Glucocorticoid Replacement in Panhypopituitarism Complicated by Myelinolysis

A Case Report

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Key Words

Hyponatremia · Adrenal insufficiency · Myelinolysis

Abstract

Objective: To report a case of glucocorticoid substitution in panhypopituitarism that can lead to uncontrolled rise in serum sodium and myelinolysis. **Clinical Presentation and Intervention:** A 42-year-old man presented with disturbed conscious level and hyponatremia. Initial data suggested glucocorticoid deficiency. Later, hormonal levels indicated panhypopituitarism. MRI of the brain led to the diagnosis of a pituitary macroadenoma. Glucocorticoid substitution was initiated immediately after admission, and possible myelinolysis subsequently became a complication. We report this case to illustrate the fact that glucocorticoid substitution can lead to rapid rise in serum sodium and myelinolysis in panhypopituitarism. **Conclusion:** This case illustrated the need to use minimum doses of glucocorticoids with close monitoring of serum sodium, in order to avoid this complication.

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Introduction

Hyponatremia is a common medical problem, occasionally occurring as a result of adrenal insufficiency – primary or secondary. In the latter case, treatment with glucocorticoids may lead to rapid correction of hyponatremia with attendant complications. We report such a case below and discuss implications for treatment.

Case Report

A 42-year-old Indian male with extreme weakness and a feeling of being unwell was admitted to Mubarak Al-Kabeer Hospital, Kuwait. A week prior to the admission he had developed gastroenteritis and had been treated elsewhere. In addition, he had complained of severe headache. He received only symptomatic therapy and felt progressively worse. He was then brought to the Emergency Department of our hospital. He had no significant prior medical problems.

Clinical examination revealed that he was ill-looking with weakness of all limbs. He was a bit confused, but there was no lateralizing neurologic deficit. He had a normal thyroid and genital examination and normal body hair. He was mildly hypotensive on admission with a BP of 90–100/60 mm Hg. The rest of the examination, including the fundi, was unremarkable.

Biochemical tests on admission revealed severe hyponatremia (105 mmol/l) with mild acidosis (HCO_3^- 18 mmol/l) and a close to normal potassium level (3.2 mmol/l). Renal function and serum glucose were normal (urea 5.8 mmol/l, creatinine 112 $\mu\text{mol/l}$, glucose

Fig. 1. Pituitary MRI demonstrating homogeneously enlarged pituitary macroadenoma extending suprasellarly in close proximity to optic chiasma.

Fig. 2. T₂-weighted MRI of the brain showing the hyperintense lesions (arrows) within the area of the basal ganglia indicative of myelinolysis.

7.1 mmol/l). At this point, serum and urine osmolality were 217 and 499 mosm/kg, respectively, and spot urine sodium was 22 mmol/l. He had an SIADH-like picture and was started empirically on dexamethasone (4 mg t.d.s.) [1] because of the suspicion of pituitary apoplexy and adrenal insufficiency. He only received 1 liter of normal saline per day for the first 3 days and oral fluid intake was restricted to 750 ml per day. Random cortisol and baseline thyroid function were requested prior to starting therapy.

Over the next 48 h he was relatively stable, urea and creatinine levels remained within normal range (urea 6.2 mmol/l, creatinine 114 µmol/l) but the urine output was markedly increased and he passed 4 liters of urine on the second day and 2.8 liters on the third day. On the third day of admission, he became more confused with

dystonic posturing of all four limbs. There was no lateralizing neurologic deficit and he had no extraocular muscle deficit or visual signs. In the preceding 48 h, his serum sodium had risen by 30 mmol/l (15 mmol/day) mainly due to a diuresis of 5 liters/day, presumably corticosteroid-induced. From the third day of admission he kept on going in and out of the acute confusional state but dystonia persisted. At times he became extremely agitated and violent while at other times he was able to communicate, albeit with dysarthria. He could also walk with assistance. However, he retained urine, and had to be kept catheterized.

His hormone profile subsequently was available: cortisol 111 nmol/l (normal > 550), free T₃ 2.8 pmol/l (normal 3.3–7.2), free T₄ 10.4 pmol/l (normal 11–24), TSH 0.2 mU/l (normal 0.3–5), testosterone 1.3 nmol/l (normal 8–35) and IGF-1 4.7 nmol/l (normal >10). He then had a brain and pituitary MRI and was found to have a homogeneously enhancing pituitary macroadenoma with suprasellar extension but no compression of either lateral structures or of the optic chiasma (fig. 1). There was no MRI evidence of hemorrhage or infarction. There were hyperintense lesions on T₂-weighted images within the basal ganglia (fig. 2). Electroencephalogram showed diffuse slowing and low voltage waves.

In retrospect, he was diagnosed to have myelinolysis as a result of glucocorticoid-induced overtly rapid sodium correction in the presence of baseline panhypopituitarism. The differential had been pituitary apoplexy, but this was dismissed after the imaging and clinical picture became clear. He was tapered to oral doses of hydrocortisone and started on thyroxine and remained free of electrolyte disturbances from day 3 of admission. He was transferred to neurosurgical follow-up on day 10.

Discussion

Hyponatremia could be the predominant presenting feature of adrenal insufficiency secondary to hypopituitarism. The pitfall of entertaining such a diagnosis is empiric glucocorticoid therapy and if this leads to rapid correction of hyponatremia, as in this case, myelinolysis as a neurologic complication can occur. It is therefore prudent that the severity of symptoms be considered in therapeutic decision-making. In adrenal disease with chronic hyponatremia, even adjunct treatment such as saline infusions are dangerous and are usually not needed if patients are asymptomatic [2]. It is important therefore that if a patient is clinically stable, even very low sodium level should not disturb the clinician and attempts to replace glucocorticoids should be approached very cautiously. Myelinolysis has been reported only once previously in a patient with hyponatremia in empty sella syndrome after substitution of glucocorticoids [3]. Ultimately, the patient, not the laboratory result, should receive treatment.

What then can we do in such situations? The answer is not clear, as withholding glucocorticoids is not free of complications. We therefore advocate, in retrospect, that the lowest possible dose of glucocorticoids should be used

and serum sodium levels must be closely monitored because of the unexpected speed with which it may increase even with careful glucocorticoid titration. If this occurs, relowering the serum sodium may be worthwhile using 5% dextrose infusions or even giving dDAVP [2]. It has been suggested that the rate of correction should be kept below 10 mmol/l during a 24-hour period [4], if possible. However, in one report of 14 cases of human myelinolysis after correction of hyponatremia [5], it was found that in 21% of the patients, correction had been done in a fashion consistent with the so-called safe guidelines. Thus, it may be impossible to define a level of correction that is always completely free of risk [4]. In our patient the cortisol replacement rapidly shut off antidiuretic hormone release (resulting in polyuria) and contributed to the rise in the serum sodium that ultimately resulted in myelinolysis. It is worthwhile to point out that the rate of rise of plasma sodium concentration is slower in patients with primary adrenal insufficiency in whom volume depletion due to aldosterone deficiency contributes to the hyponatremia. Hence, patients at real risk are those with secondary adrenal insufficiency.

Myelinolysis, as a consequence of rapid correction of hyponatremia is also known to affect extrapontine brain areas and this occurs in 10% of patients and often affects the basal ganglia, mainly the caudate and putamen [6]. Our patient developed affective changes and dystonia but did not have the classic symptoms of myelinolysis (spastic quadriparesis and pseudobulbar palsy reflecting damage to the corticospinal and corticobulbar tracts) that occur in more than 90% of these patients [5] and extrapontine myelinolysis was suspected since he had dystonia [5].

Brain imaging, the most useful diagnostic test, confirmed this suspicion. Computed tomography (CT) usually shows central pontine and extrapontine lesions as

symmetrical areas of hypodensity [7] but MRI is more sensitive; lesions appear hyperintense on T₂-weighted images and hypointense on T₁-weighted images [8]. In our patient, MRI showed hyperintense lesions at the caudate nucleus (fig. 2). Because myelinolytic lesions may not be apparent on scans within the first 2 weeks of illness, a later scan may be necessary to confirm the diagnosis [5]. Indeed the initial CT in this patient was negative.

Medications aimed at alleviating symptoms of myelinolysis such as depression, psychosis or parkinsonism may be effective, but myelinolysis cannot be specifically treated. Corticosteroids do not appear to be effective [5]. Preliminary data from studies in animals suggest that relowering serum sodium in the initial hours and days after rapid correction may be beneficial [9]. But it was not known whether or not this strategy would have been safe or effective in our patient. The outcome of patients with myelinolysis varies; some die and others recover completely. Many patients improve gradually or only partially [4]. It is therefore likely that our patient might improve, albeit gradually.

Conclusion

This case illustrated the problems associated with empiric glucocorticoid treatment of suspected hypopituitarism and the need to use minimum dose of glucocorticoids (1 mg t.d.s. of dexamethasone) with close monitoring of serum sodium, otherwise, uncontrolled correction of sodium can lead to potentially fatal consequences as noted here. Adjunct treatment of hyponatremia, such as saline, is not recommended in such cases. However, if the blood pressure does not respond to dexamethasone, only then would judicious use of saline be considered.

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