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Syndrome of Inappropriate Antidiuretic Hormone Secretion in a Mini-Breed Puppy Associated With Aspiration Pneumonia

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A 3-month-old intact male Prague ratter was presented to the emergency service for evaluation of progressive lethargy, weakness, coughing and labour breathing after an episode of resistance to oral deworming. The patient exhibited depression, increased respiratory effort and cyanosis at initial presentation. Results of first diagnostic work-up (complete blood cell count, biochemistry panel and thoracic x-rays) were all consistent with aspiration pneumonia. The puppy was initially treated with balanced isotonic crystalloids, broad spectrum antibiotics, nebulization with thoracic coupage and was transferred to an infant incubator with a sustained FiO2 of 40-50%. Twenty-four hours after ICU admission the patient's condition suffered a worsening and the dog was orthopneic, severely depressed with episodes of intermittent dysphoria and seizuring. New thoracic radiographs and several samples of blood and urine were collected to go further in the diagnostic workup revealing severe hyponatremia, severe plasma hypotonicity, high natriuresis and metabolic acidosis with a worsening of the radiological pulmonary pattern. Based on these new clinical findings a diagnosis of SIADH was established. Emergency treatment with hypertonic 3% saline solution and loop diuretics was started like a sodium supplement and to inhibit water resorption in renal tubules, thus reducing the volume overload. The goal of this treatment was to achieve a progressive and controlled increase of plasma sodium concentration and promoting the excretion of positive body water imbalance. The patient's condition improved clinically over the following days, treatment was progressively discontinued and the dog was discharged 7 days after admission.

To the author's knowledge this is the first report of a puppy younger than 12 weeks with respiratory distress developing SIADH associated to aspiration pneumonia.

Introduction

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is an unusual hormonal disorder that may occur during the hospitalization period because a patient's secretion of antidiuretic hormone (ADH) is not inhibited by hypotonicity of extracellular fluid and, consequently, water retention takes place and dilutional hyponatremia develops.[1] Clinically, this disorder is characterized by severe hyponatremia, hypoosmolality, inappropriately concentrated urine and high urine sodium excretion.[2] In human medicine, hypotonic hyponatremia is widely described as the most common electrolyte imbalance in hospital environment and SIADH is well known as the most common cause of symptomatic hyponatremia that presents an important contributing factor of morbidity and mortality.[3-5]

Although this syndrome has been mainly associated to cerebral injury, pulmonary pathologies, malignancies or use of certain drugs in canine species, its references in the veterinary literature are scarce and thus its prevalence and effect in small animals have not been well defined yet. In this case report, the authors describe emergency treatment and clinical management of severe hyponatremia and associated complications in a mini-breed puppy with SIADH secondary to aspiration pneumonia.

Case description

A 3-month-old, intact male, 0.760 kg Prague Ratter was presented to Veterinary Teaching Hospital of Universitat Autònoma de Barcelona for evaluation of progressive lethargy, weakness, anorexia, coughing, and labor breathing. The day before presentation the puppy was vaccinated against parvovirus and prescribed oral deworming medication for at home administration. According to the owner, the puppy struggled during the administration, and labored breathing started immediately after, worsening over the subsequent hours.

On physical examination, main findings were depression, cyanosis, and labored breathing with a restrictive respiratory pattern. Pulmonary auscultation revealed unilateral abnormalities including fine crackles and increased adventitious respiratory sounds in the right cranial lung lobe, raising suspicion for bronchoaspiration. The rest of the physical examination evidenced weak synchronous metatarsal pulses, cyanotic mucous membranes, slight hypothermia (36.4°C), decreased skin turgor, discomfort on abdominal palpation (aerophagia), and low body condition score (4/9).

On admission, 110 mm Hg of systolic blood pressure was obtained by Doppler (Ultrasonographic Doppler flow detector, Parks Medical Electronics Inc, Aloha, OR) using the dorsal metatarsal artery. Pretreatment packed cell volume and total plasma protein were 28% and 5.2 g/dL, respectively (reference range [RR]: 29%-33.8% and 4.5-6.5 g/dL). Blood glucose was 5.3 mmol/L (99 mg/dL; RR: 3.5-6.4 mmol/L [65-118 mg/dL]) and plasma lactate performed on the same blood sample was low (RR: < 0.6-2.5 mmol/L).

Hereupon, oxygen (flow) supplementation at 2-3 L/min was initiated and a left cephalic intravenous catheter was placed. Initially, fluid therapy was instituted with a balanced isotonic

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Table 1
Results of Initial Blood Cell Count

Complete Blood Cell Count			Reference Range
RBC ($\times 10^6/\mu L$)		3.85	4.3-5.1
Hemoglobin (g/dL)		8.5	9.4-11.2
Hematocrit (%)		28	29-33.8
MCV (fL)		66.5	63.3-68.1
MCHC (pg)		31.7	30.8-34.4
MCH (g/dL)		22.1	20.6-23
White cell count ($\times 10^3/\mu L$)		22.4	1.3-20.1
Segmented neutrophils	75%	16.8	0.7-11.4
Bands	1%	0.22	0-0.6
Lymphocytes	14%	31.3	0.35-6.5
Monocytes	10%	2.24	0.07-2.1
Eosinophils	0%	0	0-1.5
Basophils	0%	0	0-0.2
Platelet count ($\times 10^3/\mu L$)		369	200-500
Reticulocytes count ($\times 10^3/\mu L$)	0.9%	32.6	0 to <80

MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; MCH, mean corpuscular hemoglobin; RBC, red blood cell count.

crystalloid solution (Lactated Ringer's, B.Braun Medical S.A., Barcelona, Spain) at a rate of 5 mL/h (160 mL/kg/d) to restore the hydration deficits and to provide the maintenance requirements. Afterwards, the patient was transferred to an infant incubator where supplemental humidified oxygen supply was adjusted to provide a sustained FiO_2 of 40%-50%. Temperature, heart and respiratory rate, respiratory effort, breathing pattern, oxygen saturation, systolic/mean/diastolic blood pressure, color of mucous membranes, capillary refill time, and glucose levels were monitored every 1- 4 hours. During initial stabilization, the diagnostic workup was initiated and several blood samples for hematologic and biochemistry determinations were submitted for analysis (Tables 1 and 2). Furthermore, thoracic X-rays were also performed under (light) sedation with butorphanol (Butorphanol, Pfizer Inc, New York, USA) at 0.1 mg/kg intravenously (IV) and midazolam (Midazolam, Laboratorios Normon S.A, Madrid, Spain) at 0.2 mg/kg IV, showing a severe focal alveolointerstitial pattern in the right cranial lung lobe, consistent with aspiration pneumonia.

Complete blood cell count and blood smear showed a mild normocytic, normochromic and nonregenerative anemia, moderate inflammatory leukogram with neutrophilic leucocytosis, monocytosis and slight toxic changes in the neutrophils (Table 1).

Table 2
Results of Initial Serum Biochemistry Analysis

Serum Chemistry panel		Reference Range	Units
Glucose	99	65-118	mg/dL
	5.3	3.5-6.4	mmol/L
Lactate	Low	<0.6-2.5	mmol/L
Total proteins	5.2	4.5-6.5	g/dL
	52	45-65	g/L
Creatinine	0.37	0.5-1.5	mg/dL
	32.7	44.2-132.6	mmol/L
Albumin	2.1	2.6-3.3	g/dL
	21	26-33	g/L
ALT	9	21-102	UI/L
Potassium	3.75	4.37-5.35	mmol/L
Sodium	130.4	141-152	mmol/L
Chloride	101.9	105-115	mmol/L
Basal cortisol	1.69	0.5-6	µg/dL
Thyroxine (T_4)	0.897	1.3-2.9	µg/dL
Thyrotropin (TSH)	0.089	0-0-5	ng/dL

ALT, alanine aminotransferase.

Serum biochemistry revealed electrolyte imbalances such as moderate hyponatremia, mild hyplochloremia and mild hypokalemia (Table 2). Additional tests performed included whole blood real-time polymerase chain reaction for distemper, and fecal examination for parasites. Both tests resulted negative.

One hour following admission, a broad spectrum antimicrobial treatment based on cephazolin (Cephazolin, Laboratorios Normon SA, Madrid, Spain) at 25 mg/kg/IV q8h and enrofloxacin (Enrofloxacin, Bayer AG, Leverkusen, Germany) at 5 mg/kg/IV q24h was initiated. Nebulizations (q6h) with 0.9% NaCl and thoracic coupage were also scheduled. Butorphanol (0.1 mg/kg/IV) was administered as needed for handling purposes or for management of punctual episodes of anxiety.

Finally, food was withheld for 12 hours, and subsequently frequent feedings (q4h) of canned food were offered intermittently according to the patient's level of consciousness and degree of respiratory compromise.

Hemodynamic and respiratory parameters were monitored continuously through the intensive care unit (ICU) stay. Packed cell volume, serum total protein, plasma electrolytes (Na^+, K^+, and Cl^-) and glycemic controls were scheduled every 1-8 hours during hospitalization.

During the first 12 hours of admission in the ICU the patient remained hemodynamically stable. However, a mild but progressive worsening respiratory pattern was observed throughout the night. Twenty-four hours postadmission the dog became orthopneic and severely depressed with episodes of intermittent dysphoria and seizuring. Seizures were controlled with an intravenous bolus of diazepam (Diazepam, Roche, Basel, Switzerland) at 0.7 mg/kg. New thoracic radiographs were performed. Also, blood and urine samples were collected to investigate the new clinical signs.

The new radiological study of the thorax revealed a worsening of the pulmonary alveolointerstitial pattern with the appearance of bronchograms and diffuse interstitial pattern which extended into the right cranial and middle lung lobes. Urine electrolyte profile was performed and the rest of indicators such as electrolytes plasma concentration, serum osmolality, blood glucose, venous blood gas, and complete urinalysis were also determined. Plasma sodium reached a concentration of 110.8 mmol/L (RR: 141-152 mmol/L). Effective plasma osmolarity fell to 221.6 mOsm/L (RR: 285-295 mOsm/L). Urine sodium concentration was 137.4 mmol/L (adequate amount, <40 mmol/L) and urine osmolality was 274 mOsm/kg (adequate amount, <150 mOsm/kg). Urine specific gravity at the time of urine electrolyte concentration measurement was 1053 g/L (RR for puppies 4-24 weeks old: 1030-1050 g/L). Venous blood gases revealed metabolic acidosis (pH = 7.21; RR: 7.31-7.42; HCO_3^- = 15.1 mmol/L; RR: 20-29 mmol/L; standardized base excess = −11.7 mmol/L; RR: −4 to +1 mmol/L) without respiratory compensation (pCO_2 = 41 mm Hg; RR: 32-49 mm Hg) (Table 3). Testing for thyroid function and serum cortisol concentration was also performed but it did not show any significant abnormality (Table 2).

According to the veterinary literature, puppies have total thyroxine (TT4) values more than those considered within the RR for adults.[6] In our patient, total thyroxine values were within the RR using adult values. It is the author opinion that this finding could be related to a euthyroid sick syndrome.

Finally, based on such clinical signs and clinicopathological findings, a diagnosis of SIADH was established. Owing to the severity of the hypotonicity and the presence of hyponatremic encephalopathy, emergency treatment with hypertonic saline (Hypertonic NaCl solution (7.5 g/100 mL), BBraun Vet Care, Barcelona, Spain) diluted to a 3% solution was initiated at a rate of 0.3 mL/h (9.5 mL/kg/d, 0.4 mL/kg/h) and 2 bolus of furosemide (Furosemide, Sanofi—Aventis SA, Paris, France), first at 1 mg/kg/IV