Adipsic Hypernatremia in a Dog with Antithyroid Antibodies in Cerebrospinal Fluid and Serum

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(Received 10 November 2006/Accepted 14 February 2007)

Abstract. A 4-year-old, male Labrador retriever, weighing 27 kg, presented with abrupt clinical signs including mental retardation, circling and head pressing. The dog never ingested water by choice. An adipsia of the dog was persisted and developed to hypernatremia with artifactual hyperchloremia. Serial endocrine results and image findings were suggestive of a hypothyroidism. The dog revealed the presence of antithyroid antibodies in the cerebrospinal fluid and serum. With the administration of levothyroxine sodium, his neurolgic signs were alleviated within the first week of treatment and adipsia was also resolved.

Key words: adipsia, canine, hypothyroidism.

Normal physiological responses to hyperosmolality include the release of arginine vasopressin (AVP) and the stimulation of thirst centers in the hypothalamus [15]. Animals with adipsic or hypodipsic disorders deny thirst and make no efforts to drink despite their markedly elevated plasma osmolality and plasma sodium levels resulting from pure water deficits. Hypodipsic hypernatremia has been reported in dogs with brain malformations [4, 12, 20] and granulomatous meningoencephalitis [13], which are thought to result from defective osmo-regulation of AVP or hypothalamic dysfunctions.

Hypothyroidism is a common diagnosed endocrinopathy in dogs [5, 16]. Because of the multisystemic effects of thyroid hormones, the clinical signs of hypothyroidism are wide ranging. The behavioral changes associated with hypothyroidism are apathy, lethargy, intolerance of cold and aggression [1, 6]. Also, neuromuscular signs can include facial nerve paralysis, weakness, knuckling or feet dragging, vestibular signs, seizures, ataxia and circling [16]. Lymphocytic thyroiditis, which is a cause of hypothyroidism in dogs, is analogous to Hashimoto’s thyroiditis (HT) of human [17]. This disorder is a disease characterized by infiltration of the thyroid gland by lymphocytes, plasma cells, and macrophages and autoantibodies (AA) predominantly can develop against thyroglobulin (Tg) [2, 22]. Recently, neurological disorder associated with HT has been named “Hashimoto’s encephalopathy” (HE) or “encephalopathy associated with autoimmune thyroiditis” and has come to be regarded as a clinical entity in human medicine [7]. HE may be distinct from myxedema encephalopathy associated with hypothyroidism [9]. This case report describes the clinical findings of a dog with adipsia, which may be related to hypothyroidism.

A 4-year-old, male Labrador retriever, weighing 27 kg, presented to Veterinary Medical Center at Chungbuk National University with clinical signs including adipsia, mental retardation, circling and head pressing. The dog had been healthy except for an abnormal vocalization for six days prior to admission. The dog had no particular history such as head trauma and had not received vaccination within seven months. On presentation, the dog remained in a lateral recumbent position and did respond only noxious stimuli and showed circling when awaked. The rectal temperature, respiratory rate, mucosal color and capillary refill time were within normal ranges except for a regular bradycardic pattern detected by electrocardiography (43 to 52 beats per minute). The dog did not reveal other neurological deficits on the general neurological examination.

Serum biochemical analyses revealed hypernatremia with normal anion gap, hyperchloremia and elevated creatine kinase (Table 1). Potassium concentration was within reference range. Serum hyperosmolality was mainly attributed to hypernatremia. In particular, the dog never made efforts to drink water despite an increased plasma osmolality. No abnormalities of arterial blood gas analysis and urinalysis were found. Urine specific gravity was 1.036. Also, remarkable signs were not detected on survey radiographs and abdominal ultrasonography.

The dog was hospitalized for additional tests and medical treatments with closed monitoring. Fluid therapy consisting of 0.45% sodium chloride plus 2.5% dextrose was initiated to correct the hypernatremia. The rate of sodium decrease was set not to exceed 0.5 mEq/h to avoid cerebral osmotic dysequilibrium and edema. Water was added to a canned prescription diet (h/d®, Hill’s Pet Nutrition, Topeka, KS, U.S.A.) as the dog had an appetite. Over the next 24 hr, serum sodium and chloride concentrations and osmolality decreased in response to fluid therapy.

However, the condition of the dog was not improved.
When the intravenous supplementation of fluid ceased, the persistent adipsia relapsed into mild hypernatremia with artifactural hyperchloremia and hyperosmolality (Table 1). Thyroid gland function was evaluated by use of a serum sample collected on day 2. Both serum total T4 and free T4 concentrations were low (Table 2). Serum aldosterone concentration, which was analyzed to rule out hyperaldosteronism, was within reference range.

On day 5, to examine the presence of intracranial lesion, cerebrospinal fluid (CSF) collection and computed tomographic (CT) scans of the brain were performed. The CSF analysis showed increased total protein (200 mg/dl; reference interval [RI] <35 mg/dl) and sodium concentration (159 mEq/l; RI 135–150 mEq/l). Total nucleated cell count of the CSF was within the normal range (1 cells/µl; RI 0–6 cells/µl) and no evidence of etiologic agents was also observed. Antithyroid antibodies including T3 (0.3%) and T4 (0.4%) autoantibodies were detected in the CSF. Test results of antithyroid antibodies in the CSF were unavailable until 10 days later because the sample was analyzed elsewhere. Remarkable findings were not detected on CT scans of the entire brain with transverse slices taken every 2 mm.

On day 8, the magnetic resonance imaging (MRI) scans of the entire brain showed multi-focal hyperintense foci without mass lesion which was consistent with fluid accumulation in the cerebral cortex on T2-weighted imaging (Fig. 1). Also, there was no enhancement of cerebral cortex after intravenous administration of gadolinium contrast medium (Magnevist, Schering Korea, Seoul, Korea). Thyroid gland function was also re-evaluated by test of thyrotropin-releasing hormone (TRH) stimulation and by measurement of serum thyroglobulin autoantibodies (TgAA) level. Serum canine thyroid-stimulating hormone (cTSH) concentrations of samples obtained before and 30 min after intravenous administration of 0.2 mg of protirelin tartrate (Cerebrain, Shinpoong Pharm., Seoul, Korea) were 0.03 and 0.133 ng/ml, respectively (RI 0.00–0.60 ng/ml). Both basal total T4 concentration and total T4 concentration measured at 4 hr after administration of protirelin tartrate were consecutively low. The TgAA level was very high and T3 and T4 autoantibodies were also detected in the serum (Table 2). On the basis of these findings, the dog was presumptively diagnosed as hypothyroidism. Levothyroxine sodium (Synthyroid, Bukwang Pharm., Seoul, Korea) of 0.02 mg/kg was administered orally every 12 hr. On day 14, the neurologic signs including mental retardation, aimless wandering and circling were alleviated, and an effort to drink water was made. Serum sodium concentration was normalized, and the dog was discharged. Following up, his cerebral edema findings disappeared on MRI scans on day 41 (Fig. 1). The dog is healthy without abnormal signs.

The histories, clinical manifestations and laboratory findings suggested that hypernatremia observed in this case was caused purely from no water intake due to adipsia and not

### Table 1. Serial blood analysis data of the dog with adipsic hypernatremia

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5†</th>
<th>Day 6</th>
<th>Reference interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol/l)</td>
<td>168</td>
<td>157</td>
<td>152</td>
<td>140</td>
<td>149</td>
<td>162</td>
<td>141–152</td>
</tr>
<tr>
<td>Chloride (mmol/l)</td>
<td>131</td>
<td>125</td>
<td>117</td>
<td>111</td>
<td>ND</td>
<td>126</td>
<td>105–115</td>
</tr>
<tr>
<td>Corrected chloride* (mmol/l)</td>
<td>113</td>
<td>116.2</td>
<td>112.4</td>
<td>115.7</td>
<td>ND</td>
<td>113.5</td>
<td>107–113</td>
</tr>
<tr>
<td>Total protein (g/dl)</td>
<td>6.6</td>
<td>6.1</td>
<td>6.6</td>
<td>ND</td>
<td>ND</td>
<td>7.1</td>
<td>5.4–7.1</td>
</tr>
<tr>
<td>CK (IU/l)</td>
<td>1,165</td>
<td>1,991</td>
<td>2,070</td>
<td>ND</td>
<td>ND</td>
<td>142</td>
<td>42–530</td>
</tr>
<tr>
<td>Osmolality (mOsm/kg)</td>
<td>346</td>
<td>331</td>
<td>326</td>
<td>302</td>
<td>ND</td>
<td>347</td>
<td>290–310</td>
</tr>
</tbody>
</table>

* Chloride concentration x 146/sodium concentration.
† The time when hypotonic fluid therapy was stopped.

CK, Creatinine kinase; ND, Not done.

### Table 2. Results of endocrine tests in the dog with adipsic hypernatremia

<table>
<thead>
<tr>
<th>Analytes</th>
<th>Day 2</th>
<th>Day 8</th>
<th>Reference interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal TT4 (mmol/l)</td>
<td>0.35</td>
<td>0.75</td>
<td>1.6–3.2</td>
</tr>
<tr>
<td>TT4 at 4 hr post-TRH stimulation (mmol/l)</td>
<td>ND</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>fT4 (pmol/l)</td>
<td>3</td>
<td>ND</td>
<td>8–40</td>
</tr>
<tr>
<td>TgAA (%)</td>
<td>ND</td>
<td>87</td>
<td>&lt;25</td>
</tr>
<tr>
<td>cTSH (mg/ml)</td>
<td>ND</td>
<td>0.03</td>
<td>0.00–0.60</td>
</tr>
<tr>
<td>T3AA (%)</td>
<td>ND</td>
<td>3.1</td>
<td>0–2</td>
</tr>
<tr>
<td>T4AA (%)</td>
<td>ND</td>
<td>2.9</td>
<td>0–2</td>
</tr>
<tr>
<td>Aldosterone (pg/ml)</td>
<td>13.8</td>
<td>ND</td>
<td>2–96</td>
</tr>
</tbody>
</table>

TT4, Total thyroxine measured by radioimmunoassay; fT4, Free thyroxine measured by equilibrium dialysis; TgAA, Thyroglobulin autoantibody; cTSH, Canine thyroid-stimulating hormone; T3AA, Triiodothyronine autoantibody; T4AA, Thyroxine autoantibody; ND, Not done.

For the unit (%) of autoantibodies, the absorbance value of patient sample was divided by the value of positive sample and it was multiplied by 100 to achieve percentage.
Sick-euthyroid syndrome. The literatures that explain the concurrent hypothyroidism because of phenomenon such as decide whether the dog with neuropathic abnormalities had hypothyrodism [8]. Moreover, it may be difficult to cal findings support the diagnosis of hypothyroidism [8, 21].

In conjunction with low levels of thyroxines and other clinical signs, laboratory tests, image findings and responses to treatments supported that the dog had hypothyroidism. In the TRH stimulation test, the total T4 concentrations were consecutively low, although the cTSH concentrations showed a marked increase. Also, significantly elevated AA against Tg was detected in serum. This presence of TgAA in conjunction with low levels of thyroxines and other clinical findings support the diagnosis of hypothyroidism [8, 21].

Central nervous system signs are not common in dogs with hypothyroidism [8]. Moreover, it may be difficult to decide whether the dog with neuropathic abnormalities had concurrent hypothyroidism because of phenomenon such as sick-euthyroid syndrome. The literatures that explain the direct association between adipsia and hypothyroidism are lack in veterinary medicine. It was only reported in human medicine that some patients with hypothalamic adipsia had concurrent hypothyroidism, although the mechanisms was not clear [11]. In the present case, the clinical manifestations and diagnostic findings including the presence of antithyroid antibodies in the CSF and serum were similar to those of HE of humans. HE of humans may present as a decline in cognitive function or as confusion, seizures, myoclonus, tremulousness, amnestic syndrome, or a stroke-like event [19]. The diagnosis of HE requires an encephalopathy associated with the existence of anti-thyroid antibodies [18], CSF abnormalities such as elevated protein, electroencephalographic (EEG) abnormalities and excellent steroid responsiveness. MRI findings vary and are non-specific and reversible [3, 7]. However, etiologically, HE may be a controversial diagnosis, as it lacks a precise pathophysiologic basis in both humans and animals [14]. So, a possible explanation for the adipsia in this case is that acute edematous status, such as fluid accumulation in the brain, could affect the thirst center in the hypothalamus. Moreover, the demented condition resulting from hypothyroid crisis might have interfered with an appropriate thirst mechanism.

The case reported here describes the development of adipsic hypernatremia in a dog showing abnormal thyroid function and presence of antithyroid antibodies in the CSF and serum. This phenomenon has not been previously documented in dogs, and it may be a complex complication in hypothyroidism.

REFERENCES


