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Bócio hiperplásico em ovelhas no semiárido Paraibano, Brasil: relato de caso

Hyperplastic goiter in sheep in the semi-arid region of Paraiba, Brazil: case report

Bocio hiperplásico en ovejas en la región semiárida de la Paraíba, Brasil: un reporte de caso

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Resumo

O objetivo deste trabalho foi descrever os achados clínicos, anatomopatológicos e as concentrações séricas de triiodotironina (T3) e tiroxina (T4) livres de um surto de deficiência de iodo (I) em ovinos na região semiárida do Brasil. O surto foi observado em uma propriedade localizada no município de Sousa, Oeste do Estado da Paraíba, zona semiárida do Nordeste do Brasil. O lote estudado era composto por 10 animais que apresentavam aumento de volume da porção proximal do pescoço, ventral ao arco da mandíbula de consistência firme sendo sugestivo de bócio. Foram coletadas amostras da tireoide dos 10 animais que apresentavam hiperplasia da glândula. Além disso, amostras de sangue foram coletadas para análise sérica dos hormônios tireoidianos. Os achados clínicos, as características macroscópicas e os achados histológicos observados nestes casos são idênticos àqueles descritos na literatura para bócio adquirido e constituem evidências que permitem o diagnóstico definitivo desta condição. As concentrações médias observadas nos animais foram: T3 (0.5±0.08 pmol/L) e T4 (10.93±2.88 pmol/L) livres. Tomando como base os achados epidemiológicos, sinais clínicos, lesões anatomopatológicas e a análise sérica dos hormônios tireoidianos, podemos afirmar que ocorreu o surto de bócio adquirido em virtude de falhas na alimentação e suplementação mineral dos animais. Desta forma, para se prevenir o aparecimento deste transtorno nutricional, é de suma importância que seja fornecida aos animais uma alimentação e suplementação mineral balanceada, considerando consideração as necessidades para a espécie e substâncias bocígenas alimentares.

Palavras-chave: Deficiência mineral; Iodo; Metabolismo; Ruminante; Hormônios.

Abstract

The aim of this study was to describe the clinical and anatomopathological findings and serum concentrations of free triiodothyronine (T3) and thyroxine (T4) from an outbreak of iodine (I) deficiency in sheep in the semi-arid region of Brazil. The outbreak was observed in a property located in the municipality of Sousa, West of the State of Paraiba, a semi-arid zone of Northeast Brazil. The studied lot was composed of 14 animals, between 12 and 18 months old, male, and mixed breed. The animals presented an increase in volume in the proximal portion of the neck, ventral to the mandibular arch, of firm consistency, suggesting a goiter. Thyroid samples were collected from animals that presented gland hyperplasia. In addition, blood samples were collected for serum analysis of thyroid hormones. The clinical findings, macroscopic characteristics, and histological findings observed in these cases are identical to those described in the literature for acquired goiter and constitute evidence that allows the definitive diagnosis of this condition. The mean concentrations observed in animals were: Free T3 (0.5±0.08 pmol/L) and Free T4 (10.93±2.88 pmol/L). Based on the epidemiological findings, clinical signs, anatomopathological lesions, and serum analysis of thyroid hormones, we can affirm the outbreak of acquired goiter occurred due to inadequacies in feeding and mineral supplementation of the animals. Thus, in order to prevent the appearance of this nutritional disorder, it is of utmost importance that animals are provided with a balanced mineral diet and supplementation, taking into account the needs of the species and antithyroid feed substances.

Keywords: Mineral deficiency; Iodine; Metabolism; Ruminant; Hormones.

Resumen

El objetivo de este estudio fue describir los hallazgos clínicos y anatomopatológicos y las concentraciones séricas de triyodotironina libre (T3) y tiroxina (T4) de un brote de deficiencia de yodo (I) en ovejas en la región semiárida de Brasil. El brote se observó en una propiedad ubicada en el municipio de Sousa, al oeste del estado de Paraíba, una zona semiárida del noreste de Brasil. El lote estudiado estaba compuesto por 14 animales, de entre 12 y 18 meses de edad, machos y mestizos. Los animales presentaron un aumento de volumen en la porción proximal del cuello, ventral al arco mandibular, de consistencia firme, lo que sugiere un bocio. Se recogieron muestras de tiroides de animales que presentaban hiperplasia de glándulas. Además, se recogieron muestras de sangre para el análisis de suero de las

hormonas tiroideas. Los hallazgos clínicos, las características macroscópicas y los hallazgos histológicos observados en estos casos son idénticos a los descritos en la literatura para el bocio adquirido y constituyen evidencia que permite el diagnóstico definitivo de esta afección. Las concentraciones medias observadas en los animales fueron: libre T3 (0.5±0.08 pmol/L) y libre T4 (10.93±2.88 pmol/L). Con base en los hallazgos epidemiológicos, los signos clínicos, las lesiones anatomopatológicas y el análisis sérico de las hormonas tiroideas, podemos afirmar que el brote de bocio adquirido se produjo debido a las deficiencias en la alimentación y la suplementación mineral de los animales. Por lo tanto, para evitar la aparición de este trastorno nutricional, es de suma importancia que los animales reciban una dieta mineral y suplementos equilibrados, teniendo en cuenta las necesidades de las especies y las sustancias de alimentación antitiroideas.

Palabras clave: Deficiencia mineral; Yodo; Metabolismo; Rumiante; Hormonas.

1. Introduction

Mineral deficiencies are correlated to certain geographic areas and, when accentuated, may be responsible for low socioeconomic indicators in certain regions where the population depends mainly on livestock production (Tokarnia et al., 2010). In Brazil, the situation of mineral deficiencies in farm animals is relatively well known, however, there are still regions of the country, as is the case in the Northeast region, where there are reports of a lack of essential macro minerals and trace elements, with fewer studies compared to other regions of the country. Among the trace elements, iodine has a fundamental role in animal physiology and is considered an essential element for farm animals, is required in low amounts in the animal organism.

In some regions of Brazil, iodine deficiency has been reported over various decades, such as by Martins (1946), who diagnosed stillborn goats with congenital goiter due to maternal iodine deficiency in São Paulo and Megale (1949), who identified congenital goiter in calves, in Minas Gerais State. The most recent works are reported by Almeida et al. (2013), who recorded cases in goats in São Paulo state, Panziera et al., (2014), who also recorded congenital goiter in goats in the northwest of Rio Grande do Sul and Martins et al., (2018) with cattle in the Center-South region of Mato Grosso. According to Riet-Correa (2007), the occurrence is more frequent in areas that are far from the sea and where rainfall is low.

The expression goiter is a clinical term applied to describe an increase in the thyroid gland volume, of non-neoplastic and non-inflammatory origin, which affects many species,

from domestic, marine, and wild mammals to humans (Capen, 2007; Ecco and Langohr, 2010; Laperle, 2013). The goiter can be classified as congenital, when the animal is born with an altered thyroid gland, or acquired, due to food suppression and hormonal control mechanisms. Although goiters frequently affect goats, there are few literary descriptions in this species (Al-ani et al., 1998; Ozmen et al., 2005; Cheema et al., 2010), in addition to in other species such as sheep, cattle, and horses (Capen, 2007; Riet-correa, 2007; Tokarnia et al., 2010; La Perle, 2013).

A deficiency or excess of iodine in the diet, antithyroid compounds, and genetic defects in the enzymes responsible for the synthesis of thyroid hormones, can cause the thyroid gland to swell, in addition to altering the synthesis and secretion of triiodothyronine (T3) and thyroxine (T4) (Capen, 2007; La Perle, 2013; Behringer et al., 2018). In addition, they play important functions in the animal organism related to protein metabolism, immunocompetence, and the reproductive system (Martins et al., 2018). For Ecco and Langohr (2010) and La Perle (2013), iodine has a fundamental role in the synthesis of thyroid hormones (T3 and T4) and its deficiency is the main cause of goiter in domestic animals.

There are no record of iodine deficiency cases, in the semi-arid region of the Brazilian Northeast or the negative aspects that this deficiency causes in livestock breeding systems. In view of the above, the objective was to describe pioneering clinical and anatomopathological findings and serum T3 and T4 concentrations of an outbreak of iodine deficiency in sheep in the semi-arid region of the state of Paraiba, Brazil.

2. Material and Methods

The outbreak was observed in a property located in the municipality of Sousa, in the western region of the Paraiba State, in the semi-arid zone of Brazilian northeast. At the property, the animals were in a fattening system, distributed in batches according to age, and reared in a semi-intensive regime. The animals grazed in native pasture areas, in the morning, associated with Tifton grass, and with the offer of corn bran and soy in the afternoon, with a proportion of 80/20 of each ingredient in the period they were confined, in addition to a supply of water and mineralized salt ad libitum. On the property, there was an average herd of 1,500 sheep. Of this total, biological material was collected from 10 animals, which were between 12 and 18 months old, being mixed-breed animals and all males.

The animals were subjected to a clinical examination on the property, anamnesis data were recorded, and blood collection was performed. Subsequently, 10 of the animals were

referred to the Veterinary Pathology Sector of the Federal University of Campina Grande (LVP-UFCG). Blood samples were collected by jugular venipuncture in tubes without anticoagulant to obtain serum. Subsequently, the animals that presented a volume increase in the neck's proximal portion, ventral to the mandibular arch, of firm consistency, and being suggestive of goiter, were euthanized for macroscopic evaluation. Samples of thyroid tissue were stored in 10% formal solution for further histopathological analysis.

After clot retraction, the tubes containing blood were centrifuged at 3500 rpm for 10 minutes and the serum was aliquoted in polyethylene tubes and stored in a freezer at -20ºC to quantify thyroid hormones (Free T3 and T4). The thyroid fragments were submitted to histological processing and cut to 5 µm thick, before being stained by the hematoxylin-eosin method for microscopic analysis.

At the analysis time, serum samples were thawed at room temperature, homogenized by vortexing, and centrifuged again at 3000 rpm for 10 minutes. The serum concentrations of Free T3 and T4 were determined using the electrochemiluminescence method (ECLIA), with a commercial kit and the equipment BECKMAN COUNTER - ACCESS 2®. Hormonal analyzes were performed at the Analytical Chemistry Laboratory of the Research Support Center (CENAPESQ) of the Federal Rural University of Pernambuco.

3. Results and Discussion

3.1. Clinical Aspects

All sheep presented clinical signs similar to those described in the literature for goiter, which basically consisted of an increase in the palpable volume of the cranial ventral cervical region (Figures 1A and 1B) (Ozmen et al., 2005; Campbell et al., 2012; Hassan et al., 2013). Panziera et al. (2014), found, in addition to the accentuated symmetrical volume in the lobes of the thyroid gland, diffuse alopecia and a marked increase in symmetrical volume in the lobes of the thyroid gland, a clinical sign that was not registered in the animals of the current study. Hassan et al. (2013), did not observe alopecia, however, they registered that the hair was rough, in addition to which, during auscultation and palpation of the neck area, the authors observed the presence of pulsation. In the clinical examination, rectal temperature and respiration rates were normal. Ozmen et al. (2005) reported subnormal growth and absence of normal wool development.

The animals presented a good nutritional status, with a body score between 3.5 and

4.0, and did not present skin and hair alterations. In the anamnesis, there were no deaths related to the current cause, but due to several causes, such as mortality of newborns who did not receive adequate delivery assistance.

Figure 1 – Increased palpable volume in the cranial ventral cervical region of the evaluated animals.

Source: Authors' elaboration.

The animals consumed native pasture in the morning, supplemented with corn bran and soy, with a proportion of 80/20 of each ingredient in the period they were confined, in addition to water and mineralized salt ad libitum. It is important to consider these observations, since the lack of mineral supplementation, or even the offer of foods that are antithyroid agents, define this disease in a rearing system, whether extensive or intensive, in which it can present in the congenital form or not. Almeida et al. (2013), explains that the cases of goiter reported in the national literature are quite scarce and, when reported, consist of the congenital form. In this case, the outbreak was associated with an acquired form, since the animals developed the disease during their productive life.

As the animals were supplemented with mineral salt specific for the sheep species, it is assumed that another risk factor has been defined in this situation, such as the ingestion of feed considered to be antithyrotic, as is the case of soy present in their diet. In addition to simple deficiency, there are several food substances, known as goitrogens (Ozmen et al., 2005). These substances can be found in different vegetables, such as the cruciferous vegetables (cabbage, cabbage, broccoli) and soy, cassava, flaxseed, and sorghum that contain antithyroid substances that block the uptake of iodine by the thyroid gland and prevent the formation of thyroxine (Ikeda et al., 2000; Knowles and Grace, 2015).

These same authors found that soy diet and iodine deficiency synergistically induced hyperplasia of thyroid follicular cells in rats, reinforcing the hypothesis of soy as a risk factor for the appearance of goiter in these animals, unrelated to mineralization. The soy protein diet has been shown to increase T4, Free T4, and TSH levels in animals, while T3 is generally unaffected (Forsythe, 1995). According to this same author, the basic premise is that feeding with soy protein decreases the plasma cholesterol concentration, causing an increase in the plasma concentrations of thyroxine, and as Ikeda et al. (2000) and Son et al. (2001) reported, feeding soy protein to laboratory animals consistently raises plasma thyroxine concentrations.

Also, this rise in plasma thyroxine concentrations precedes the alteration in plasma cholesterol concentrations: a necessary requirement for the hypothesis of a causative effect. Possible mechanisms are also presented about how a dietary protein source affects plasma thyroxine (Forsythe, 1995).

Martins et al. (2018) also report that some minerals are capable of interfering with the thyroid functioning, such as calcium, which when present in large amounts in the blood, can develop goiter, due to the intestinal decrease in the absorption of iodine in the intestine. Another element that influences the thyroid is selenium, as a lack of this trace element favors the development of goiter, since it is related to the formation of enzymes that convert T4 into T3 (Matamoros et al., 2003). In the northeastern region, it is common to use maniçoba hay (genus Manihot), and this forage contains cyanogenic glycosides, due to the formation of thiocyanide, which prevents the absorption of iodine by the thyroid, but, in this case, there was no record of previous consumption of this forage and for a long period, which could imply as another risk factor (Knowles and Grace, 2015).

3.2. Quantification of Free T3 and T4

The average serum concentration of the Free T4 hormone was 10.93±2.88 pmol/L and the Free T3 was 0.5±0.08 pmol/L (Table 1). The values of Free T4 and Free T3 found are lower than those observed by Anderson et al. (1988), with 24.71±0.78 pmol/L and 3.99±0.36 pmol/L and Nazifi et al. (2008), with 20.24±0.47 pmol/l and 4.68±0.14 pmol/l. For Atessahim et al. (2002) the normal values of T4 Free range from 19.56±0.90 pmol/L, and T3 Free range from 4.40±0.12 pmol/L.

The concentrations of Free T4 were higher than the data observed by Ozem et al. (2005), who found mean values of 2.65±0,43 pmol/L for goiter sheep; and Osório et al. (2017), who registered an average of 7.10±2.91 pmol/L to Free T4 of sheep under seven

months of age and both sexes. Ozmen et al. (2005) found that while serum levels of Free T4 were much lower than normal before treatment, the level of these hormones became more or less normal after 2 months of treatment. After treatment, the serum concentration of Free T4 was 25.17 pmol/L.

Table 1 - Values of mean, median, standard deviation, minimum and maximum serum concentration of free T3 and T4 hormones in sheep (n=10) with hyperplastic goiter.

Animals	Free T3 (pmol/L)	Free T4 (pmol/L)
1	0.43	10.55
2	0.63	4.11
3	0.54	12.48
4	0.48	12.99
5	0.56	12.61
6	0.54	13.12
7	0.44	9.39
8	0.42	12.61
9	0.42	10.55
10*	-	-
Average	0.50	10.93
Standard deviation	0.08	2.88
Minimum	0.42	4.11
Maximum	0.63	13.12

* The blood sample from sheep 10 was not viable for analysis. Source: Authors' elaboration.

Few studies have recorded cases of goiter in sheep in which they have quantified thyroid hormones in their free form, as it is common to verify records with Total T4 and T3 (Kallfez and Erali, 1973; Reap et al., 1978; Bowers et al., 1993; Starling et al., 2005; Todini, 2007; Iveta et al., 2011; Hassan et al., 2013 and Farman et al., 2018); whereas Anderson et al. (1988) and Oznem et al. (2005), quantified Total and Free T4 and T3. Alterations in serum concentrations of Free T4 and Free T3 generally followed those of Total T4 and T3,

respectively, as observed by Fazio et al. (2007), since this assumption was confirmed by the existence of positive and significant correlations between the concentrations of Total T3 with Free T3 and Total T4 with Free T4. In this context, it is important to consider the discussion about the different works published with sheep with goiters and that the quantified hormones were not in free form.

It is widely known that variations in the concentration of thyroid hormones in sheep can be identified between authors, which may be attributed to differences in analytical methods, as well as variations in dietary composition, animal's physiological aspects, and geophysical characteristics of the environment. According to Matamoros et al. (2003) and Fazio et al. (2014), it is necessary to understand the functions of thyroid hormones to be able to properly interpret endocrine disorders and evaluate their possible applications in farm animals. According to Huszenicza et al., (2002) these hormonal alterations represent an important adaptation mechanism of the organism when faced with risk factors.

Matamoros et al. (2003), reinforce that the serum quantification of thyroid hormones is appropriate to affirm damage or aggravation related to the thyroid gland. In fact, many endogenous and exogenous factors that affect thyroid function can lead to misinterpretation when comparing with reference values. Based on the reports, it appears that the animals in the current study presented low concentrations of both hormones and are in agreement with other authors who reported cases of goiter, with diagnoses established through clinical signs, blood concentrations of these hormones, and anatomopathological aspects.

The use of Free T3 and T4 in the current study is in agreement with the observations of Gouveia et al. (2016), who mentions that the serum dosage of Free T3 and T4 (instead of Total T3 and T4) is advantageous in that it reflects the individual's true metabolic state and remains relatively constant, being less frequently influenced by levels of carrier proteins. Although the free fractions of T3 and T4, which have biological effects on tissues, are very small (<0.1% of the total), they are responsible for the regulation of cellular metabolism and for the control of TSH (thyroid-stimulating hormone) and TRH (thyrotropin-releasing hormone) from the hypothalamic-pituitary-thyroid axis (González and Silva, 2017; Behringer, et al., 2018).

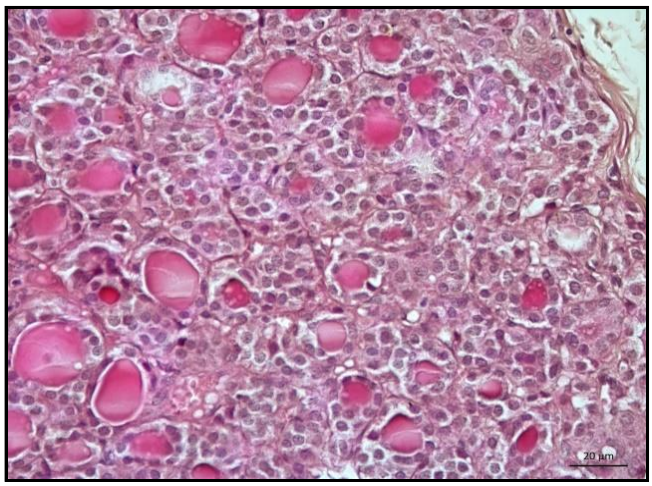
The absence of reference values for thyroid hormones, especially in free form, in sheep in Brazil may be one of the factors that contribute to the lack of thyroid disorders diagnosis, particularly of goiter cases, as recorded in this outbreak. In this way, the data recorded here provide an important reference that will enable discussion of data obtained in new cases.

3.3. Pathology

Macroscopically, the thyroid samples presented a slight increase in volume, of both lobes of the gland. The lobes were firm, dark red in color, and compact. Similar characteristics have been described by Panziera et al. (2014) and Macedo et al., (2011); these latter authors, when evaluating the birth defects in cattle from the Central Region of Rio Grande do Sul, found a goiter casuistry of 1.9%. Campbell et al. (2012) also found enlarged, firm, and dark thyroid glands, of homogeneous consistency in all lambs, in addition to alopecia, which was not identified in any of the animals in the current study.

Histologically, the findings are similar to those described in the literature in cases of goiter (Capen, 2007; Ecco and Langohr, 2010; Campbell et al., 2012) as shown in Figure 2. There is follicular hyperplasia and marked heterogeneity in the size of the follicles that are lined by a layer of cube-shaped epithelial cells. Ozmen et al. (2005) and Panziera et al. (2014), also observed marked follicular hyperplasia with heterogeneous size between the follicles, similar to the results found. These authors attributed the cause of the goiter to the absence of mineral supplementation with iodine for goats, thus characterizing the congenital form. Macedo et al. (2011), in their study, described multiple follicles with flattening of the epithelium lining due to colloidal repletion and dilation.

Figure 2 – Hyperplasia of thyroid follicles.



Source: Authors' elaboration.

The clinical findings, macroscopic characteristics, and histological findings observed in these cases are identical to those described for goiter and constitute evidence that allows the definitive diagnosis of this condition (Al-ani et al., 1998; Ozmen et al., 2005; Cheema et

al., 2010).

The relationship between histopathological data and the low concentrations of thyroid hormones found in the blood of these animals is based on the fact that follicular cells are those that synthesize and secrete thyroglobulin, which combines with iodine to form metabolically active thyroid hormones (triiodothyronine and thyroxine) (Ozmen et al., 2005), and as thyroid hormones contain iodine, their deficiency, due to the likely effect of goitrogens, resulted in insufficient production of thyroid hormones and, consequently, the animals evolved to the clinical framework of goiter.

4. Conclusions

Thus, the diagnosis of acquired goiter can be stated, based on epidemiological findings, clinical signs, and anatomopathological lesions, as well as on the quantitative serum analysis of thyroid hormones (Free T3 and Free T4). The cause of goiter in the sheep examined in this study was determined as a probable iodine deficiency related to feed (soybean meal), which interfered with the thyroid hormones metabolism.

To avoid its occurrence, feed management must be corrected in order to provide a balanced diet and mineral supplementation for the animals, taking into account the needs of the species and antithyroid feed substances.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the research, publication or authorship of this article.

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