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Case Series

Internal Medicine Section

Panhypopituitarism following Haemotoxic Snake Envenomation: A Case Series Emphasising Early Diagnosis

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ABSTRACT

Snake envenomation remains a significant health problem in tropical regions. Haemotoxic snake bite commonly causes Acute Kidney Injury (AKI) and coagulopathy; however, panhypopituitarism is rare and frequently overlooked. Delayed diagnosis may result in serious morbidity due to unrecognised adrenal/thyroid insufficiency. This case series describes the clinical presentation, hormonal profile, radiological findings, and outcomes of four patients who developed panhypopituitarism following haemotoxic snake envenomation, highlighting the importance of early diagnosis. Patients presented within weeks to months after the snake bite with features such as fatigue, hypotension, hyponatraemia, and hypoglycaemia. Hormonal evaluation revealed secondary adrenal insufficiency and central hypothyroidism in all cases, with associated secondary hypogonadism in some patients. Magnetic Resonance Imaging (MRI) of the pituitary demonstrated features consistent with empty sella syndrome. All patients received appropriate hormone replacement therapy, resulting in significant clinical and biochemical improvements. A high index of suspicion is required, and early endocrine evaluation should be carried out in patients with persistent or unexplained symptoms following envenomation. Timely diagnosis and hormone replacement therapy can lead to favourable outcomes.

Keywords: Adrenal insufficiency, Capillary leak syndrome, Central hypothyroidism, Pituitary apoplexy, Viper bite

INTRODUCTION

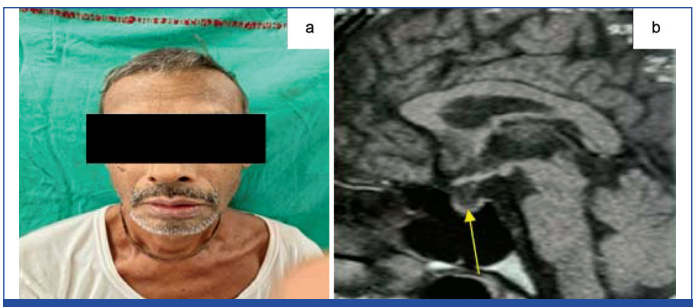
Snake bite envenomation remains a major public health challenge in major tropical countries of the world, including India, where Russell's viper is responsible for most haemotoxic bites and accounts for considerable morbidity and mortality [1,2]. AKI develops in approximately 20-30% of haemotoxic envenomations [3,4]. While renal and haematological complications are well recognised, endocrine consequences, particularly pituitary dysfunction, remain underdiagnosed despite their potential to significantly worsen outcomes. The pituitary gland is vulnerable to pituitary apoplexy following envenomation [5]. There is a scarcity of evidence documenting early pituitary dysfunction in patients recovering from snake bite envenomation. This case series aims to describe it.

Patients with clinical suspicion of panhypopituitarism, who attended our tertiary care centre between September and November 2025 and developed post-viper bite AKI, were included in this case series

CASE SERIES

Case 1

A 60-year-old male (a farmer by occupation from a rural area and a known hypertensive (on amlodipine 5 mg), sustained a haemotoxic viper snakebite over the right ankle and subsequently developed multiple episodes of vomiting and increasing local pain and swelling, prompting admission at the local hospital. The 20-minutes Whole Blood Clotting Time (WBCT) was non clotted, indicating coagulopathy. He received 30 vials of Anti-Snake Venom (ASV) administered in three cycles. Altered renal parameters (urea 71 mg/dL, creatinine 1.84 mg/dL) with reduced urine output suggested systemic envenomation. Then he was referred to our tertiary care centre. On day 2, he was diagnosed with AKI secondary to haemotoxic envenomation, he underwent five cycles of Haemodialysis (HD). On day 13, he was haemodynamically stable with Blood Pressure (BP) 120/80 mmHg, with improvement of renal parameters. He was discharged on day 14. Two weeks later (on day 28), he re-presented to our tertiary care centre [Table/Fig-1a] with persistent generalised weakness, reduced effort tolerance, and recurrent dizziness. On admission, his Blood Pressure (BP) was 80/60 mmHg with postural hypotension. By day 29, sustained hypotension without antihypertensive medication prompted an endocrine evaluation which revealed low morning serum cortisol, low Thyroid-Stimulating Hormone (TSH), low free thyroxine (FT4), and markedly reduced testosterone with suppressed Luteinising Hormone (LH), confirming multi-axis pituitary dysfunction. MRI of the hypothalamic-pituitary region revealed a completely empty sella [Table/Fig-1b]. These findings were consistent with secondary adrenal insufficiency, central hypothyroidism, and secondary hypogonadism, establishing a diagnosis of panhypopituitarism as an early endocrine complication of haemotoxic envenomation. He was initiated with injection hydrocortisone 100 mg twice daily for three days, followed by oral hydrocortisone 10 mg twice daily (6 AM and 4 PM) along with oral-thyroxine 75 µg supplementation, resulting in marked symptomatic improvement. He was discharged on oral hydrocortisone and l-thyroxine on day 33 of post-snake bite and advised to continue it. He was doing well as per routine Outpatient Department (OPD) follow-up visits and continuing his medications.

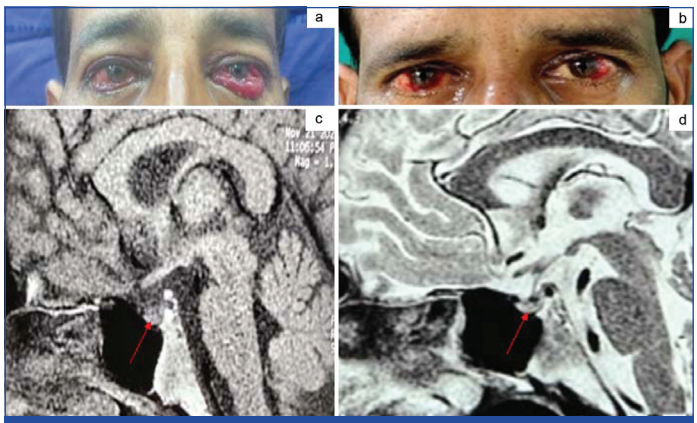


[Table/Fig-1]: a) Facial appearance not suggestive of typical panhypopituitarism; b) Magnetic Resonance Imaging (MRI) T1-weighted plain image of the hypothalamic-pituitary region showing a complete empty sella (yellow arrow).

Case 2

A 37-year-old male villager sustained a haemotoxic viper bite on the right hand and visited the local hospital within one hour of the bite. A 20-minute WBCT was non clotted twice, and he received 20 vials of ASV. He subsequently developed vomiting, conjunctival

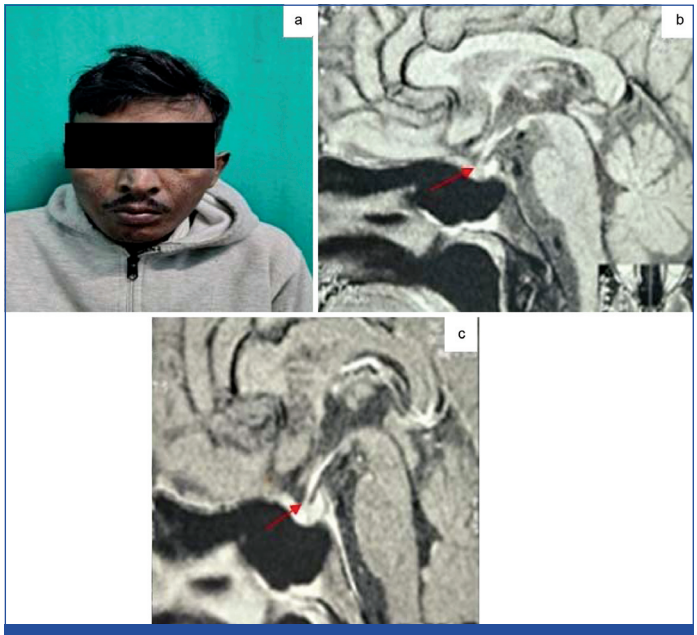
redness with oedema [Table/Fig-2a] and gross haematuria, and due to rapid progression of symptoms, he was referred to our tertiary care hospital with baseline urea 49.8 mg/dL and creatinine 1.2 mg/dL and admitted at emergency general medicine ward. On admission (day 2), his BP was 138/70 mmHg. As the 20-minute WBCT remained non clotted, urine analysis showed Red Blood Cells (RBCs); an additional 20 vials of ASV were given. On day 3, he developed oliguria, worsening coagulopathy requiring eight units of fresh frozen plasma, and respiratory distress with bilateral basal crepitations, prompting transfer to the Critical Care Unit (CCU) under general medicine department. Laboratory tests showed Na-131 mmol/L, K-4.2 mmol/L, urea-178 mg/dL, and creatinine-8.4 mg/dL. He was started on high-dose methylprednisolone (750 mg intravenous infusion once daily for 5 days) in view of capillary leakage syndrome and continued HD. Conjunctival signs [Table/Fig-2b] and urine output gradually improved, and the patient shifted to the emergency general medicine ward from CCU. During the hospital course on day 17, he developed sudden hypotension with a BP of 70/50 mmHg, requiring intravenous fluids. On day 18, he again experienced hypotension with palpitations and sweating, along with hypoglycaemia {random Capillary Blood Glucose (CBG) 47 mg/dL}, requiring 25% dextrose and initiation of inotrope infusion. Despite supportive therapy, his BP and glucose continued to fluctuate. Ongoing hypotension prompted an endocrine evaluation with morning cortisol, FT4, and TSH. Results were consistent with secondary adrenal insufficiency, central hypothyroidism, and central hypogonadism. An MRI of the hypothalamic-pituitary region revealed a partial empty sella [Table/Fig-2c,d]. Injection hydrocortisone 100 mg twice daily for three days followed by oral hydrocortisone 20 mg/day along with oral l-thyroxine 75 mcg/day was started. Over subsequent days, his haemodynamics improved steadily with BP 110/72 mmHg; inotrope was discontinued with normalisation of CBG. Gradually his urine output increased following dialysis, and creatinine began trending downward, allowing dialysis to be withheld. On day 29, he was haemodynamically stable with BP 110/70 mmHg, random CBG 110 mg/dL, off inotropes and i.v. fluids, and tolerating oral hydrocortisone 20 mg in two divided doses, and l-thyroxine 75 mcg/day and was discharged with instructions for follow-up after one week and then monthly. The patient was educated regarding the stress dose of hydrocortisone. On follow-up there was marked improvement of general wellbeing. He was treated with intramuscular testosterone ester (250 mg) every four weeks for the management of central hypogonadism.



[Table/Fig-2]: a) Haematotoxic viper snake bite shows conjunctival chemosis and congestion due to capillary leak syndrome (b) the resolving phase on day 14; c,d) Magnetic Resonance Imaging (MRI) of the hypothalamic-pituitary region showing a partial empty sella on T1 and T2 sequences (red arrows) respectively.

Case 3

A 36-year-old male [Table/Fig-3a] presented to the emergency department of nearest local rural hospital two hours after sustaining a Russell's viper snake bite over the left foot, with progressive local swelling and pain. At the local rural hospital, the 20-minute WBCT was non clotted. After receiving 10 vials of ASV, he was referred to our tertiary care hospital. His BP was 110/74 mmHg, Pulse Rate (PR) 90/min, and random CBG 128 mg/dL, but the repeat 20-minute WBCT remained non clotted, prompting additional 30-vial ASV administration. Baseline renal parameters were normal with urea at 21.37 mg/dL and creatinine at 0.76 mg/dL. On day 2, he developed AKI with urea 60.3 mg/dL and creatinine 2.35 mg/dL, requiring HD. On days 3 and 4, renal parameters worsened, with creatinine at 2.71 mg/dL. On day 5, he developed hypotension and hypoglycaemia with a random CBG of 56 mg/dL, requiring 25% dextrose. Due to clinical instability, he was shifted to the CCU. On Day 6, recurrent hypoglycaemic episodes occurred. On day 8, though urine output improved, conjunctival oedema and respiratory distress appeared, prompting initiation of i.v. methylprednisolone (750 mg intravenous infusion) for suspected capillary leak syndrome. By day 10, renal parameters were improved with increased urine output. Conjunctival oedema and respiratory symptoms resolved. On day 13, he became haemodynamically stable with BP 120/70 mmHg, PR 66/min, and random CBG 187 mg/dL and was hence shifted to the general ward, and HD was gradually withheld as renal recovery progressed. Two weeks after discharge (day 28), he was admitted to the medicine emergency with generalised weakness, dizziness, and reduced effort tolerance, with BP of 90/60 mmHg and the presence of a postural drop. Due to persistence of symptoms, a morning endocrine profile was sent which later revealed low cortisol; low FT4 with inappropriately low TSH; low fasting glucose (60 mg/dL); and hyponatraemia (131 mmol/L), confirming secondary adrenal insufficiency and central hypothyroidism. MRI of the hypothalamic-pituitary region showed a partial empty sella [Table/Fig-3b,c]. Panhypopituitarism was diagnosed following a haemotoxic envenomation and AKI-requiring HD. Oral hydrocortisone 15 mg/day (10 mg at 6 AM and 5 mg at 4 PM), followed by l-thyroxine 75 µg/day, was initiated, resulting in marked symptomatic and biochemical (normalisation of CBG and sodium) improvement. Patient was discharged on day 35 with stable vitals (BP: 112/70, PR: 82/min). He remains under regular follow-up at the medicine OPD.

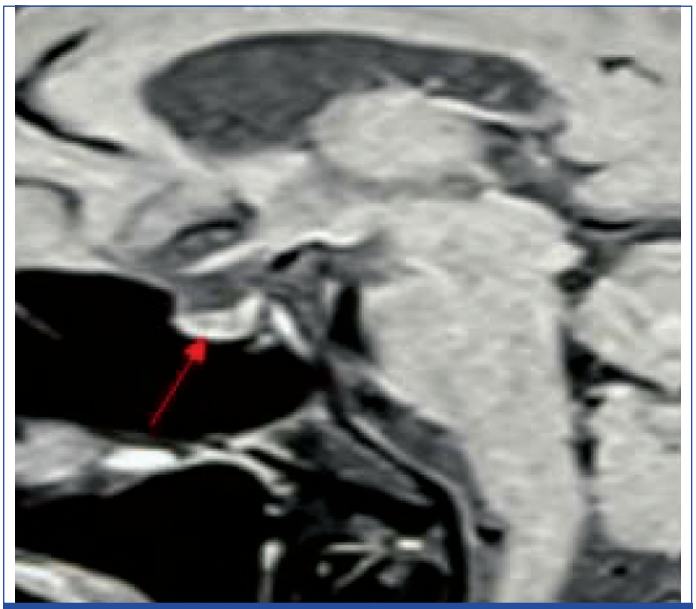


[Table/Fig-3]: a) Lack of typical panhypopituitarism in facial appearance; b,c) Magnetic Resonance Imaging (MRI) of the hypothalamic–pituitary region showing partial empty sella on T1 {b); red arrow} and T1-contrast images {c); red arrow}.

Case 4

A 49-year-old male, a daily wage worker, presented to the general medicine emergency department of our tertiary care hospital with intermittent fever with chills for the preceding three days. Fever was associated with dysuria, and increased frequency of micturition. He had a history of haemotoxic viper bite over right leg two months

prior, for which he was initially treated at a local hospital with 30 vials of ASV and subsequently referred to another tertiary care centre, where he developed AKI requiring multiple cycles of HD. During the hospital course (day 37 post-envenomation), he developed persistent hypotension with BP of 90/60 mmHg and recurrent hypoglycaemic episodes, necessitating hormonal evaluation and he was diagnosed with panhypopituitarism [Table/Fig-4]. He was treated with injection hydrocortisone 100 mg every 12 hourly and he improved clinically. His renal parameters became normal and was discharged on day 44 post snake bite). On discharge, he was advised oral hydrocortisone 25 mg/day in three divided doses (10 mg at 6 AM, 10 mg at 12 noon, and 5 mg at 5 PM) along with l-thyroxine 100 µg/day. After 13 days of discharge he developed fever with chills. He was not aware of stress-dose steroid supplementation and he missed the hydrocortisone dose during the recent febrile illness. He developed generalised weakness and dizziness for which he presented to general medicine emergency of our tertiary care institution (day 60 post snake bite). On examination, his vitals were unstable with BP 70/54 mmHg, PR 104/min, CBG 80 mg/dL. A clinical diagnosis of adrenal crisis in a known panhypopituitarism patient was made. The adrenal crisis was precipitated by a Urinary Tract Infection (UTI). He was managed with intravenous (0.9%) normal saline (NS) two litres bolus and followed by three litres of NS over 24 hours, injection hydrocortisone 100 mg bolus followed by 100 mg every six hourly, injectable broad-spectrum antimicrobials (piperacillin 4g and tazobactam 0.5g) intravenous eight hourly for UTI and oral l-thyroxine 100 mcg/day at the general medicine CCU. He improved gradually and was discharged after one week of admission (day 67 post snake bite) with oral hydrocortisone 25 mg/day in three divided doses (10 mg at 6 AM, 10 mg at 12 noon, and 5 mg at 5 PM), and l-thyroxine 100 mcg/day. He was counselled regarding stress dose of steroids.



[Table/Fig-4]: Magnetic Resonance Imaging (MRI) of the hypothalamic-pituitary region showing a partial empty sella (red arrow) on a T1-weighted plain image.

The summary of all four cases is shown in [Table/Fig-5].

Blood parameters					
Parameters	Case 1 (60 years, Male)[¥]	Case 2 (37 years, Male)	Case 3 (36 years, Male)	Case 4 (49 years, Male)	Reference range
Day after snake bite	Day 29	Day 18	Day 30	Day 37	
Sodium	140	128.60	131	134	136-146 mmol/L
Potassium	4.43	3.77	4.70	3.4	3.50-5.50 mmol/L
Creatinine	1.72	8.4	0.98	0.6	0.70-1.20 mg/dL
FT4[£]	0.50 ng/dL (0.78-2.19)	0.29 ng/dL (0.93-1.70)	0.397 ng/dL (0.7-1.79)	0.37 ng/dL (0.93-1.70)	
TSH	0.20	0.069	0.22	0.143	0.27-4.20 µIU/mL
8-9 AM serum cortisol	5.06	1.00	3.50	3.21	6.70-22.60 µg/dL
Prolactin	24.40	4.84	<0.50[€]	1.98	3.70-17.90 ng/mL
Fasting morning total testosterone	0.20	<0.08	13.11	ND	2.49-21.60 nmol/L
FSH	3.80	<0.30	4.60	ND	1.55-9.74 mIU/mL
LH	0.50	<0.10	5.43	ND	1.24-8.62 mIU/mL
Imaging					
MRI of hypothalamic-pituitary region	Complete empty sella [Table/Fig-1b]	Partial empty sella [Table/Fig-2c,d]	Partial empty sella [Table/Fig-3b,c]	Partial empty sella [Table/Fig-4]	

[Table/Fig-5]: Summary of relevant investigations from all the four cases.
FSH: follicle stimulating hormone; FT4: Free thyroxine; LH: Luteinising hormone; MRI: Magnetic resonance imaging; ND: Not done; TSH: Thyroid stimulating hormone; [¥]Age, and gender of the patient is mentioned within the third bracket "[]"; [£]Laboratory and assay specific FT4 reference ranges are mentioned within the first bracket "()"; [€]A prolactin concentration below the assay's lower limit of detection may be observed in pituitary apoplexy, likely reflecting extensive necrosis of lactotroph cells

DISCUSSION

Haemotoxic snake envenomation is a well-established cause of AKI, coagulopathy, and capillary leak syndrome in India [1-4]. The association between Russell's viper envenomation and hypopituitarism was systematically described by Antonypillai CN et al., who reported delayed pituitary dysfunction occurring in years after the bite [5]. Delayed hypopituitarism was documented in South Indian patients presenting with fatigue, hypotension, and hyponatraemia long after apparent recovery [6]. In contrast, this case series demonstrated that pituitary dysfunction can manifest as early as 2-6 weeks following the acute insult, substantially narrowing the previously accepted delayed window. However, some evidence from India indicates that pituitary dysfunction may occur much earlier, including during the acute hospitalisation or early recovery phase [7]. A case report documented early cortisol deficiency and central hypothyroidism following haemotoxic snake bite [8].

Hyponatraemia, hypotension, altered sensorium, and hypoglycaemia — hallmark features of adrenal and thyroid insufficiency — are often misattribute to AKI, dialysis-related metabolic fluctuations, or sepsis, resulting in delayed endocrine evaluation [3,6,8,9]. This is clinically significant because timely initiation of glucocorticoid and thyroid hormone replacement can be lifesaving and can rapidly stabilise haemodynamic and metabolic disturbances [10].

In line with the present series findings, endocrine dysfunction manifested during early recovery rather than years later, indicating a shorter temporal course of pituitary insult. The present study observations are further supported by Bhat S et al., who identified AKI-requiring dialysis and severe vasculotoxicity (capillary leak syndrome, as in case 2, case 3) as strong predictors of subsequent hypopituitarism [11]. Notably, all patients in this series required renal replacement therapy in the form of HD, confirming that AKI requiring HD is a strong clinical predictor of subsequent panhypopituitarism [8,11].

From a pathophysiological view, pituitary injury has been attributed to microvascular thrombosis, disseminated intravascular coagulation, hypotensive ischaemia, and capillary leak, which were present in the present study patients also [5,6]. This mechanism closely mirrors the ischaemic necrosis described in Sheehan's syndrome and explains the predominance of secondary adrenal insufficiency and central hypothyroidism observed in the present cases.

With respect to imaging, previous studies have reported empty sella, pituitary haemorrhage, or even normal pituitary MRI findings [6,7]. In the present series, patients similarly demonstrated partial (case 2, 3, 4)/complete (case 1) empty sella, but biochemical testing remains the diagnostic gold standard.

All published series demonstrated rapid and sustained clinical improvement following hydrocortisone and l-thyroxine replacement, confirming both diagnostic accuracy and therapeutic reversibility [5-8,10]. This response across literature supports the urgency of early identification, because untreated adrenal insufficiency carries a considerable risk of morbidity and mortality [10]. Most of the reported cases of post-snake bite hypopituitarism have been reported from tropical countries like India and Sri Lanka, reflecting the geographic distribution of Russell's viper envenomation [5-8].

CONCLUSION(S)

Despite the high regional burden of snake bite envenomation in India, routine endocrine surveillance is not yet included in standard post-envenomation follow-up guidelines, representing a critical gap in care delivery that is directly exposed by this case series. This case series highlights the need for early pituitary-directed endocrine evaluation to prevent unwanted morbidity and mortality, as well as to ensure better quality of life for the patients.

Authors' contribution: RM, KR: Concept and design of the study; JFW: Collection of samples; RM, UM: Acquisition, analysis, and interpretation of data; RM, SD: Drafting of the article; KR, UM: Supervision.

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