Reset Osmostat in a 47-Year-Old Woman with Cerebral Palsy

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The reset osmostat variation of the syndrome of inappropriate antidiuretic hormone (SIADH) is thought to account for up to one third of SIADH cases.[1] Most commonly, it can cause hyponatremia in patients who are quadriplegic, psychotic, or chronically malnourished, such as those with tuberculosis or alcoholism.[5–7] Recent case reports have also noted the reset osmostat in several other states, including health.[8] Because the reset osmostat is a diagnosis of exclusion, its workup requires consideration of all other causes of hyponatremia; thus, its investigation can help the primary care physician understand more thoroughly the low-sodium state. Furthermore, as the following case illustrates, its diagnosis can have important consequences for the overall management of a patient's fluid and nutritional status.

Case Report

A 46-year-old woman with cerebral palsy was brought to the hospital by her caretakers for persistent fevers. Five days before admission her physician had prescribed a course of levofloxacin to treat a urinary tract infection, but her caretakers stated that her temperature had continued to go as high as 103°F. The *Escherichia coli* that was isolated from her urine was sensitive to levofloxacin, and she was admitted for further workup of her fevers.

The patient received 90% of her fluid and nutrition by means of a J-tube, which had been inserted 1 year earlier to prevent aspiration. She was also taking medication for hypothyroidism. Her other medical problems were related directly or indirectly to her cerebral palsy: spastic dystonia, mental retardation, decubitus ulcers, and deep venous thrombosis. Her medications were levothyroxine, psyllium mucilloid (Metamucil), multivitamins, zinc, and iron, as well as bisacodyl, docusate, and ibuprofen as needed.

When admitted, her temperature was 39.6°C, blood pressure 124/60 mmHg, pulse 94 beats per minute, and respirations 28/min. Findings from an examination of her head, eyes, ears, nose, and throat were unremarkable. Her lungs were notable for left-side basilar crackles. Her heart sounds were regular without murmur or gallops. Her liver size was normal, and her J-tube site was free from signs of infection. Neurologic findings of spastic movements and dystonic posturing were consistent with previous examinations. She had a stage 4 decubitus ulcer over her coccyx, which had formed a sinus tract 2 cm deep. The wound appeared to be without signs of surrounding cellulitis and had granulation tissue at the base.

In reviewing her medical record, we noted that the patient had been hospitalized for fevers several months earlier, and an exhaustive workup had not discovered the source. Although we repeated many of the laboratory and imaging studies (urine and blood cultures, chest films, a tagged white cell scan, abdominal and pelvic computed tomograms) and performed a number of specialized laboratory tests (eg, erythrocyte sedimentation rate, rheumatoid factor, antinuclear antibodies), we were unable to discover an organic cause of her fevers. We finally attributed her elevated temperature to emotionally induced hyperthermia, a phenomenon found in cerebral palsy patients when they are placed in unfamiliar settings.[4] Notably, when she was first found to be febrile, the patient had recently changed home care facilities, and now she was in the hospital. Our second clinical task focused on enhancing her fluid and nutritional state while we continued to evaluate the source of her fevers.

At admission she was incidentally noted to have a sodium level of 124 mEq/L. Our search of the patient's medical record also showed that she had had consistently low sodium levels of 125 to 130 mEq/L within the last several years. Whereas her

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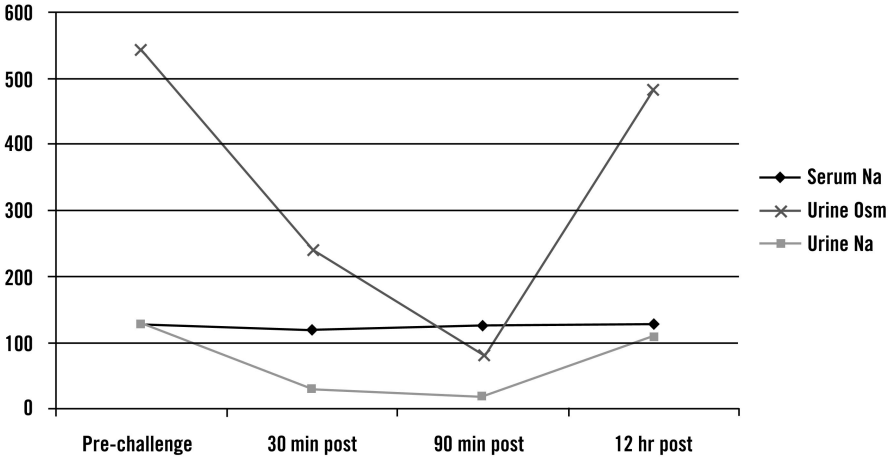

Figure 1. Free-water challenge in a patient with reset osmostat. Unlike with the syndrome of inappropriate antidiuretic hormone, an appropriate decrease in urine osmolality to < 100 mOsm/kg with free-water challenge indicates normal response to lowered serum sodium. This physiologic response is identical to that of the normal patient: antidiuretic hormone is released only when serum sodium levels decrease below the osmostat setting. Once the serum sodium level is raised to this point, antidiuretic hormone release stops (sodium levels between an osmolality of 128 to 130 mOsm/kg in our patient). The drop in urine sodium levels parallels the drop in urine osmolality and provides additional evidence the patient's kidneys are functioning normally.

admission workup centered on the cause and treatment of her fever, the team decided that it would be important to evaluate and treat her hyponatremia. We wanted to correct any abnormality that could adversely affect her already compromised neurologic state. The workup of her hyponatremia began by comparing measured with calculated serum sodium levels to exclude laboratory error. Next, we spoke with her primary care physician to confirm our clinical impression that she did not have a hypovolemic type of hyponatremia, specifically heart failure, cirrhosis, or nephrosis. Although the patient had a history of hypothyroidism, a normal thyroid-stimulating hormone level confirmed that her condition was adequately treated.

Based on the available data, the team made a presumptive diagnosis of the SIADH and asked that fluid be restricted to 2 L/d. A nutritionist consulted on the second day of admission had recommended increasing her protein intake to accommodate her increased metabolic needs from the elevated body temperatures. The nutritionist cautioned us that fluid restriction would necessitate cutting her protein intake, because any feeding formulation required mixing with water. After several days of fluid restriction, her sodium levels failed to rise above a high of 131 mEq/L.

At that point a decision was made to confirm the diagnosis of SIADH with further workup. A review of her medication list did not show any medications associated with SIADH (eg, antipsychotics, tricyclic antidepressants). A cortisone-stimulation test resulted in an appropriate rise in serum cortisol levels in response to adrenocorticotropic hormone stimulus, thus precluding hypoadrenalism as a cause of hyponatremia. The patient's consistently normal blood urea nitrogen and creatinine levels indicated that kidney function was intact, and several urinalyses showed no evidence of renal parenchymal damage. It thus appeared the patient had SIADH, and because fluid restriction failed to increase her sodium levels, the diagnosis of reset osmostat was implied.

To confirm this diagnosis, we gave the patient a free-water challenge of 1 L delivered through her J-tube over 30 minutes. Serum and urine osmolalities and sodium levels were measured before the challenge and then at 30 minutes, 90 minutes, and 12 hours afterward. An examination of data presented in Figure 1 shows the patient's ability to dilute her urine appropriately and maximally with the free-water challenge. Thus, the diagnosis of reset osmostat was confirmed.

Discussion

Hyponatremia is often diagnosed incidentally when a patient is hospitalized for another reason. As this

case illustrates, however, ignoring it or only partially working it up can have a profound effect on therapy. The evaluation of our patient's hyponatremia was guided by a generally agreed-on approach described in several texts and review articles.[1–3] Here we focus our discussion on the salient features of the SIADH and reset osmostat.

To understand the most common cause of persistent hyponatremia, the euvolemic SIADH state, one should recall that disorders of sodium balance are caused by a primary problem with water metabolism. In effect, a low-sodium value indicates that the kidneys are unable to rid the body of free water appropriately. This situation occurs only in two fundamental situations: either an inappropriate secretion of antidiuretic hormone or an intrinsic renal problem. In the nephron the critical area for free-water metabolism is the collecting duct. The concentration gradient established by the ascending loop of Henle and the distal convoluted tubule cause the filtrate to become maximally dilute (50–100 mOsm/kg) as it reaches the distal convoluted tubule in the cortex. In the absence of antidiuretic hormone, the filtrate remains dilute, and a dilute urine is excreted. Once antidiuretic hormone is present, it causes specialized water channels to open along the collecting duct. Water then moves into the interstitium following the concentration gradient, and an increasingly concentrated urine is formed.

Renal disease can prevent the nephron from ever establishing the above-mentioned gradient, and the body cannot excrete excess free water. Thus, hyponatremia can occur with interstitial nephropathy, medullary cystic disease, polycystic kidney disease, type 2 (bicarbonate-wasting) acidosis, or partial urinary obstruction. Numerous disorders have been associated with inappropriate antidiuretic hormone secretion and a normally functioning kidney, most commonly pulmonic, intracerebral, neoplastic diseases and certain medications. Hyponatremia found with hypothyroidism and hypoadrenalism is also thought to be related to inappropriate antidiuretic hormone release.

In our patient we confirmed the reset osmostat variation of SIADH by giving a free-water challenge through her J-tube. Her ability to excrete free water appropriately can be noted most remarkably at 90 minutes after the challenge, when her urine osmolality and sodium level decreased to less than 100 and to 19 mOsm/kg, respectively. She secreted a maximally dilute urine and appropriately retained sodium. Other evidence in support of the diagnosis included the patient's failure to correct her sodium level with free-water restriction. Interestingly, several authors have confirmed a high incidence of reset osmostat in paraplegic and quadriplegic patients, and they hypothesize a central cause for the disorder. It might be reasonable to suppose our patient with cerebral palsy has a similar mechanism.

Conclusions

We are admonished to "treat the patient, not the laboratory value." The reset osmostat, once diagnosed, certainly confirms the importance of this advice. For the chronically ill patient in whom the nutritional status and fluid balance can be of great importance, fluid restriction not only can present a practical problem but also can prevent the patient from receiving adequate caloric intake. Furthermore, it is precisely such patients who tend to develop hyponatremia as a result of the reset osmostat. Because it has been suggested that one third of the SIADH might be due to the reset osmostat, we recommend that physicians consider investigating this possibility when appropriate, in particular when fluid restriction might cause problems.

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