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Case Series

Hypopituitarism Presenting as Heart Failure-A Case Series

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ABSTRACT

Hypopituitarism, an uncommon endocrine disorder, presents a diagnostic challenge due to its variable and often vague manifestations. It can have severe, life-threatening complications including heart failure. In this case series, we reported five cases with hypopituitarism presented as heart failure, each exhibited unique etiologies and presentations. Out of these, two cases were associated with Sheehan's syndrome, two with Empty Sella Syndrome, and one with isolated ACTH deficiency. Clinical evaluation, hormonal assays, and imaging studies were instrumental in confirming diagnoses. Hormone replacement therapy led to symptomatic and functional cardiac recovery in these patients, highlighting the importance of considering hypopituitarism in cases of unexplained heart failure. This series emphasizes early recognition and appropriate treatment of hypopituitarism to prevent significant morbidity and mortality.

Keywords: Cardiomyopathy, Cortisol, Empty Sella, Growth Hormone, Heart Failure, Hypopituitarism, Panhypopituitarism, Pituitary Gland.

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INTRODUCTION

Hypopituitarism is an infrequent problem encountered by physicians, world over. However, it is to be kept in mind that its diagnosis poses a formidable challenge for most clinicians because of its varied etiology and presentation which is usually vague and nonspecific thus, eluding the real diagnosis for quite some time. The presentation is variable and late cases may be seen due to partial ischemic injury of the pituitary gland and gradual loss of endocrine function. It is important to pick the illness well in time to avoid unnecessary morbidity and mortality.[1] The prevalence of this disease has been estimated at 45 cases per 100000 population.[2] Heart failure (HF) is an uncommon but treatable complication of untreated hypopituitarism and it is imperative to consider it as a cause of unexplained congestive cardiac failure in a young patient. Five cases are presented here, out of which two appeared most likely to be due to Sheehan's syndrome (SS), two due to Empty Sella Syndrome and in one the etiology appeared to be isolated ACTH deficiency. In two cases, mild left ventricular dysfunction was found (those due to SS) and clinically they presented with signs of incipient HF.

METHODOLOGY

This case series included a total of five case reports collected from patients diagnosed with hypopituitarism presenting as HF. Cases 1,2 & 5 were reported at Military Hospital, Rawalpindi, and cases 3 & 4 reported at POF, Hospital, Wah Cantt. Cases were selected based on hypopituitarism linked to cardiac complications. Patients with clinical and laboratory evidence of hypopituitarism alongside cardiac symptoms were included in the study, while patients with other primary cardiac diseases were excluded.

Each patient underwent a detailed diagnostic and therapeutic process. Standardized procedures common to all cases included clinical evaluations for signs and symptoms of hypopituitarism and HF, as well as imaging and laboratory tests to confirm hormone deficiencies. Routine diagnostic tools used included MRI imaging of the pituitary gland, echocardiography to assess cardiac function, and a range of hormone assays measuring cortisol, ACTH, TSH, LH, FSH, and prolactin levels. These laboratory investigations were instrumental in confirming hypopituitarism and assessing the endocrine status of each patient. When indicated, additional tests, such as a short Synacthen test, were employed to further evaluate adrenal function.

Ethical standards were maintained throughout the study, adhering to institutional guidelines. Written informed consent was obtained from each patient prior to data collection, including consent for publication of de-identified information in a case

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series format. Treatment protocols were tailored according to each patient's specific clinical condition. Thyroxine, hydrocortisone, and, where needed, estrogen-progesterone replacement were administered, dosages were adjusted based on regular follow-up lab tests and clinical evaluations to optimize recovery and minimize the risk of adverse outcomes. All patients received follow-up to assess the impact of therapy on both cardiac and endocrine health outcomes.

CASE:1

A 40 years old lady presented with complaints of weakness, lethargy and lack of interest in day-to-day activities as a house wife for 6 years. Her menses had ceased about six years back after the home delivery of her last child during which she had excessive bleeding. She had been treated by a physician in her home town but had shown no improvement. Examination revealed lack of normal effect and delayed relaxation of the tendon jerks. Blood pressure revealed a postural drop of 30 mmHg.

Laboratory values have been presented in Table-I

Her echocardiography revealed mild left ventricular dysfunction with ejection fraction (EF) of 45%. She was finally diagnosed as suffering from Sheehan's syndrome. She was placed on a replacement regimen of Thyroxine 150 ug per day and Prednisolone 7.5 mg per day orally to which she remarkably responded. Her left ventricular function returned to normal after six months.

CASE:2

A 53 years old lady presented with five years history of vague complaints. She had been on Dothiepin hydrochloride 75 mg per day for the last five years without any benefit. Examination revealed hypothyroid features, lying systolic blood pressure of 80 mmHg and diastolic blood pressure of 10 mmHg, with a postural drop of 20 mmHg. She had four children the youngest being 20 years old. There was no history of post-partum haemorrhage and she had breast fed all her children. She was amenorrheic for the last 12 years. Her left ventricular function on 2D echocardiography was only mildly reduced with EF of 50%. Imaging with MRI showed an enlarged Sella Turcica with no visible pituitary tissue, confirming the diagnosis of primary empty Sella Syndrome (Figure-1a). A plain X-ray of the pituitary fossa also demonstrated increased dimensions, consistent with the MRI findings (Figure-1b). Laboratory values have been presented in Table-I.

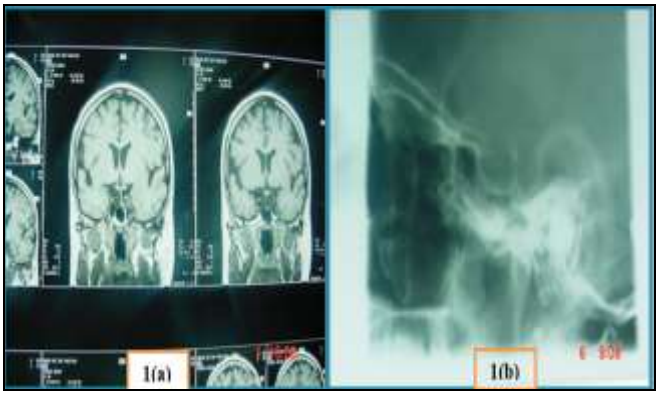

Figure (1a): MRI Brain and Pituitary Gland (No Pituitary Tissue, Enlargement of Sella) (1b): Plain X-ray Pituitary Fossa (Increased Dimensions of Pituitary Fossa)

She was prescribed Thyroxine 150 ug per day, Prednisolone 7.5 mg per day and estrogen progesterone oral contraceptive pill. Subsequent to the replacement therapy she made a good symptomatic recovery. Her mild LV systolic dysfunction also returned to normal after 3-months.

CASE:3

A 70 years old male presented with history of dyspepsia, backache and generalized weakness of about 10 years duration. Physical examination revealed severe orthostatic hypotension, with blood pressure dropping from 70 mmHg systolic when lying down to 40 mmHg upon standing. There was no hyperpigmentation in the buccal mucosa or over the skin. Rest of the examination was unremarkable.

Keeping in view the possibility of hypo-adrenalism some laboratory values were obtained which have been presented in Table-I.

MRI of the pituitary could not be done as he developed atrial fibrillation during the course of investigations. 2D-echocardiography revealed pre-served LV systolic function with ejection fraction of 50%.

Keeping in view his impaired short Synacthen test in mind he was administered prednisolone in a dose of 5 mg per day to which he showed good symptomatic improvement as reduction of his pulse pressure from 30 mmHg to 10 mmHg. This appeared to be a case of partial hypopituitarism with isolated ACTH deficiency. His LV systolic function improved with EF rising to 55%.

Table I: Laboratory and Clinical Findings of Cases

Test		Case-1	Case-2	Case-3	Case-4	Case-5
ACTH (9AM) (pg/ml)		-	10	43.6	17.4	10
Cortisol (9 AM) (ug/dl)		1.7	Undetectable	4.2	5.69	0.83
FSH (mIU/ml)		9.60	1.2	9.51	6.7	< 0.1
LH (mIU/ml)		2.80	1.7	6.8	1.7	0.2
Prolactin (ng/ml)		-	6.95	5.04	1.04	-
TSH (mIU/L)		2.63	3.73	0.224	4.4	0.35
T3(ng/ml)		0.42	0.50	1	0.63	0.70
T4 (ng/ml)		20.66	23.40	70.4	0.445	33.40
Short Synacthen Test	S Cortisol Baseline (ug/dl)	-	Cortisol was undetectable	2.4	-	-
	S Cortisol 30 min (ug/dl)	-		10.4	-	-
	S Cortisol 60 min (ug/dl)	-		13.6	-	-
Random Blood Glucose (mmol/L)		-	-	-	3.8	-
Urea (mmol/L)		-	-	-	4.2	-
Creatinine (µmol/L)		-	-	-	109	-
Sodium (mmol/L)		-	-	-	138	-
Potassium (mmol/L)		-	-	-	4.1	-
DHEA-S (µg/dL)		-	-	-	15	-
Growth Hormone (Basal) (mIU/L)		-	-	-	0.2	-
USG Pelvis		-	-	-	Atrophic uterus and ovaries	-
Dexa Scan		-	-	-	Osteoporosis	-
MRI Brain and Pituitary		-	-	-	Empty Sella with CSF intensity signal in the pituitary fossa, reduced gland size	Reduced in size
Echocardiographic Findings		EF:45%	EF:50%	EF:50%	EF:43%	Preserved EF

FSH=Follicle-Stimulating Hormone; LH=Luteinizing Hormone; TSH=Thyroid Stimulating Hormone; T4=Thyroxine; T3=Triiodothyronine; DHEA-S=Dehydroepiandrosterone Sulfate; USG=Ultrasonography; MRI=Magnetic Resonance Imaging

CASE:4

A 30 years old house wife presented with progressive vague ill health weakness, easy fatigability, shortness of breath and inability to cope with daily activities for the last five years and aggravation of these complaints for the last one year. On examination she looked pale, somewhat dyspneic and was unable to sit unsupported. She had been brought to the hospital on a stretcher with a Folley's catheter in situ. She had ceased menstrual cycles for the last ten years. Her blood pressure was 80/60 mmHg and chest auscultation revealed basal crepitations. The relaxation phase of tendon jerks was delayed suggesting hypothyroidism. Her echocardiography showed EF of 43%. Keeping the possibility of pituitary insufficiency due to low blood pressure and amenorrhea she was administered Tab Dexamethasone 0.75 mg per day followed by oral Thyroxine 50 ug per day due to her precarious condition after drawing blood for laboratory tests. Her investigations have been depicted in Table-I.

Her general condition improved as she was discharged home while taking Tab Hydrocortisone 20 mg per day, Tab Thyroxine 100 ug per day, Tab Vitamin D and calcium (elemental) 125 IU and 500 mg per day respectively along with estrogen/progesterone replacement. Her left ventricular function recovered after six months. At 10 months of follow-up, she was doing well and returned to a normal life. She recalls having severe post-partum haemorrhage at the time of her second delivery about ten years back. Hence, she was a case of Sheehan's syndrome.

CASE:5

A 54 years old woman presented to the emergency department with history of loss of consciousness. She was initially evaluated at another tertiary care hospital where routine evaluations including CT scan brain were unremarkable. There was no previous medical history of note neither was she a diabetic. She had not been on any medication. Preliminary evaluation at the second hospital revealed hypoglycemia, which was promptly corrected. However, following the correction of hypoglycemia, her condition remained unchanged. Hypopituitarism was suspected and investigations to that effect

initiated. Pending the results of the investigations she was treated with intravenous hydrocortisone and Thyroxine through nasogastric tube to which she favorably responded. Details of laboratory findings have been given in Table-I.

She was discharged home with advice to take Hydrocortisone tablets 10 mg in the morning 5 mg in the afternoon and 5 mg in the evening. Thyroxine was advised in a dose of 100 ug per day.

Hydrocortisone is used for ACTH deficiency and now it is recommended to give 10 mg in the morning, 5 mg in the afternoon and 5mg in the evening. The dose of hydrocortisone has to be increased during stressful situations. The patients and the healthcare team should be trained to increase the dose in special situations like prolonged exercise, surgery, vomiting and diarrhea and during pregnancy. Thyroxin is used for TSH deficiency starting at a dose of 100 ug per day. In elderly and patients with ischemic heart disease the initial dose is 25 ug per day. The treatment regimen may have to be modified during transition from childhood to adulthood and during pregnancy. In primary adrenal failure mineralocorticoid deficiency has to be corrected whereas in secondary hypopituitarism it is not required. Overdosing with steroids can lead to osteoporosis, deranged glucose metabolism and increased cardiovascular mortality. About 95% of orally administered hydrocortisone is bioavailable and peak serum levels are achieved after about one hour. It is mandatory to exclude adrenal insufficiency before initiating thyroxin therapy because this can lead to acute adrenal crisis if this is overlooked. Thyroxin should be given in the morning before breakfast.

DISCUSSION

Hypopituitarism, marked by partial or complete hormone loss, typically requires >75% pituitary damage for symptoms to appear. Though rare, it presents diagnostic challenges and is linked to high cardiovascular morbidity and mortality. In this case series, cases 2&5 and 1&4 were due to Empty Sella Syndrome and SS respectively, improved with Thyroxin and prednisolone, and case-3 due to isolated ACTH deficiency. The series underscores the need for vigilance in diagnosing endocrine disorders, especially in unexplained HF patients.

Sheehan's disease is prevalent in less developed regions,[3] linked to factors like increased pituitary volume during pregnancy, small Sella size, coagulopathy, and autoimmunity.[4] Our cases aligned with findings by Giri *et al.*,[5] where delayed diagnosis followed severe postpartum hemorrhage, showing hypopituitarism's gradual progression. Unlike a published case with preserved menstruation and spontaneous pregnancies, our patients exhibited typical reproductive dysfunction, reflecting the syndrome's variability. Timely hormone replacement therapy led to significant improvement, highlighting the importance of vigilance and individualized follow-up in postpartum-hemorrhage patients.

Despite symptomatic improvement with treatment, cardiovascular mortality remains high in hypopituitarism,[6] primarily due to growth hormone deficiency (GHD) and cardiomyopathy, as adrenal insufficiency, hypothyroidism, and GHD independently contribute to HF.[7] Hypothyroidism reduces myocardial contractility, output, and heart rate while increasing vascular resistance, and hypoadrenalism causes hypovolemic hypotension. GHD, especially from childhood, decreases LV wall thickness and mass, raising cardiovascular risk. In our series, LV dysfunction resolved fully with hormone therapy, aligning with reports of its cardiomyopathy reversal and cardiac function restoration.

Further comparison to a case by Yoshino *et al.*[8] involving a 77-year-old woman with decompensated HF due to secondary hypothyroidism and hypopituitarism, showed symptom improvement after targeted hormone replacement therapy. This mirrors our cases, where cardiac dysfunction was linked to endocrine disorders. Both cases initially stabilized with conventional HF treatments, but symptoms persisted until the underlying endocrine disorder was identified and treated. This highlights the need to consider hormonal deficiencies in managing HF, especially with atypical presentations. While our cases involved various comorbidities, Yoshino's patient improved largely due to hormone replacement, stressing the importance of addressing endocrine causes.

Similarly, a published case,[9] of a 42-year-old male with HF due to Panhypopituitarism and empty Sella syndrome compares to our empty Sella syndrome cases. Similar to our case, the patient had severe cardiovascular symptoms, including reduced ejection fraction, and showed significant improvement after hormone replacement therapy, highlighting the efficacy of endocrine treatment for hypopituitarism-related cardiac dysfunction. While the male required testosterone for hypogonadism, our female patients

did not, reflecting sex-specific treatment differences. Additionally, the presence of hereditary hemochromatosis in this case emphasizes the need for comprehensive assessments in hypopituitarism cases with HF.

The cited case of hereditary hemochromatosis emphasizes assessing comorbidities in hypopituitarism with HF, as they impact treatment and prognosis. Clinicians should suspect hypopituitarism in unexplained HF, especially with risk factors like postpartum hemorrhage. Prompt endocrine evaluation and hormone replacement therapy can significantly improve cardiac function, as shown in the cited case and our patients,[10] highlighting the importance of early diagnosis and treatment in reversing hypopituitarism-associated cardiomyopathy followed by improved outcomes.

Conclusively, our case series highlighted the critical, yet often under-recognized, relationship between hypopituitarism and reversible heart failure. Prompt diagnosis and targeted hormone replacement therapy led to significant clinical and cardiac recovery in all cases, emphasizing the need for heightened awareness of hypopituitarism as a differential diagnosis in unexplained heart failure. Early endocrine intervention can mitigate severe complications, underscoring its clinical importance in improving patient outcomes.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript:

IA & AHS: Study concept, study design, drafting the Case series, approval of the final version to be published

AS: Study concept, data acquisition, critical review, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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