CASE REPORT

Symptomatic Hypotonic Hyponatremia Presenting at High Altitude

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We present a case of altered mental status and seizure that occurred at an altitude known to cause high altitude-related illnesses. Based on the presenting symptoms, the patient was initially transferred to the hospital with a presumptive diagnosis of high altitude cerebral edema. On review of imaging and laboratory data, she was found to be experiencing symptomatic hypotonic hyponatremia. This case presented an interesting diagnostic challenge and underscores the importance of maintaining a broad differential diagnosis when evaluating a patient with altered mental status from an alpine setting.

Key words: hyponatremia, exertional associated hyponatremia (EAH), syndrome of inappropriate antidiuretic hormone (SIADH), hypertonic saline (HTS), high altitude cerebral edema, search and rescue

Introduction

Recreation in our national parks is an increasingly popular way for people to spend their free time and experience the natural beauty of our nation.¹ Unfortunately, traumatic injuries, environmental illness, and exacerbation of underlying medical conditions are not uncommon in wilderness settings. Although trauma-related complaints comprise the majority of presenting illness in mountainous wilderness settings, altered mental status and seizure may occur at high altitude,² and individual case fatality for medical complaints including altitude illness is disproportionately high.³ Providers who care for these patients need to consider the spectrum of disease that is encompassed by wilderness and environmental medicine, although not excluding uncommon presentations of common conditions.

Case Report

PREHOSPITAL CLINICAL HISTORY

A previously healthy 29-year-old woman presented to our medical center after a 3-day hiking and camping trip in the Sierra Nevada Mountains of central California in midsummer. Roughly 48 hours before her presentation at the hospital, the patient drove from sea level to an altitude of 2400 m (7800 feet). Once at this altitude she participated in multiple strenuous hikes above 2500 m

(8000 feet). In the 24 hours immediately preceding her presentation at the hospital, the patient started to complain of a headache, became progressively weaker, and began to experience nausea, vomiting, and diarrhea. She had 5 episodes of emesis. By midday she required assistance ambulating back to her camp as a result of fatigue and dizziness. Although it is unclear whether she experienced ataxia, she was noted to have fallen from a height of 0.6 m (2 feet) while attempting to squat to urinate. Once back at camp she rested in her tent and continued to be anorexic and progressively lethargic.

At 2100 hours she experienced a witnessed seizure with tonic-clonic activity followed by a sustained state of altered mental status while resting in her tent. A cell phone call reached the National Park authorities, and Parkmedics were dispatched to the scene. By the time of arrival at 0215 hours, Parkmedics found the patient obtunded and vomiting.

Parkmedic assessment at the scene demonstrated a patient who was not protecting her airway owing to a decreased mental status and who was at high risk of aspiration of emesis. She responded to pain with eye opening, verbal groans, and localizing to pain (E2V2M5 = 9), representing a Glasgow Coma Score (GCS) of 9. Her airway was secured in the field with the placement of a King LT-D, a sterile, single-use supraglottic airway commonly known as a “Kingtube.” Her respiratory rate before securing her airway was even and unlabored at a normal rate. Her breath sounds were equal without rales.

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Initial heart rate was 78 beats/min and blood pressure was 110/60 mm Hg. Her finger-stick glucose reading was 169 mg/dL. Pupils were equal at 4 mm and reactive to light, with gross neurological examination showing movement of all 4 extremities to pain and an absence of facial droop. Limited skin examination was remarkable for the absence of rash, skin mottling, or external signs of trauma, and she was noted to be pink, warm, and dry.

According to her traveling companions, she had a history of gradual-onset malaise and flulike symptoms with ascent above 2500 m (8000 feet) and a chief complaint of headache unresponsive to aspirin and ibuprofen self-administered 3 times (1300, 1500, 1700 hours) before seizure onset at 2100 hours. She had no known preexisting medical conditions or medication use. She did not have a history of alcohol or substance abuse.

The Parkmedic established Base Hospital contact with the Medical Control for Sequoia Kings Canyon National Park (SEKI) through the park's dispatch at 0320 hours. Orders from the Base Hospital Physician included administering 1 L normal saline bolus, 4 mg of ondansetron intravenously (IV), serial neurological examinations, and a recommendation to litter-carry the patient to an elevation below 2500 m (8000 feet). The exact elevation of the patient was only known at that time to be over 2500 m (8000 feet), and the precise altitude was not known. The backcountry evacuation to a suitable landing zone by litter-carry was estimated to take approximately 3 hours. Immediate transport by air ambulance was precluded by the darkness of night. The litter team rendezvoused with flight paramedics at the trailhead at 0730 hours, and the patient was evacuated by helicopter to Community Regional Medical Center, which is at an elevation of 216 m (415 feet).

HOSPITAL PRESENTATION

The air ambulance landed at 0845 hours with the patient. En route, the patient's supraglottic airway adjunct had been exchanged for an endotracheal tube using rapid-sequence intubation by the prehospital flight nursing crew. On arrival to the hospital, the patient's vital signs were stable with a heart rate of 91 beats/min and blood pressure of 123/78 mm Hg, and her finger-stick glucose reading remained normal at 133 mg/dL. She was mechanically ventilated with oxygen saturation at 100% on 60% inspired oxygen. Portable chest x-ray demonstrated patchy air space opacities in the left upper and lower lobes and right upper lobe. She was administered 500 mL normal saline IV and 10 mg of dexamethasone IV, and had imaging and laboratory studies initiated. The patient was admitted to the medical intensive care unit with a battery of laboratory and imaging tests pending.

Among the initial tests conducted were a computed topography (CT) scan of the head and serum blood work including chemistry panel, liver function studies, complete blood count, and urinalysis. Further testing in the emergency department included a magnetic resonance image (MRI) of the brain and lumbar puncture. Intravenous saline at 100 mL/h was included as part of the patient's initial treatment. Additionally, early consultations with the neurology and neurosurgical services were requested, and an electroencephalogram (EEG) was performed several hours after her initial hospital arrival. The emergency medicine and intensivist teams considered a broad differential including meningitis, encephalitis, electrolyte abnormalities, accidental or intentional toxidrome, Addisonian crisis, myxedema coma, primary epilepsy, nonconvulsive status epilepticus, spontaneous intracranial hemorrhage, acute mountain sickness, and high altitude cerebral edema. The initial clinical impression was high altitude cerebral edema.

The head CT suggested mild edema of the basilar structures. The initial blood work revealed a mild leukocytosis at $13.4 \times 10^3/\mu\text{L}$, ketones in the urine, and a hypotonic hyponatremia with initial serum sodium at 122 mEq/L and osmolality at 268 mOsm/kg. Blood urea nitrogen (BUN) level was 6 mg/dL (normal range, 6–20 mg/dL) and initial creatinine was 0.5 mg/dL (normal range, 0.5–1.1 mg/dL). Random urine sodium several hours after arrival was elevated at 13 mmol/L (maximally dilute level <5 mmol/L), and measured urine osmolality was 65 mOsm/kg (normal range, 35–1400 mOsm/kg). Liver function studies were normal. The brain MRI, including fluid-attenuated inversion recovery (FLAIR) images, did not show any signs of cerebral edema or other disease. The EEG revealed mild slowing without seizure activity. The results of the lumbar puncture, including opening pressure, were normal. A repeat chemistry panel drawn 6 hours after admission revealed the serum sodium had increased to 131 mEq/L.

During the next 48 hours the serum sodium was closely monitored, and the patient was treated with alternating IV normal saline and 5% dextrose in water to increase her serum sodium by 10 mEq/L in each 24-hour period. After 48 hours in the medical intensive care unit, the patient was successfully extubated without complication, and by the morning of the third hospital day her serum sodium was 141 mEq/L. She was alert and oriented without any neurological deficit. She was discharged into the care of her family. The final diagnosis was symptomatic hypotonic hyponatremia.

Discussion

This case brings up several areas of discussion pertinent to those directing prehospital care, receiving and

stabilizing the undifferentiated patient, and treating and managing the course of patients from wilderness settings. Prehospital care delivery in our system is also briefly reviewed as it pertains to this case report as well as the clinical rationale used to arrive at the final diagnosis.

The National Park Service has a unique scope of practice in prehospital settings with the 30-plus year history of the federally recognized Parkmedic level of certification. Parkmedics are park rangers with specialty medical training. Their training is similar to an Emergency Medical Technician-Intermediate, but with an expanded pharmacological and procedural scope of practice. Parkmedics are able to establish a definitive airway, administer several dozen different medications, and make protocol-based medical decisions in cases of radio failure. In SEKI the only diagnostic testing available in the field is for vital signs, pulse oximetry, and finger-stick glucose reading. A portable machine to determine blood chemistry levels (ie, iSTAT) is not available in SEKI, but is used regularly in other national parks such as Grand Canyon National Park. Parkmedics in SEKI provide emergency medical services under protocols written, reviewed, and revised by emergency medicine residents at an academic regional medical center and level 1 trauma facility. Parkmedics can call for medical direction from the field to the regional medical center's emergency department, where physicians provide consultation via a phone patch. A phone patch is performed manually at a base station, where radio transmissions are connected to a transceiver to provide emergency communication to places that do not have telephone network access.

Evacuation options in the alpine wilderness setting include litter-carry, stock evacuation (often by mule), and aeromedical transport. Litter-carrying is the least expedient of the 3, demanding both significant time and personnel resources. Federal rescue organizations, excluding the military, are prohibited from flying in mountainous terrain at night as it is deemed an unnecessary risk. In our case, the patient fell into this no-fly period, leaving litter evacuation the only viable option besides staying the night and awaiting daytime air evacuation for definitive diagnosis and management.

Altitude illness, high on the initial differential diagnosis, is generally considered on a spectrum that runs from altitude-related headache to acute mountain sickness (AMS), and ultimately high altitude cerebral edema (HACE). The vast majority of travelers at high altitude experience some degree of altitude-related illness; however, when a headache is associated with fatigue, dizziness, anorexia, irritability, or nausea and vomiting, AMS is diagnosed. A diagnosis of HACE is made when the above symptoms are followed by onset of ataxia,

confusion, disorientation, and impaired judgment. Coma and seizures may then ensue.^{3,4} HACE is often seen concurrently in patients also suffering from high altitude pulmonary edema (HAPE), most commonly seen the second night at elevation.³ The timing for our patient's symptoms fits, but it would be unusual for such a high degree of neurologic impairment as a result of altitude with a complete absence of pulmonary symptoms. The altitude at which the patient was recreating, 2400 m to over 2500 m (7800–8000 feet) was within the range known to cause HACE. The lowest reported elevation for a case of HACE is 2100 m (7000 feet).³ The pathophysiology of HACE is believed to be that of vasogenic edema triggered by an environment with a reduced partial pressure of oxygen, resulting in an increased intracranial pressure that then leads to its clinical manifestations.⁴ Increased intracranial pressures and cerebral edema manifesting with radiographic findings on both CT and MRI FLAIR images, as well as significantly elevated opening pressure on lumbar puncture, are generally considered confirmatory tests.^{3,4}

The clinical rationale at first was centered on the possibility of HACE, as we thought this was consistent with the historical features and the lack of focal symptoms. The CT scan of the head demonstrated some possible mild edema of some of the basilar structures, but there was no major edema present or loss of anatomical resolution. Serum sodium at the time of her arrival was 122 mEq/L, with other electrolytes appearing relatively normal. Furthermore, MRI of the brain failed to demonstrate significant edema on the FLAIR images, making that entity somewhat unlikely. A lumbar puncture was also performed, and the patient underwent a stat EEG to rule out status seizures. Although encephalitis and meningitis were thought to be unlikely, she was empirically treated with broad-spectrum antibiotics on admission pending the final results.

Additional history was given that during the early portion of the trip the patient consumed liberal amounts of filtered water but very little food and no electrolytes. In the 24 hours immediately preceding her presentation at the hospital, the patient started to complain of a headache, and her companions noted a decrease in oral intake. Although concurrent AMS may have contributed to the rapid development of her symptoms, it was believed that the most likely diagnosis was symptomatic hyponatremia, likely related to significant salt losses from sweating with a large free water replacement. Given the concerns of raising her sodium too rapidly, therapeutic treatment including changing her maintenance fluids from normal saline to 5% dextrose in water, as the patient's sodium rose much more rapidly than expected with initial management. Hormonal agents such as desmopressin (DDAVP) were

considered to limit free water losses with inappropriate rise in serum sodium, although this was not necessary during her clinical course.

Hyponatremia, the final diagnosis in the case presented, is a common and often serious medical condition that generally has a high prevalence among hospitalized patients and residents of skilled-nursing facilities. However, significant hyponatremia can also occur among otherwise healthy patients who participate in endurance sports and other exertional activities.⁵ Management of hyponatremia based on rate of onset and volume status, adapted from the review article by Vaidya et al,⁶ can be noted in the Figure. Exercise-associated hyponatremia (EAH) has been well documented among marathoners and triathletes in the last 15 years,^{7–18} and has also been known to occur in hikers.^{19,20} Clinical symptoms of EAH include nausea, vomiting, confusion, altered mental status, and seizure. EAH has been known to result in fatalities and can be more severe among women, especially those of menstruant age.⁵ It is not clear why women experience a more severe clinical course of EAH; current theories attribute it to altered sensitization of cerebral vasculature and altered neuronal volume regulation induced by female hormones.⁵ Many published cases of EAH meet the diagnostic criteria for syndrome of inappropriate antidiuretic hormone (SIADH), and elevated inflammatory markers, including interleukin 6 (IL-6) have been considered responsible for

increased levels of antidiuretic hormone, also known as arginine vasopressin in this population.²¹ A diagnosis of SIADH should only be made when normal adrenal and renal function is confirmed in a patient who presents with normovolemic hypoosmolar hyponatremia. In retrospect, this patient's random urine sodium, as well as a serum cortisol, should have been drawn promptly during the initial workup when her head CT demonstrated only mild edema at the basilar structures. Our patient was presumptively treated with steroids for several days to treat an initial diagnosis of HACE. These factors would have made a diagnosis of SIADH difficult to establish, and should serve as a precaution to those treating patients who present with hyponatremia while recreating at altitude.

Treatment of presumed EAH is evolving from an approach of slow calibrated normal saline (NS) infusion while following serial sodium levels to the one-time administration of hypertonic saline (HTS) at concentrations of 1.8%, 3%, or 5% after noting low serum sodium. Cases of hyponatremia that go unrecognized at presentation have been reported to be fatal.^{7,8} Several case reports support NS alone as effective treatment in a diverse population of patients from ultra-endurance events,²² those presenting with very low sodium (initial level of 107 mEq/L),²³ as well as 1 pediatric case of EAH in a patient with cystic fibrosis.²⁴ Although our patient was successfully treated with NS, 1 case report describes

Figure. The suggested management of hyposmolar hyponatremia based on rate of onset and volume status, adapted from the review article by Vaidya et al.⁶

2 female marathon runners, both previously well, whose diagnosis of EAH was treated with NS with subsequent deaths secondary to cerebral and pulmonary edema.⁸ Furosemide and mannitol have also been reported as efficacious in the treatment of EAH.^{9,10,25} The use of HTS has produced good outcomes in marathoners,^{7,11,12,16,17} ironman triathletes,^{13,14} and gym enthusiasts.¹⁵ Several case series at endurance events have followed, showing similar outcomes in those who received NS or HTS, often with more-rapid recovery times, and even emergency department discharge in those receiving 1.8% and 3% HTS.^{15,16} Administration of 5% HTS has also been reported with a rapid full recovery.¹⁸ The legitimate concern for poor neurologic outcome with the use of HTS in the hypotonic normovolemic state of EAH has not been realized clinically.

Conclusions

We present a case of headache, nausea, vomiting, fatigue, anorexia, and ultimately seizure with altered mental status occurring at high altitude. Prehospital management and evacuation were performed with a presumed diagnosis of altitude illness. After evacuation, stabilization, and diagnostic evaluation, these symptoms appear to be related to symptomatic hypotonic hyponatremia. When encountering a similar patient in the future, we recommend treating high altitude illness presumptively with early rapid descent and administration of steroids in cases of altered mental status, even if this creates a diagnostic challenge in the inpatient setting for a possible diagnosis of SIADH-caused hyponatremia.

When normovolemic hypotonic hyponatremia is suggested early on in the patient's course, a rapid serum electrolyte assessment should be done when this technology is available in the field. The expanded use of this technology in the prehospital setting in locations known for strenuous recreational activities is recommended. Once in the hospital setting, urine sodium, urine osmolality, and adrenal function should be evaluated as promptly as possible to exclude SIADH. Normal saline therapy of symptomatic hypotonic hyponatremia can be effective, as in this case, and can be presumptively started in the prehospital setting even in the absence of known electrolyte values. An initial normal saline bolus would be effective therapeutically in both hyponatremia and hypernatremia cases, which can share similar clinical presentations. We note growing evidence supporting the early use of HTS to promote a faster recovery in similar cases, and this has been employed in the prehospital setting when the infrastructure to check serum electrolytes is in place. It is unclear whether high altitude

exposure presents an additional risk factor to developing an SIADH-type state with moderate exertion, producing symptomatic normovolemic hypotonic hyponatremia.

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