3. Discussion

The recovery from focal dystonia after betahistine withdrawal strongly suggests a causative link with prolonged use of betahistine. A literature search revealed a single case of movement disorder involving acute OMD following betahistine treatment.[3] It is surprising that only two patients with focal dystonia have been reported after betahistine treatment, considering its widespread use worldwide. The limited ability of the drug to cross the blood-brain barrier may explain the rare occurrence of this betahistine adverse effect. A reported case of delirium triggered by betahistine in a patient with supposed blood–brain barrier disruption caused by a recent cerebral infarction seemed to support such a hypothesis.[4]

In our patient, an elevated plasma betahistine level attributable to long-term use may have enabled the drug to cross the blood-brain barrier and accumulate in the brain.

Betahistine, a drug largely used in the treatment of Ménière's disease, is a structural analog of histamine, with weak H1 receptor agonist and strong H3 receptor antagonist activities.[5] Betahistine upregulates the histamine turnover and releases it into the histaminergic system, most probably by blocking the presynaptic histamine H3 receptors.[6]

Histamine terminals and receptors are widely distributed in motor areas.[7] A high density of H3 receptors was found in the striatum projections of rats[8] and humans.[9]

The brain histaminergic system appears to be involved in dyskinesia. Diphenhydramene, a H1 antagonist, for instance, is considered to be effective in all types of dyskinesias,[10,11] and interestingly, dyskinesia has also been reported after antihistamine use.[12]

Some more recent experimental data demonstrated that H3 activation *in vitro* strongly inhibited the dopamine D1 receptor-dependent release of [3(H)]gamma-amino butyric acid from the rat striatum[13] and indicated a role of H3 receptors in modulating dopaminergic transmission.[14]

The case reported here, although exceptional, shows a relationship between oromandibular dyskinesia and histamine, suggesting the role of histaminergic pathways in the pathophysiology of orofacial movement disorders.

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Extreme correction of hyponatremia in a patient treated with intravenous conivaptan

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ABSTRACT

Intravenous administration of conivaptan, an arginine vasopressin (AVP) receptor antagonist, has been demonstrated to be a safe and effective therapy for euvolemic and hypervolemic hyponatremia. In this case report, we report an extremely rapid correction of serum sodium with a typical dosing regimen of conivaptan. The patient was a 24 year woman who presented with nausea and vomiting, and was found on imaging to have two intracranial tumors, one of which was a large pituitary macroadenoma. Her serum sodium declined to 121 mmol/L and intravenous conivaptan therapy was started. After approximately 25 mg of conivaptan, her sodium increased 16 mmol/L over 8.5 hours. Fortunately, in this case, this correction was well tolerated, and the patient experienced no adverse effects of such a dramatic correction of serum sodium. Despite the good clinical result in this case, it should serve as a warning regarding the use of conivaptan, that although a gradual steady improvement in serum sodium can be expected in the majority of patients, more extreme corrections can be inadvertently achieved with even moderate doses. Thus, the exact clinical situation should be taken into consideration, especially in cases of subacute to chronic hyponatremia, where such an extreme correction could lead to neurologic devastation.

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1. Introduction

Hyponatremia is a common electrolyte disturbance.[1] Serum sodium concentrations less than 135 mEq/L have been reported in up to 28–40% of hospitalized patients.[2] Significant degrees of hyponatremia, with serum sodium concentrations less than 130 mEq/L, have been documented in 6.2% of hospitalized patients.[1] Serum sodium levels in the 130–135 range are also clinically important in neurosurgical patients, and can lead to severe symptoms or even seizures. Intravenous administration of conivaptan, an arginine vasopressin (AVP) receptor antagonist, has been demonstrated to be a safe and effective therapy for euvolemic and hypervolemic hyponatremia.[3] In this report, we detail the clinical findings in a patient with an extreme response in conivaptan therapy.

2. Case report

A 24-year-old woman developed intractable nausea and vomiting after running approximately 2 miles. Evaluation included a CT scan of the head that demonstrated a partially calcified mass of the fourth ventricle. MRI scan of the brain confirmed a $1.3 \times 1.1 \times 2.0$ heterogeneous mass centered in the fourth ventricle (Fig. 1). There was no hydrocephalus. A separate $2.5 \times 0.5 \times 2.0$ cm heterogeneous mass was located in the pituitary gland (Fig. 1). The lesion extended into the suprasellar cistern, possibly invading the right cavernous sinus, displaced the pituitary gland towards the left, and had a central area suggestive of degeneration or necrosis. She was hospitalized and treated with glucocorticoids. Her nausea resolved immediately. A review was remarkable for the absence of other neurologic symptoms as well as symptoms and signs of anterior pituitary hormone excess or deficiency. There were no symptoms of diabetes insipidus. The neurological examination was normal. There were no clinical features of acromegaly, Cushing's syndrome, hyperthyroidism, hyperprolactinemia, or hypothyroidism. Laboratory studies on admission are depicted in Supplementary Table 1.

The patient was initially started on normal saline with 20 meq/L KCl at 100 mL/h on admission, her initial serum sodium was 134 mmol/L, and she maintained stable serum sodium measurements, followed by a precipitous decline. Over the course of the subsequent 72 hours, and despite continued treatment with supraphysiologic doses of glucocorticoids, the serum sodium level declined to 121 mmol/L (Fig. 2), and subsequent repeat blood evaluation confirmed that this was an accurate value. There were no other neurologic symptoms or signs.

Our assessment was that the patient was euvolemic prior to the administration of conivaptan. The urine output roughly matched her intravenous fluid and oral intake for several hours following admission. She was not tachycardic, or hypotensive throughout the admission, and did not demonstrate signs of dehydration (dry mucous membranes) or fluid overload. The patient's serum osmolality tested immediately prior to administration of conivaptan was 284 and the specific gravity was 1.030, suggesting inappropriate urine concentration.

Given a severe drop in sodium in the setting of a brain tumor, we felt that the addition of fluid restriction was not safe as a single intervention, and decided to add conivaptan to avoid the complications of sudden decreases in sodium in a patient with symptomatic brain masses. The patient with treated a 20 mg conivaptan loading dose followed by a 20 mg dose given as a continuous infusion over 24 hours. Additionally she was placed on a 1000 ml/24 hour fluid restriction.

The conivaptan loading dose was started at 9:30 a.m on the 2nd hospital day, with a subsequent intravenous infusion. Serum

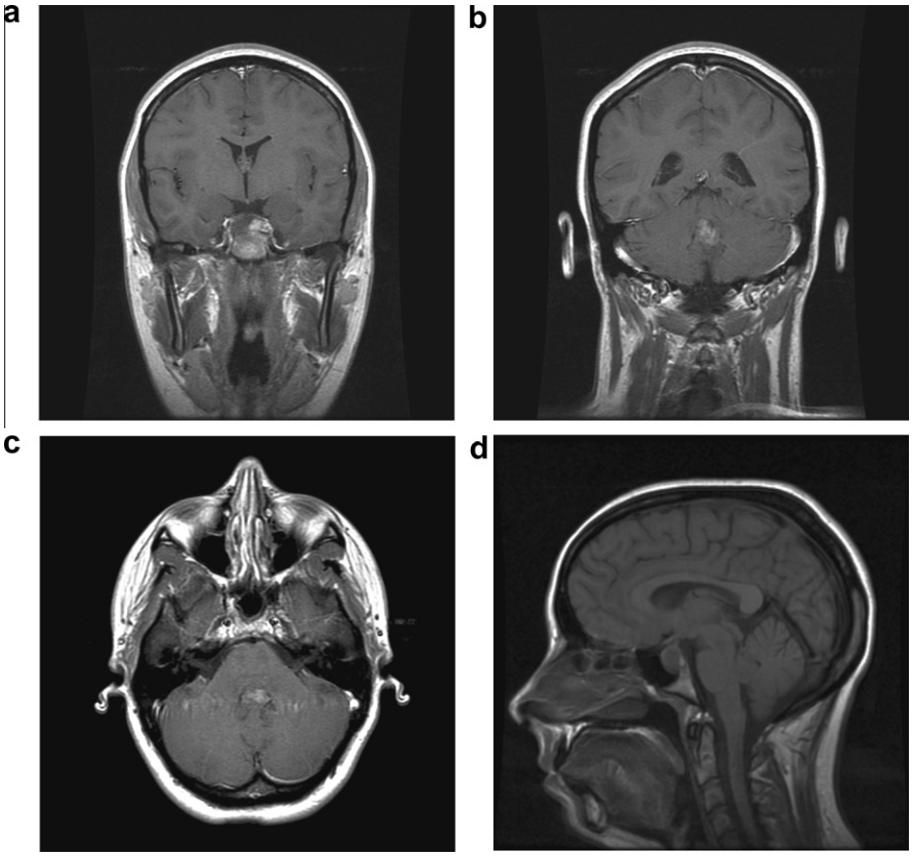

Fig. 1. (a,b) Coronal and (c) axial T1-weighted gadolinium enhanced MRI through the sella (a) and 4th ventricle (b,c) demonstrating the sellar and 4th ventricular tumors. (d) Sagittal MR without gadolinium demonstrating both lesions.