BRIEF RESEARCH COMMUNICATION

Hypopituitarism: A Rare but Often Neglected Condition

Divendu Bhushan[1], Mukta Agarwal[2], Rahul K Shukla[3]

Abstract

Pituitary insufficiency is an uncommon disorder. The most common cause is compression due to a pituitary mass. Other causes include inflammatory damage and vascular injury like postpartum pituitary apoplexy. Postpartum pituitary apoplexy, also known as Sheehan's syndrome, leads to hormonal deficiencies and causes postpartum amenorrhea, lactational failure, chronic hyponatremia, hypoglycemia, and loss of secondary sexual characters. Here we are discussing the clinical course of 15 female patients of panhypopituitarism. Most of them had a history of postpartum hemorrhage. Knowledge about this entity is essential as it is a treatable condition and ignorance could prove to be fatal.

Keywords: Lactation failure, Panhypopituitarism, Recurrent hyponatremia, Secondary amenorrhea.

Indian Journal of Critical Care Medicine (2020): 10.5005/jp-journals-10071-23422

Introduction

Hypopituitarism is defined as deficiency of one or more hormones secreted from the anterior pituitary gland. Vascular injury is an important cause after sellar and parasellar mass compression. Postpartum pituitary apoplexy, as a result of postpartum hemorrhage, is an endocrine emergency, which is not uncommon to find in developing countries where facility of institutional deliveries is still in the struggling phase. Pituitary is a highly vascularized organ and its size and vascularity increases in pregnancy. Lack of institutional deliveries, postpartum hemorrhage (PPH), and unavailability of blood and blood products are common culprits for increased incidence of Sheehan's syndrome in developing countries. The effect of acute deficiency of pituitary hormones may persist for long and causes much morbidity to the patients in long-term.[1] The long-term effects of deficient hormones cripple the patient for years and may even lead to death. Here we are presenting 15 cases of the Sheehan's syndrome of which two succumbed to their illness.

Aims and Objectives

- To know the different presentations of pan-hypopituitarism.
- To know the prevalence of undiagnosed Sheehan's syndrome in our part of the world.
- To assess the improvement with treatment in diagnosed hypopituitarism patients.

Materials and Methods

The present study was done at a tertiary care center of Eastern India, catering mainly to rural and semiurban population. The study duration was five years (2013–2018).

Inclusion Criteria

All females presented with seizures, unconsciousness, hypotension, hyponatremia, and hypoglycemia, which on further evaluation were found to have pituitary hormone deficiency, may or may not be Sheehan's syndrome.

Exclusion Criteria

- Male hypopituitarism
- Any alternative diagnosis that was presented with same clinical profile

[1,3]Department of General Medicine, All India Institute of Medical Sciences, Patna, Bihar, India

[2]Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, Patna, Bihar, India

Corresponding Author: Divendu Bhushan, Department of General Medicine, All India Institute of Medical Sciences, Patna, Bihar, India, Phone: +91 9661216010, e-mail: divendub@gmail.com

How to cite this article: Bhushan D, Agarwal M, Shukla RK. Hypopituitarism: A Rare but Often Neglected Condition. Indian J Crit Care Med 2020;24(5):350–352.

Source of support: Nil

Conflict of interest: None

All patients presented with symptoms of altered sensorium, seizures, recurrent vomiting, anemia with hypotension (mean arterial BP < 70 mm Hg), and hyponatremia (serum sodium less than 135 mEq/L) were included in the study. Other common causes of hyponatremia like drug-induced, volume depletion, and decreased sodium intake were ruled out. These patients were further subjected to serum TSH, FT4, cortisol, FSH, and LH estimation. Patients with decreased serum FSH, LH and cortisol, FT4, and normal or slightly raised serum TSH were diagnosed as hypopituitarism. Retrospectively, when these patients were asked about their obstetric history in detail, all except one patient revealed a positive history of PPH and lactation failure. There was history of blood transfusion in five patients out of 15 enrolled patients.

Results

During the defined time period, we enrolled a total 15 patients of female pan-hypopituitarism, which were discussed in detail here. Five patients were excluded from the study (one male hypopituitarism, two patients had drug-induced hyponatremia, and two patients were diagnosed as case of sepsis with sick euthyroid syndrome.)

It is important to note that 12 out of 15 hypopituitary cases presented in emergency room, and history of multiple hospital admissions was present in 4 patients, where despite diagnosing

hypothyroidism, the condition remained undiagnosed and patients demographic profile of patients described in Table 1.

We diagnosed 15 cases of panhypopituitarism in last 5 years. Most of them ($n = 12$) presented in emergency department due to one of the fatal complication of this illness (Fig. 1). Age of patients ranged from 31 to 61 years (mean = 42 years). The average time between last postpartum amenorrhea and present complaints was 20 years. Most of them ($n = 10$) had a history of excessive PPH. Five of them had home delivery, and rest had hospital deliveries. There was a history of blood transfusion during the postpartum period in four cases. No patient was diagnosed to be having pituitary insufficiency during her postpartum period. Two of these patients were diagnosed about pituitary insufficiency in the recent past, but they left the treatment by their own. Patients with history of PPH had a history of postpartum amenorrhea and lactational failure, except one who had excessive bleeding after second-trimester abortion. Presenting symptoms were extreme lethargy, recurrent hyponatremia causing decreased sensorium, hypoglycemia, and weight loss in decreasing frequency (Table 2). Clinically all patients had low normal blood pressure except one who presented with refractory shock. The mean pulse rate at presentation was 64 minutes. All had loss of secondary sexual characters like loss of pubic and axillary hair and breast atrophy. Most of them had fine facial wrinkling especially at corner of eyes (Fig. 2A).

Indications for admissions from the emergency department ($n = 12$) were hyponatremia, altered sensorium, hypoglycemia, seizure, and refractory shock in decreasing order (Fig. 1). All of them get admitted to the intensive care unit. On investigation, mean hemoglobin, total leukocyte count, and platelet count were 11.2 g% (range 8–11.9), 4300 cumm (2,350–10,180), and 84,000 cumm (range 10,000–201,000) respectively. Mean blood urea and creatinine were 49.5 mg% and 1.6 mg%, respectively. Two patients had acute kidney injury at presentation. Mean serum sodium, potassium, and glucose were 123 mEq/dL, 5.1 mEq/dL, and 84 mg%, respectively. There was one patient who had history of hyponatremia and rapid correction of which causes extrapontine myelinolysis. On 6 month follow-up her limb movements improved but dysarthria persisted. One patient with recurrent hyponatremia and vomiting found to have autoimmune pancreatitis. We investigate her for infiltrative diseases like IgG4-related disease and sarcoidosis, but all investigations were negative.

Mean serum TSH, FT4, and FT3 were 2.32 IU/mL, 0.20 ng/dL, and 1.01 pmol/L, respectively. Low in FT4 and FT3 along with low, normal, or slightly high TSH is suggestive of secondary hypothyroidism inappropriate setting. Mean serum cortisol (morning fasting) was 2.1 µg/dL (Table 3). Serum LH, FSH, and prolactin were below normal range in all except one who presented post-abortion. It may

Table 1: Demographic profile of patients. All patient's age range between 31 years and 61 years with mean age of patients was 42 and interval since last child birth was 20 years

Parameter	*No. of patients (n = 15)*	*Percentage*
Age		
20–30 years	1	6.7
30–40 years	5	33.3
40–50 years	5	33.3
>50 years	4	26.7
Interval since last delivery		
<10 years	5	33.3
>10 years	10	66.7
Residence		
Rural	11	73.3
Urban	4	26.7

Table 2: Symptoms of patients (total no of patients: 15)

Symptoms	*n (no. of patients)*
Lethargy	13
Recurrent hospital admission	10
Postpartum amenorrhea	10
Lactational failure	10
Decreased secondary sexual characters	13
Alopecia	7
Weight loss	8
Weight gain	4
Emotional slowness	6
Recurrent hyponatremia	8
Recurrent hypoglycemia	3

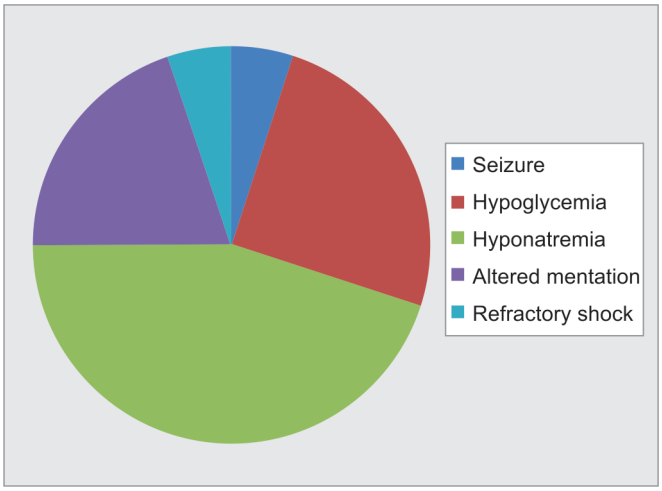
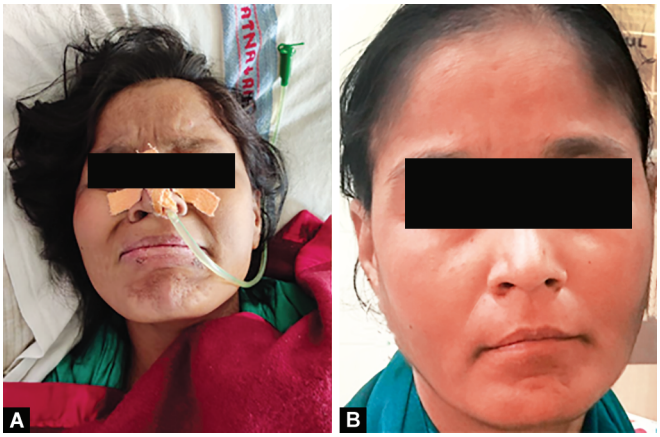


Fig. 1: Presenting symptoms of the admitted patients through emergency room



Figs 2A and B: (A) Patient at admission diagnosed to have hypopituitarism, had facial wrinkling, emotional liability; (B) 2 months after treatment

Table 3: Investigations of all patients

Parameter	*Range*	*Mean*
Mean arterial pressure (mm Hg)	40–110	94
Serum sodium (mEq/L)	101–132	123
Serum TSH (IU/mL)	1.04–6.47	2.32
Serum FT4 (ng/dL)	0.08–1.4	0.20
Serum cortisol (µg/dL)	1.19–3.1	2.1

Table 4: Patient's outcome with treatment

Parameter	*No. of patients (n = 15)*	*Percentage*
Improvement in symptoms	13	86.7
Did not survive	2	13.3

be due to partial deficiency of hormones. The MRI of all patients showed empty sella. Two patients did not survive: one who had resistant shock and another, acute renal failure leading to anuria, metabolic acidosis, and death (Table 4). Rest all survived well and are in regular follow-up. There is marked improvement in general activity, blood pressure, dyselectrolytemia, and facial coarsening of patient (Fig. 2B).

Discussion

The diseases that affect multisystem and chronic in nature are difficult to diagnose. Sheehan's syndrome is one of them. In a study of 60 patients, the average period between last obstetrical event and recognition of the disease is about 13 years.[2] In our research, it is 20 years long period. It usually presented as a lactational failure or failure to resume menses. But quite often these are overlooked. Presentations vary from person to person and many a times patient lands up in the emergency department for hypoglycemia, seizure, altered sensorium, and unexplained shock. Although the acute presentation is rare, clinical features depend upon a mixture of hormonal deficiencies. The most common presentation is lethargy, drowsiness, and slow speech. Although most patients with history of PPH have postpartum amenorrhea and lactational failure, they did not seek physician opinion for this. The reason may be that lactational failure can be considered due to various effects like mother's general condition and poor nutrition status. Most of the patients are multipara, so perhaps they are not varied about the missing periods. Even they might take it as a boon that if there are no menses, there will not be any chance of getting pregnant again. Lethargy can be contributed by hypothyroidism, GH, and cortisol deficiency. Hyponatremia is caused by hypothyroidism, cortisol deficiency, and diabetes insipidus.[3] In adults, deficiency of GH hormone is less well appreciated. It can lead to increased adiposity, lethargy, and fine facial wrinkling.[4] Deficiency of LH and FSH leads to secondary amenorrhea. The absence of amenorrhea does not rule out the diagnosis.[5,6] Biochemically hypoglycemia is also a common finding, caused by cortisol and GH deficiency.[7] Other rare presentations are congestive cardiac failure, acute renal failure, and focal neurological deficit.[8,9] Anemia, thrombocytopenia, and pancytopenia were also reported in decreasing frequency. Here in our study, only one patient presented with pancytopenia who recovered fully on replacing glucocorticoid and thyroid hormone.[1] Important causes of mortality are shock, cardiovascular events, hypoglycemia, and acute renal failure.

Treatment includes supplementation of hormones required for sustaining life. This includes thyroid and cortisol replacement. Cortisol replacement should be done before thyroid because otherwise adrenal crisis can precipitate.[10] Replacing sex steroid is essential if fertility is desired. Treatment with recombinant GH is not recommended to all patients. The exact mortality rate is not known, but if diagnosis or treatment delayed, then mortality can occur.

Conclusion

We should screen patients for pituitary insufficiency who are presenting with recurrent hyponatremia, hypoglycemia, low blood pressure, and extreme lethargy.

References

1. Shivaprasad C. Sheehan's syndrome: newer advances. Indian J Endocrinol Metab 2011;15(Suppl 3):S203–S207. . Available from: http://www.ncbi.nlm.nih.gov/pubmed/22029025.
2. Gei-Guardia O, Soto-Herrera E, Gei-Brealey A, Chen-Ku C. Sheehan syndrome in Costa Rica: clinical experience with 60 cases. Endocr Pract 2011;;17(3):337–344. . Available from: http://journals.aace.com/doi/abs/10.4158/EP10145.OR.
3. Bunch TJ, Dunn WF, Basu A, Gosman RI. Hyponatremia and hypoglycemia in acute Sheehan's syndrome. Gynecol Endocrinol 2002;16(5):419–423. DOI: 10.1080/gye.16.5.419.423. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12587538.
4. Keleştimur F. GH deficiency and the degree of hypopituitarism. Clin Endocrinol (Oxf) 1995;42(4):443–444. DOI: 10.1111/j.1365-2265.1995.tb02659.x. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7750202.
5. Keleştimur F. Sheehan's syndrome. Pituitary 2003;6(4):181–188. DOI: 10.1023/B:PITU.0000023425.20854.8e. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15237929.
6. Huang YY, Ting MK, Hsu BR, Tsai JS. Demonstration of reserved anterior pituitary function among patients with amenorrhea after postpartum hemorrhage. Gynecol Endocrinol 2000;14(2):99–104. DOI: 10.3109/09513590009167667. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10836196.
7. Kumar N, Singh P, Kumar J, Dhanwal DK. Recurrent hypoglycaemia: a delayed presentation of Sheehan syndrome. BMJ Case Reports 2014;2014:bcr2013200991. . Available from: http://www.ncbi.nlm.nih.gov/pubmed/24842349.
8. Laway B, Allaqaband F, Kotwal S, Wani I, Banday K, Bhat M. Acute renal failure: a rare presentation of Sheehan's syndrome. Indian J Endocrinol Metab 2012;16(2):306. DOI: 10.4103/2230-8210.93777. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22470876.
9. Raina S, Jearth V, Sharma A, Sharma R, Mistry K. Postpartum pituitary apoplexy with isolated oculomotor nerve palsy: a rare medical emergency. J Neurosci Rural Pract 2015;6(4):598. DOI: 10.4103/0976-3147.165348. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26752912.
10. Zeni D, Rissetti G, Ongaratti B, Pereira-Lima JF, Rech CGSL, Oliveira M da C. Evaluation of treatment of central hypothyroidism vs primary hypothyroidism in relation to levothyroxine replacement dose. Endocr Pract 2019;25(7):663–668. DOI: 10.4158/EP-2018-0533. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30865544.