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Primary adipsia and severe hypernatremia in a Pit Bull dog

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ABSTRACT: *Primary adipsia is a rare condition in which there is failure in the activation threshold of the hypothalamic osmoreceptors, leading to osmolality imbalance. Here, we reported the case of a Pit Bull dog with an altered level of consciousness (started after weaning) and adipsia. There was an increase in plasma osmolality (444 mOsm/kg), sodium (223.7 mg/dL), and chlorine (173 mg/dL) levels. Based on the suspicion of primary adipsia, water was administered via a nasogastric tube, with clinical improvement. The owner was instructed to supply water with food. Eight months after discharge, the dog returned with parvovirus and died. In the anatomopathological examination, no structural changes were observed in the central nervous system. To our knowledge, this is the first report of hypernatremia due to adipsia in a Pit Bull dog, showing that this is a differential diagnosis that should be considered in this breed.*
Key words: *congenital, neurology, osmolality, osmoreceptors, sodium.*

Adipsia primária e hipernatremia severa em um cão Pit Bull

RESUMO: *Adipsia primária é uma rara condição em que há falha no limiar de ativação dos osmoreceptores hipotalâmicos, levando ao desequilíbrio da osmolalidade. Este artigo tem como objetivo relatar o caso de um cão da raça Pit Bull apresentando alteração no nível de consciência (iniciado após o desmame) e adipsia. Foi verificado aumento da osmolalidade plasmática (444 mOsm/kg), sódio (223,7 mg/dL) e cloro (173 mg/dL). Baseado na suspeita de adipsia primária, iniciou-se administração de água via sonda nasogástrica, com melhora clínica. O tutor foi orientado a fornecer água junto a alimentação. Oito meses após alta, o paciente retornou com parvovirose e veio a óbito. No exame anatomopatológico, não foram observadas alterações estruturais no sistema nervoso central. Este é o primeiro relato de hipernatremia por adipsia em um cão Pit Bull, mostrando que este é um diagnóstico diferencial que deve ser considerado nesta raça.*
Palavras-chave: *congênito, neurologia, osmolalidade, osmorreceptores, sódio.*

Primary hypodipsia or adipsia is an uncommon disease (RIGGS 2002). In veterinary medicine, few reports show no structural abnormalities in the central nervous system (CRAWFORD et al. 1984, KANG et al. 2007). In these cases, the absence of thirst occurs due to a malfunction in the hypothalamic receptors, which are unable to detect an increase in plasma osmolality and thus generate stimuli that signal the need for water intake, generating adipsia. In this report, we describe the first case of primary adipsia in a Pit Bull dog with no structural abnormalities.

A 3-month-old male Pit Bull dog was brought to the Veterinary Hospital with sporadic diarrhea, depression interspersed with periods of agitation, and vocalization for 8 days. The animal had undergone veterinary care in the previous week with the same history, when a blood count was performed, but no abnormalities were found.

In the anamnesis, the owner reported worsening of the animal's general condition during the hottest periods of the day, with severe lethargy and cutaneous hyperemia, besides normorexia. On physical examination, the dog's physiological parameters were within the normal range, except hydration (dehydration estimated at 6%) (DIBARTOLA & BATEMAN 2006). Neurological evaluation showed altered consciousness (depression alternating with moments of agitation and disorientation), lack of proprioception, and increased spinal reflexes in the four limbs; however, examination of the cranial nerves showed no abnormalities. In addition, cutaneous hyperemia and associated seborrhea were observed. Blood and urine samples were collected for the laboratory tests, and

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supportive treatment was immediately initiated to correct losses and dehydration, with isotonic fluid therapy (Ringer's lactate solution) at an IV flow rate of 5 mL/kg/h and antibiotic therapy (metronidazole 15 mg/kg BID) due to sporadic diarrhea.

Blood count, arterial blood gas, and serum levels of albumin, globulin, and total protein were within the reference range for the species. However, plasma levels of sodium, chlorine, and plasma osmolality were markedly high in the first evaluation of the animal (Table 1, day 1 - morning). Urinalysis showed hypersthenuria (Table 1), and the rapid antigen test for distemper virus (SensPert® C Ag) was negative. New dose of plasma electrolytes 6 h after the first examination revealed persistence of hypernatremia, hyperchloremia, and hyperosmolality (Table 1, day 1 - afternoon). From these results, the owner was questioned to determine the etiology of the persistent hypernatremia. The owner reported that the animal had a total lack of interest in the free intake of water, which led to forced administration since the weaning period.

Due to the possibility of isovolemic hypernatremia, the infusion of Ringer's lactate solution was replaced with water intake via a nasogastric tube, due to extreme resistance to forced administration. The daily volume of water intake was calculated according to the formula: daily water intake (mL) = 30 × live weight + 70 (KIRK & BISTNER, 2006), with 20 mL administered every 2 h. On day after the beginning of treatment (day 2), chlorine, osmolality, and urinary density remained high (Table 1, day 2), and despite the reduction of 1.2 mmol/L/h in the plasma sodium concentration (to 197.8 mmol/L), worsening of neurological signs was noted. Clinical signs were controlled with diazepam (0.5 mg/kg, IV, single dose) and phenobarbital (2 mg/kg, IV, single dose). The animal remained hospitalized, with water administration via a nasogastric tube, metronidazole (15 mg/kg BID), and *ad libitum* feeding. After 48 h of treatment (day 4), the plasma sodium level reached a concentration of 173 mmol/L, accompanied by the reduction of chlorine, osmolality, and improvement of the general clinical picture (Table 1, day 4). In the second urinalysis performed that day, isostenuria was the only abnormality observed.

Based on the dog's clinical improvement, the owner was instructed to add 250 mL of water to the food daily, since the animal was eating normally despite the lack of interest in spontaneous water intake and an intense resistance to forced oral administration. Total remission of neurological signs and normalization of plasma sodium, chlorine, and osmolality levels (Table 1, day 7) occurred 6 days after the initiation of oral water therapy, despite persistent isostenuria. The owner did not return for the scheduled follow-up appointments, but he informed via phone call that after 30 days, there was a complete improvement of the initially reported condition.

Eight months after the first visit, the animal returned in hypovolemic and septic shock due to gastroenteritis (melena and emesis), with an evolution of 7 days, and generalized deep pyodermitis. Laboratory tests revealed pancytopenia, azotemia, increased alanine aminotransferase (ALT), hypersthenuria, and a positive rapid parvovirus (Alere) antigen test. Despite the initiation of therapy, the animal died on the same day. Necropsy and histopathological examinations revealed diffuse and marked necrotizing enteritis and demodicosis with hyperkeratosis, but no abnormalities were found in the other organs, including the central nervous system.

The diagnosis of primary hypodipsia or adipsia is based on the history of non-ingestion of water associated with serum hyperosmolarity and the ability to concentrate urine (MCCLURE & DVIR 2013), which can be acquired (as in trauma or neoplasia) or congenital (HARDY 1999). In this report, the diagnosis of primary adipsia was based on the history of non-ingestion of water, associated

Table 1 - Evolution of urinary density, sodium, chlorine, and osmolality levels over 6 days of treatment of a dog with primary adipsia.

Laboratory exams	----------Day 1----------		Day 2	Day 4	Day 7	Reference range
	Morning	Afternoon				
Sodium (mg/dL)	223.7	212.6	197.8	173	146.4	140-150
Osmolality (mOsm/kg)	444	414	385	339	291	280-310
Urinary density	1.05	-	1.05	1.015	1.015	1.015-1.025
Chlorine (mg/dL)	173	165.7	153.3	132.4	107.1	98-107

with clinical and laboratory abnormalities, reinforced by the fact that the onset of clinical signs occurred concurrently with the weaning period. In addition, there was a complete remission of the clinical signs in response to the treatment administered.

To our knowledge, this is the first case of primary adipsia observed in a Pit Bull dog. An altered mental state is common, since neurological signs develop due to persistent hyperosmolarity of the extracellular fluid, which severely affects the cells of the central nervous system, leading to the observed clinical abnormalities (KANG et al. 2007). As noted in this case, the worsening of neurological signs is common during rehydration as a consequence of cerebral edema, which developed due to a rapid drop in sodium levels (RIGGS, 2002).

Integumentary and gastrointestinal system may also be compromised in dogs with primary adipsia, and erythema and seborrhea have already been described (MCCLUE & DVIR, 2013), as observed in this case. These dermatological abnormalities tend to disappear after plasma sodium normalization (MCCLUE & DVIR, 2013), and it is speculated that they occur due to chronic dehydration of the stratum corneum (CHAPMAN et al. 2009). This animal also had intermittent gastrointestinal signs, as mentioned in a report on hypodipsic hypernatremia (CHAPMAN et al. 2009), but this does not justify the electrolytic alteration.

In primary adipsia, after sodium correction, isosthenuria occurs due to the dysfunction of hypothalamic osmoreceptors. These osmoreceptors fail to recognize the need for the secretion of vasopressin in an adequate osmolarity range, resulting in low urinary density in situations of normal serum osmolarity (DERUBERTS et al. 1974, HAWKS et al. 1991, ABREU 2002, GOLDKAMP & SCHAER 2007), as observed in this study.

The possibility of inadequate access to water was ruled out since the owner reported offering *ad libitum* fresh water, and since other puppies of the litter were healthy. After the correction of dehydration by fluid therapy, the animal continued to present hypernatremia and hyperosmolality, and hypovolemia was ruled out as the cause of the increased serum sodium. High serum sodium concentration without any signs of dehydration characterizes isovolemic hypernatremia (MCCURIE & DVIR, 2013; GUILLAUMIN & DIBARTOLA 2017).

The severity of clinical signs is directly related to the high plasma concentration of sodium (HARDY 1989, ABREU 2002, GUILLAUMIN & DIBARTOLA 2017). Treatment is considered challenging and is associated with high mortality rates (GUILLAUMIN & DIBARTOLA 2017). Treatment includes the correction of hyperosmolarity through the parenteral administration of hypotonic fluids (0.45% NaCl or 5% dextrose). However, oral or nasogastric tube administration is preferred (MCCURIE & DVIR 2013, GUILLAUMIN & DIBARTOLA 2017), as was the case in this study.

The correction of hypertonicity should be performed slowly and gradually to avoid the development of cerebral edema (HARDY 1989). In our case, despite efforts, there was a drop of 1.2 mmol/L/h sodium, which resulted in worsening of the neurological signs, which was attributed to the development of cerebral edema, since the decrease in plasma sodium should be between 0.5 mmol/L/h and 1 mmol/L/h (GOLDKAMP & SCHAER 2007). Fortunately, after 2 days, there was a significant improvement in the dog's general condition, with a reduction of 25.9 mmol/L in 24 h, which is within the recommended range (CHAPMAN et al. 2009). After stabilizing the clinical condition, it is recommended that water be added to solid food (MCCURIE & DVIR, 2013), as in this case. Serum electrolyte concentrations and urinary density, along with the animal's history and response to treatment, were critical for the diagnosis of primary adipsia. Despite being rare, it should be considered as a differential diagnosis in cases of normovolemic hypernatremia.

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DECLARATION OF CONFLICT OF INTERESTS

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTIONS

SMC, SMC and GGO were responsible for the clinical care of the case reported. SMC and SMC wrote the article, GGO and AIS contributed to hematological analyzes, and MIPP and FOL was responsible for guiding, reviewing and interpreting the results achieved. All authors read and approved the final manuscript.

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