

CASE OF THE MONTH

An Unusual Case of Intractable Vomiting: Unravelling the Present, Through the Past!

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Abstract

A 54 year old lady presented to our institute with a history of low grade fever for one week associated with occasional loose stools, vomiting and severe malaise. Initial evaluation revealed low serum sodium. An initial diagnosis of acute gastroenteritis with secondary hyponatremia was made. Work up for infective causes of gastroenteritis was however negative. ENT evaluation and review of drug history did not contribute towards a diagnosis. The patient's symptoms persisted and did not respond to symptomatic treatment. Ultrasound of abdomen revealed cholelithiasis with no evidence of cholecystitis. Further evaluation revealed hypotonic hyponatremia with normal levels of urinary sodium excretion. With other causes of hyponatremia ruled out, an endocrinopathy was suspected as the likely culprit. Follow up hormonal studies revealed hypopituitarism and MRI of brain revealed a partially empty sella. On reviewing the case, a past history of amenorrhea immediately after the birth of her third child (almost 20 years ago!) was elicited. Intractable vomiting is quite an unusual presentation for Sheehan's syndrome, but a thorough case history coupled with a high index of suspicion can contribute towards identifying the cause among a series of confounding clinical and radiological findings, as in our case.

Hemoglobin of 11.3 gm/dl with a normal leucocyte and platelet count. Hepatic and renal parameters were within normal limits, but the electrolyte panel revealed hyponatremia (Na= 120 meq/L) along with hypocalcemia (Ca= 7.8 mg/dl) and normokalemia (5.36 meq/L). Serum amylase was normal (46 SU) and the thyroid profile revealed an elevated TSH (10.9 IU/ml). Ultrasound of the abdomen revealed multiple echogenic calculi (largest 7.2 mm) in gall bladder with no pericholecystic collection along with grade I fatty liver (no evidence of cholecystitis). Pancreas was normal. Non contrast CT scan of head, done on admission was normal.

Thus the initial presentation was suggestive of recurrent bouts of vomiting associated with hyponatremia and a history of low grade fever. This is a very commonly encountered scenario and the likely differentials are enlisted in Table 1. She was started on symptomatic treatment with anti-emetics and her dose of levothyroxine was escalated.

In hospital, fever charting did not reveal elevated temperature. Blood and urine cultures sent on admission were sterile. Routine microscopy and culture of stool also proved non-contributory.

The patient's symptoms did not resolve. The hyponatremia persisted and a new finding came to light in the form of an isolated elevation of alkaline phosphatase in the absence of hyperbilirubinemia and transaminitis. Clinically the patient was asymptomatic and did not complain of pain or tenderness in the abdomen. The possibility of a slipped stone in the common bile duct was considered and

Case

A 54 year old female, a nurse by profession, presented to our hospital with complaints of low grade fever with recurrent bouts of vomiting over one week associated with generalized weakness and malaise. Fever was not associated with chills and had no diurnal variation, precipitating or relieving factors. However, it was associated with 6-8 episodes of vomiting per day, which

was non-bilious, comprising primarily of food particles consumed in meals. There was no relation of vomiting with food intake. She did not complain of abdominal pain, headache, vertigo, diarrhoea, passage of worms in vomitus, decreased urine output etc.

The patient persistently complained of severe weakness and lethargy which limited her activities of daily life both at work and home even before the onset of the present illness. She was a known case of hypothyroidism, on replacement therapy with levothyroxine (50 mcg/day). She had no other comorbidities.

At admission patient was conscious, alert, afebrile and her vitals were stable. General examination revealed only mild pallor and there was no abnormality detected on systemic examination.

Laboratory evaluation revealed

Table 1: Common causes of Vomiting in adults

Cause	Leads in history
Acute Gastroenteritis	Fever, vomiting, short history
Postoperative nausea and vomiting	Recent history of operative intervention, severe post-operative pain.
Vestibular neuritis	Vertigo, dizziness, imbalance
Chemotherapy	Known malignancy on treatment
Drugs	Metformin, NSAIDS, Antidepressants etc
Cerebellar CVA	Acute onset, recurrent, intractable

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Table 2: Causes of hyponatremia

Hypervolemic	Euvolemic	Hypovolemic
Heart failure	Glucocorticoid deficiency	Diuretic therapy
Cirrhosis	Hypothyroidism	Mineralocorticoid deficiency
Chronic kidney disease	SIADH resulting from	Third space losses
	Mass lesions	Burns
	Inflammatory diseases	Pancreatitis
	Degenerative demyelinating disorders	Bowel obstruction
		Muscle Trauma
Nephrotic syndrome	Carcinoma lung, prostate, larynx, pancreas.	Salt wasting nephropathy
	Leukemia	
	Atypical pneumonia	Vomiting and diarrhea
	Chronic obstructive pulmonary disease	Cerebral salt wasting syndrome
	AIDS related complex	Sweat losses
	Drug induced	

an MRCP was done, which revealed low insertion of the common bile duct.

At this point of time, the most prominent issue of the patient was her low sodium levels. A list of differentials for hyponatremia is listed in Table 2. A systematic approach was adopted for evaluation of the same (Figure 1). Serum and urine osmolality were done which revealed a serum osmolality of 234 mOsm/kg and corresponding urine osmolality of 320 mOsm/kg, reflecting hypotonic hyponatremia. The patient was euvolemic and spot urine sodium was 123 mmol/L. There was no history of diuretic use and in the presence of hypothyroidism, an endocrinopathy was considered a likely cause.

Morning cortisol levels were analysed on two successive occasions and found to be low both times (6.5 mcg/dl and 5.79 mcg/dl respectively). The ultrasound of abdomen done on admission had shown no lesion in the adrenal glands. Thus low cortisol together with hypothyroidism suggested the presence of an anterior pituitary lesion. An MRI of brain was performed that revealed a partially empty sella (Figure 2). The differentials of a partially empty sella are discussed in Table 3. Thus we reached a diagnosis of hypopituitarism with hyponatremia. To differentiate between the causes of hypopituitarism (Table 4), we revisited the history provided by the patient on admission.

On probing, she revealed that she had become amenorrhic immediately after the birth of her third child (around 20 years back), but was unsure of the occurrence of postpartum haemorrhage. Based on this, a clinical suspicion of chronic Sheehan's syndrome was kept and an endocrine profile was done that revealed decreased FSH, LH, cortisol,

IGF-1 with elevated prolactin (Table 5). The diagnostic criteria of Sheehan's Syndrome is given in Table 6.¹ The patient was started on steroids. The likely cause of hyponatremia was thus a combination of hypocortisolism and hypothyroidism.

The vomiting episodes as well as hyponatremia, resolved after 3-4 days of steroid therapy and the patient was discharged. The complaints of weakness and lethargy have decreased and she is presently doing well.

Sheehan Syndrome also known as postpartum hypopituitarism is a clinical condition characterized by hypopituitarism resulting from injury to the pituitary gland. The most common inciting factor is postpartum haemorrhage that deprives an enlarged pituitary gland (during pregnancy) of its blood supply leading to ischemia and necrosis.¹ Other causes include arterial thrombosis, vasospasm and occlusion of hypophyseal arteries. The clinical presentation is myriad and encompasses a broad spectrum, from an acute presentation such as failure to lactate postpartum, immediate amenorrhea post childbirth to a more chronic presentation (after several months or years) with vague symptoms such as weakness, lethargy, cold intolerance etc.^{1,2}

The presentation as intractable vomiting is quite unusual, with sporadically reported cases. Hyponatremia, is reported in only 30-40% cases in 3 case series on the disease.^{3,4,5} Gei-Guedira *et al* reported a higher (60%) incidence in their series. A partially empty sella is reported in two case series at 25%³ (Dokmetas *et al*) and 45% respectively (Ozkan *et al*).⁴ The interval between the inciting delivery and final diagnosis is also variable. In

one study of 18 patients, the mean delay was 15.35 years (range= 6-33 years post delivery).⁵

The presence of hypothyroidism was also an interesting factor in our case as uncontrolled hypothyroidism may independently manifest as hyponatremia. However, several studies have challenged this traditional teaching and suggest that only severe hypothyroidism (eg. Myxedema coma) may manifest as hyponatremia.⁹ Thus, hyponatremia should not be ascribed to coexistent hypothyroidism and alternative causative factors should be actively pursued. In our case the patient had been assumed to be a case of primary hypothyroidism, but the presence of hyponatremia raises the possibility of an endocrinopathy.

Finally, vomiting is more commonly seen in acute Sheehan's syndrome, although cases presenting with hyponatremia and even rhabdomyolysis have been reported.¹⁰ This probably highlights the importance of not neglecting uncommon presentations of common diseases while formulating the differentials for a patient and the need to treat every case on its individual merit rather than to fit it into a guideline.

Conclusion

Hypoadrenalism due to pituitary insufficiency in rare cases can lead to vomiting and hyponatremia in patients who are previously normal. All symptoms as related by the patient should be analysed objectively, rather than taking them at face value. The diagnosis in our case was confounded by factors such as hypothyroidism and the presence of gall stones which can independently cause recurrent vomiting and subsequent hyponatremia. Further the patient herself was not forthcoming with the history of amenorrhea immediately after childbirth and narrated this only after specific interrogation. This further highlights the importance of menstrual history in females, which is often neglected, but as evidenced, can be a crucial part of the problem solving process.

Sheehan's syndrome contributes to only a small fraction (3.1%) of cases of hypopituitarism.⁶ Nationwide studies in Iceland report the incidence at 5/10000 (2009).⁷ Our case report serves to highlight the importance

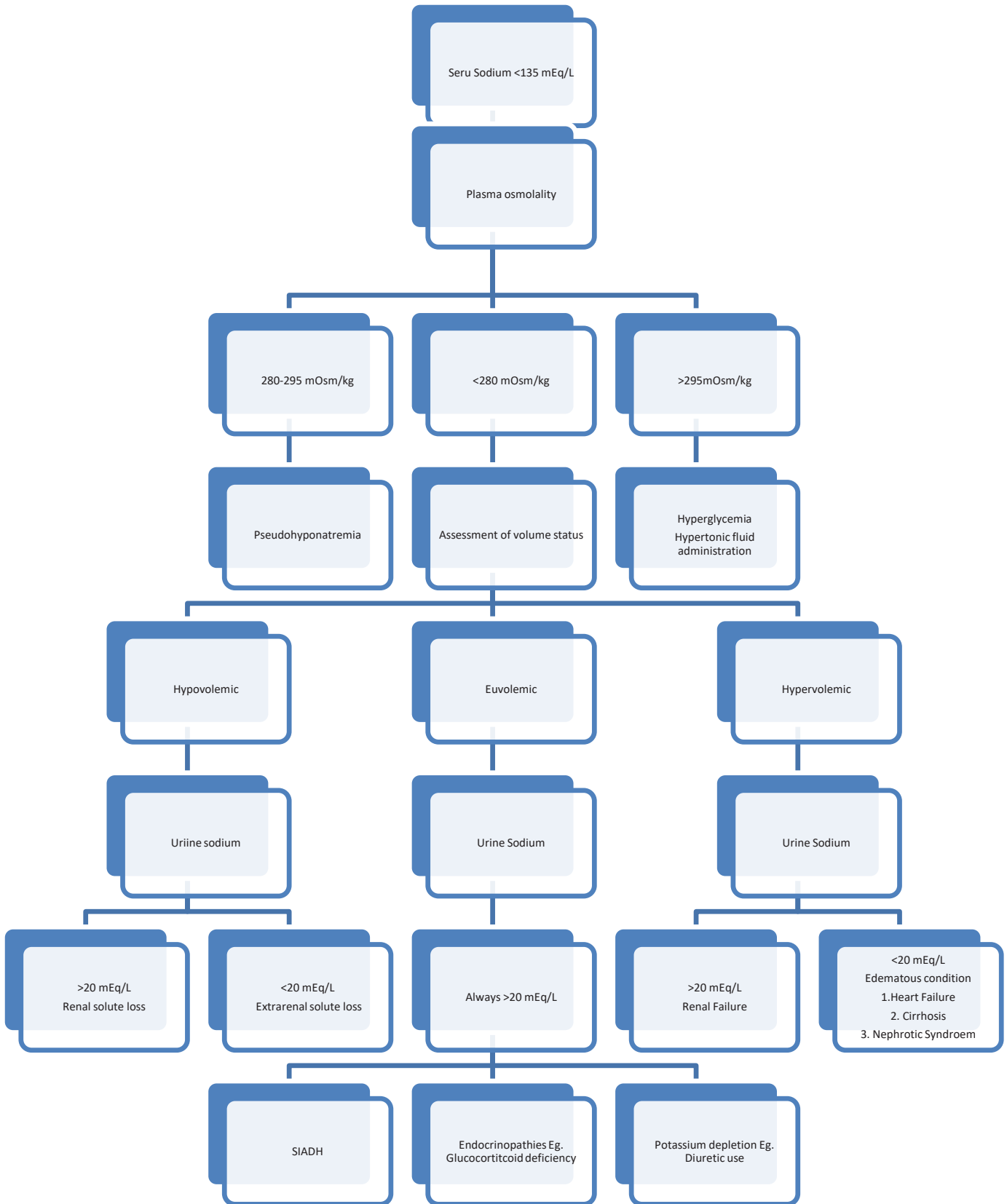


Fig. 1: Evaluation of hyponatremia

of a thorough history and systematic analysis in clinching an uncommon

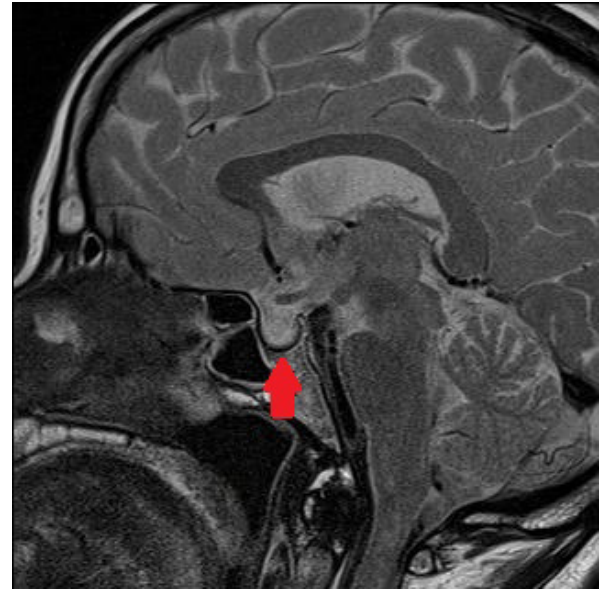
diagnosis amidst a multitude of possibilities.

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Sagittal T1 weighed MR image sella reveals partially empty sella turcica with flattened pituitary gland (Arrow).



Sagittal T2 weighed MR image reveals partially empty sella turcica (Arrow).

Fig. 2: MRI image showing partially empty sella

Table 3: Causes of empty sella syndrome

1. Primary: Small anatomical defect above the pituitary gland which increases pressure in the sella turcica and causes the gland to flatten out along the interior walls of the sella turcica cavity.
2. Secondary: Pituitary gland regressing within the cavity after an injury, surgery, or radiation therapy.

Table 4: Causes of hypopituitarism

- Congenital: Kallman Syndrome
- Infective: Basal meningitis, Encephalitis, Syphilis
- Vascular: Sheehan syndrome, carotid artery aneurysm, apoplexy
- Immunological: Pituitary antibodies
- Neoplastic: Pituitary tumours, craniopharyngioma, glioma, meningioma, pinealoblastoma, secondary metastases
- Traumatic: Skull fracture, trans-sphenoidal surgery
- Infiltration: Sarcoidosis, Hemochromatosis, Histiocytosis X
- Functional: Anorexia, Starvation, Emotional distress
- Others: Radiation, fibrosis, chemotherapy

Table 5: Hormonal analysis

Hormone analyzed	Values obtained	Normal range	Result
TSH	9.49 mIU/L	0.4-4.0 mIU/L	High
Prolactin	42.3 ng/dl	5-40 ng/dl	High
Cortisol	5.79 mcg/dl	7-28 mcg/dl	Low
LH	0.674 IU/L	14.2-52.3 IU/L	Low
FSH	1.25 mIU/ml	25.8-134.8 mIU/ml	Low
ACTH	33.64 pg/ml	10-50 pg/ml	Normal
IGF-1	3 ng/ml	97-130 ng/ml	Low

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Table 6: Diagnostic criteria of sheehan's syndrome¹

- Essential criteria for the diagnosis:
 - o Typical history of severe postpartum bleeding, particularly at last delivery
 - o A least one pituitary hormone deficiency
 - o Partial or complete empty sella on MRI or CT in chronic phase
 - Criteria which are not essential, but if present, strongly suggestive of the diagnosis
 - o Severe hypotension/shock at index delivery
 - o Postpartum amenorrhea
 - o Postpartum agalactia
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