life.

**References**