Hyponatremia in intracranial disease: perhaps not the syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

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Patients with intracranial disorders are prone to develop hyponatremia with inability to prevent the loss of sodium in their urine. This was originally referred to as "cerebral salt wasting," but more recently is thought to be secondary to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Blood volume determinations were made in 12 unselected neurosurgical patients with intracranial disease who fulfilled the laboratory criteria for SIADH. Ten of the 12 patients had significant decreases in their red blood cell mass, plasma volume, and total blood volume. The finding of a decreased blood volume in patients who fulfill the laboratory criteria for SIADH is better explained by the original concepts of cerebral salt wasting than by SIADH. The primary defect may be the inability of the kidney to conserve sodium.

KEY WORDS - hyponatremia - natriuresis - antidiuretic hormone - SIADH - inappropriate secretion of antidiuretic hormone syndrome - cerebral salt wasting

Patients with intracranial disorders are prone to develop hyponatremia with inability to prevent the loss of sodium in their urine. The hyponatremia is frequently associated with a worsening in the patient's neurological condition. The problem was referred to in the early 1950's as "cerebral salt wasting." The syndrome was defined as the inability to prevent salt loss in the urine despite depressed concentrations of sodium in the serum. These early investigators concentrated on renal loss of salt as the primary defect. They thought that the central nervous system influenced the kidney's ability to reabsorb sodium in the proximal tubule. The therapeutic implications were that progressive salt depletion may lead to peripheral vascular collapse and may jeopardize recovery from the primary illness. The early investigators treated these patients with salt replacement in excess of the amount lost in the urine. The administration of glucocorticoids and mineralocorticoids did not reverse the syndrome.

The approach to hyponatremia associated with natriuresis changed in 1957 when Schwartz, et al., defined the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). In their original paper, they described two patients with bronchogenic carcinoma who had hyponatremia and persistent loss of sodium in their urine. Extracellular volume was measured in one patient and found to be expanded. The syndrome improved with fluid restriction. Since similar findings had been seen in experimental conditions where hyponatremia resulted when normal individuals were given antidiuretic hormone (ADH) and water, Schwartz, et al., concluded that sustained inappropriate secretion of ADH was probably the cause of the abnormal laboratory findings in their patients. No direct determinations of ADH were made. Laboratory criteria to make the diagnosis of SIADH became a low serum sodium level, a low serum osmolality, a high urinary sodium, and a urinary osmolality that was inappropriately concentrated as compared to the serum osmolality. The diagnosis assumed normal renal and adrenal function and that the patients were not taking diuretics.

Since 1957, it has generally become accepted that patients with intracranial disorders who exhibit hyponatremia with excessive loss of sodium in their urine have SIADH. This syndrome has been reported to be the probable cause of hyponatremia.
Hyponatremia in intracranial disease

TABLE 1

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Day</th>
<th>Hyponatremia Developed</th>
<th>Diagnosis</th>
<th>Serum Sodium (mEq/Liter)</th>
<th>Urine Sodium (mEq/Liter)</th>
<th>RBC (ml/kg)</th>
<th>Plasma (ml/kg)</th>
<th>Total Blood Volume (ml/kg)</th>
<th>Volume Change</th>
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<tbody>
<tr>
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<td>postop aneurysm</td>
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<td>3 postop SAH</td>
<td>127</td>
<td>203</td>
<td>17.6</td>
<td>21.1</td>
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<td>11</td>
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<td>134</td>
<td>112</td>
<td>12.6</td>
<td>22.3</td>
<td>34.9</td>
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<tr>
<td>4</td>
<td>11</td>
<td>head injury</td>
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<td>43</td>
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<td>42.2</td>
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<td>132</td>
<td>80</td>
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<td>145</td>
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<td>77.4</td>
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<td>56.8</td>
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<td>72</td>
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<tr>
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<td>22.4</td>
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<tr>
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<td>10</td>
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<td>177</td>
<td>27.0</td>
<td>27.8</td>
<td>54.9</td>
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* RBC = red blood cell; SAH = subarachnoid hemorrhage.

with natriuresis in a wide variety of intracranial disorders. The traditional concepts of cerebral salt wasting have been abandoned for the concept of sustained inappropriate release of ADH. There is a marked difference between these two concepts. In cerebral salt wasting, renal salt loss leads to progressive salt and extracellular volume depletion. In SIADH, water intoxication leads to an expanded or increased extracellular volume. To further study the volume status of neurosurgical patients with intracranial disorders who developed the laboratory criteria for SIADH, we measured the intravascular blood volumes in patients who developed hyponatremia and natriuresis.

Clinical Material and Methods

Blood volume determinations were made in 12 unselected neurosurgical patients with intracranial disease who all fulfilled the laboratory criteria for SIADH: serum sodium less than 135 mEq/liter, serum osmolality less than 280 mOsm/kg, urine sodium more than 25 mEq/liter, and urine osmolality inappropriately concentrated as compared to the serum osmolality. The blood volume determinations were made within 24 to 48 hours of the time the patients fulfilled the laboratory criteria for SIADH. Eight patients had subarachnoid hemorrhage. Cerebral angiography of these patients revealed aneurysms in five patients arising from the anterior communicating artery, in one patient from the middle cerebral artery trifurcation and from the ophthalmic artery, in one patient from the internal carotid ophthalmic artery, and in one patient from the vertebral artery.

Two of the patients had undergone craniotomy for a previously unruptured aneurysm. One of these patients had a left internal carotid ophthalmic artery aneurysm and the other patient had a basilar tip aneurysm. One patient had suffered a closed head injury and one patient had a traumatic carotid cavernous sinus fistula. None of the patients were restricted as to fluid intake, and none of the patients had renal or adrenal disease or were on diuretic therapy.

Red blood cell mass was determined using chromium-51-labeled autologous erythrocytes. Plasma volume was determined with radioiodinated human serum albumin. Electrolytes were measured by flame photometer, and serum and urine osmolalities were determined using the freezing-point depression technique. Six additional blood volumes were determined in a control group, which consisted of neurosurgical patients without intracranial disease who were not restricted to bed rest. This group consisted of patients admitted to the hospital for elective disc surgery. Blood volume determinations were made as a part of their preoperative evaluation. The data are expressed in means ± standard error of the means. Statistical analysis was performed using the t-test for unpaired data.

Results

Ten of the 12 patients had decreased intravascular blood volumes despite fulfilling the laboratory criteria for SIADH (Table 1). Two of the 12 patients (Cases 7 and 10) had increased plasma and total blood volumes (Table 1). The blood volumes obtained in neurosurgical patients without intracranial disease who were not restricted to bed rest were normal (Table 2). The 10 patients with decreased blood volume had significant decreases in red blood cell mass, plasma...
volumes, and total blood volume as compared to neurosurgical patients without intracranial disease (Table 2). The mean red blood cell mass in these 10 patients was 19.1 ± 1.6 ml/kg, the plasma volume was 30.3 ± 1.9 ml/kg, and the total blood volume was 49.5 ± 2.9 ml/kg. The hyponatremia developed on an average on the 10th day of the patient's illness, with a range of 4 to 16 days. Three of the 10 patients with decreased blood volumes had determinations made in the postoperative period. The blood loss in each of these three cases was not thought to be excessive and was estimated to be 300 cc.

Illustrative Case Report

This 50-year-old white woman (Case 1) was admitted with an 8-month history of progressive loss of vision in her left eye. Her neurological examination was normal, with the exception of a left Marcus-Gunn pupil and a left paracentral scotoma. Computed tomography revealed an enhancing left parasellar mass lesion that extended into the suprasellar region. Cerebral angiogram revealed a giant internal carotid artery aneurysm arising from the suprachiasmatic segment of the internal carotid artery.

Application of a Selverstone clamp on her left common carotid artery resulted in decreased vision of her left eye as the clamp was closed. A left frontotemporal craniotomy was then performed with clipping and evacuation of the aneurysm. Postoperatively, she was alert, oriented, and without neurological deficits. On the 2nd postoperative day, she developed a mild aphasia. She was given 2 units of packed red blood cells when her hematocrit fell to 25%. On her 3rd hospital day, she was noted to be more lethargic with increased aphasia and mild right-sided weakness. Serum sodium fell to 129 mEq/liter, and she was noted to fulfill the laboratory criteria for SIADH. She was started on a mild fluid restriction. Her symptoms persisted on the 4th postoperative day, and her serum sodium continued to fall to 124 mEq/liter. A blood volume measurement was obtained on the same day and revealed contraction of the red blood cell mass, plasma volume, and total blood volume. She was given 2 units of packed red blood cells and 2 units of plasmapheresis after the blood volume studies were performed. She was noted to be more alert on the 5th postoperative day. On the 7th postoperative day, she was alert and oriented without neurological deficits. A repeat blood volume analysis obtained on the 12th hospital day revealed a normal blood volume. Serial determinations of the fluid balance parameters are summarized in Table 3.

Discussion

The finding of a decreased blood volume in patients who fulfill the laboratory criteria for SIADH is better explained by the original concepts of cerebral salt wasting than by SIADH. The primary defect may be the inability of the kidney to conserve sodium. The cause of the natriuresis is unknown but may be due to a yet undefined natriuretic factor in the brain or secondary to an alteration in the direct neural innervation to the kidney. The progressive loss of sodium leads to volume depletion. Volume depletion is a strong stimulus for secretion of ADH. Elevated levels of ADH lead to water retention, and water retention along with progressive renal loss of sodium leads to hyponatremia.

Two of the 12 patients had an expanded blood volume which is more consistent with what one might

<table>
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<tr>
<th>Parameter</th>
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<th>4</th>
<th>5</th>
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<tbody>
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<td>138</td>
<td>139</td>
<td>131</td>
<td>129</td>
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<td>1720</td>
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<td>1525</td>
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<td>1180</td>
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<tr>
<td>RBC treatment</td>
<td>2 units packed RBC</td>
<td>fluid restriction</td>
<td>2 units packed RBC, 2 units plasmanate</td>
<td>1 unit packed RBC, 1 unit plasmapheresis</td>
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</table>

* RBC = red blood cells.
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expect with true SIADH. Therefore, there appears to be a spectrum of abnormalities that one may encounter in the hyponatremic, natriuretic patient that varies from true SIADH to apparent cerebral salt wasting. The serum and urine electrolytes and osmolalities, however, may be the same in patients with either SIADH or cerebral salt wasting. Blood volume determinations may be necessary to differentiate the two groups. The findings of hyponatremia with natriuresis and decreased volume are similar to the findings that one might expect in adrenal insufficiency, salt-losing renal disease, or diuretic therapy, but none of these patients had renal or adrenal disease or were on diuretic therapy.

Although one must be cautious about extrapolating from this small series of patients to all patients with hyponatremia and natriuresis, the implications are that therapy should differ from the current treatment of SIADH with fluid restriction alone. Fluid restriction may actually aggravate an underlying volume deficit. A more appropriate treatment may be to not only restrict water but to replace the volume deficit with packed red blood cells and colloids and to replace the sodium deficit with salt.

Further experimental work to study the problem of hyponatremia and natriuresis in patients with intracranial disease will include studies on measured levels of vasopressin and salt balance and volume status studies prior to the development of the hyponatremia. If natriuresis actually precedes the development of hyponatremia, one would expect to find a negative salt balance in the days prior to the development of serum hyponatremia.

References


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