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Osteodistrofia fibrosa atípica em uma égua lactante

Atypical fibrous osteodystrophy in a lactating mare

Osteodistrofía fibrosa atípica en una yegua lactante

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Resumo

O hiperparatireoidismo secundário à nutrição é uma condição causada por altos níveis séricos de fósforo em comparação ao cálcio levando a um aumento na produção de PTH, hormônio paratireoidiano das glândulas paratireoides de maneira que a atividade osteoclástica aumente, sequestrando cálcio dos ossos e formando um tecido fibroso caracterizado como osteodistrofia que ocorre comumente nos ossos faciais. Este artigo tem como objetivo descrever um caso atípico de hiperparatireoidismo e osteodistrofia fibrosa em uma égua em lactação de 8 anos cuja face possuía um aumento focal e nodular envolvendo a narina direita e os ossos incisivos causando dificuldades respiratórias e alimentares. Os exames radiológicos foram sugestivos de osteossarcoma com o Doppler indicando circulação superficial a massa nodular. O tratamento foi efetuado com cisplatina e suplementação de cálcio. O paciente foi a óbito três dias após a realização dos procedimentos de traqueostomia temporária e biópsia. Os achados de necropsia indicaram linfadenomegalia da paratireóide, confirmada pela histopatologia além de osteodistrofia na região maxilar. Neste caso o hiperparatireoidismo não se apresentou de maneira típica, havendo uma necessidade de estudos posteriores sobre possíveis atipias da doença em países tropicais.

Palavras-chave: Equino; Hiperparatireoidismo; Osteossarcoma; Diagnóstico diferencial; Linfadenomegalia.

Abstract

Secondary nutritional hyperparathyroidism is a condition caused by increased serum phosphorus levels compared to calcium, which leads to an growth in the production of the PTH, parathyroid hormone of the parathyroid glands, increasing the osteoclastic activity withdrawing calcium from the bones, forming fibrous tissue, known as osteodystrophy, usually in the facial bones. The goal of this paper was to report an atypical case of hyperparathyroidism and fibrous osteodystrophy in a 8-year-old lactating mare, whose face enlargement was focal and nodular, involving of the right nostril and incisor bones, causing breathing and feeding difficulties. In the radiological examination the image was suggestive of osteosarcoma, with Doppler showing superficial circulation to the nodular mass. Treatment

with cisplatin and calcium supplementation was performed. The the patient died three days after a temporary tracheostomy and a biopsy procedure. At necropsy parathyroid's lymphadenomegaly was confirmed by histopathology, and osteodystrophy in the maxillary region was observed. In this case, hyperparathyroidism did not presented itself as a typical form, and there is a need for further studies on possible atypical forms of the disease on tropical countries.

Keywords: Equine; Hyperparathyroidism; Osteosarcoma; Differential diagnosis; Lymphadenomegaly.

Resumen

El hiperparatiroidismo secundario a la nutrición es una afección causada por los altos niveles de fósforo en suero en comparación con el calcio que conduce a un aumento en la producción de parathormonio, hormona paratiroidea en las glándulas paratiroides, de modo que aumenta la actividad osteoclástica, secuestrando el calcio de los huesos y formando tejido fibroso. caracterizado como osteodistrofia que ocurre comúnmente en los huesos faciales. Este artículo tiene como objetivo describir un caso atípico de hiperparatiroidismo y osteodistrofia fibrosa en una yegua lactante de 8 años cuya cara tenía un agrandamiento focal y nodular que involucraba la fosa nasal derecha y los huesos incisivos que causaban dificultades para respirar y alimentarse. Los exámenes radiológicos sugirieron osteosarcoma con Doppler que indica circulación superficial a la masa nodular. El tratamiento se realizó con suplementos de cisplatino y calcio. El paciente falleció tres días después de realizar la traqueotomía temporal y los procedimientos de biopsia. Los hallazgos de la necropsia indicaron linfadenomegalia paratiroidea, confirmada por histopatología además de osteoartritis en la región maxilar. En este caso, el hiperparatiroidismo no apareció de manera típica, con la necesidad de más estudios sobre la posible atipia de la enfermedad en los países tropicales.

Palabras clave: Equino; Hiperparatiroidismo; Osteosarcoma; Diagnóstico diferencial; Linfadenomegalia.

1. Introduction

Nutritional disturbances on horses have become preponderant for metabolic disorders that compromise homeostasis due to deficits on proteins, vitamins and minerals balance at the animal's diet (Maidana et al., 2014). Secondary hyperparathyroidism is a pathological metabolic disease caused by increased serum phosphorus levels compared to calcium, usually

associated with calcium-deficiency and oxalate-rich diets. Thus, it is characterized as a trifaceted metabolic disorder that provides elevated release of parathormone, presenting different etiopathogenesis as prospecting of clinical signs (Ospina et al., 2014; Queiroz et al., 2015).

There are different clinical signs associated with hyperparathyroidism, correlating from a parathyroid lymphadenomegaly to a deficiency in the serum phosphorus absorption by the proximal tubules of the kidneys. In Brazil, facial bone disorders are common, popularly known as "swollen face", characterized by fibrous osteodystrophy, increasing the density of the paranasal, mandibular and maxillary bones, most often in a generalized and bilateral pattern. Those lesions are consequence of calcium sequestration from the bones by parathormone, seeking to maintain homeostasis. This condition is commonly found in younger animals from one to three years (Queiroz et al., 2015).

This report proposes to discuss, a hyperparathyroidism characterized by an atypical fibrous osteodystrophy in a lactating mare, with apparent signs of neoplasia, observed by the unilateral lesion and radiological findings.

2. Metodology and case report

The nature of this paper is a case study about the lactating mare with atypical fibrous osteodystrophy. An 8-year-old lactating mare, Mangalarga Marchador breed, 402 kg, with a 4 months-old nursing foal, was admitted to the Ambulatory of the Equine Research and Extension Group of the Federal University of Alagoas (GRUPEQUI-UFAL), presenting dyspnea and increased volume in the right facial region (nasal and maxillary bones). The medical history revealed that the animal was treated by another veterinary for 3 months, when cell proliferation in the facial region (Figure 1), cachexia and suspicion of neoplasia were identified, a biopsy was performed and the mare was diagnosed with benign neoplasia. The medical records also revealed a mass growth greater than 100% over two months, resulting in breathing and feeding difficulties. The patient was raised in a semi-intensive pasture of *Panicum maximum* and received 3 kg of maintenance ration per day (12% crude protein and 2% ethereal extract).

Figure 1. Cell proliferation in facial region.

Source: own authorship.

At Figure 1 the mare showed in a lateral view (A) and a front view (B) a consistent nodular increase in the maxillary and right nasal bones, low body score and dyspnea, with total obstruction of the right nostril's ventral meatus, hypertrophied and swollen submandibular lymph nodes. Upon opening the animal's mouth, softening of teeth 101 and 102 with great hard palate hyperplasia were perceived. There were no significant alterations at the hemogram performed. In serum biochemical tests variations were observed of the renal functions with dosage of Creatinine (4.2 mg / dL) and Urea (109 mg / dL).

The radiographic exam evidenced a significant decrease in radiopacity, making it not possible to observe the right incisor bone from its rostral branch. It was also observed areas of lysis in the left and right maxillary bones, and despite the diagnosis being confirmed with biopsy, radiographic findings may suggest osteosarcoma (Figure 2).

Figure 2. Radiographic findings**.**

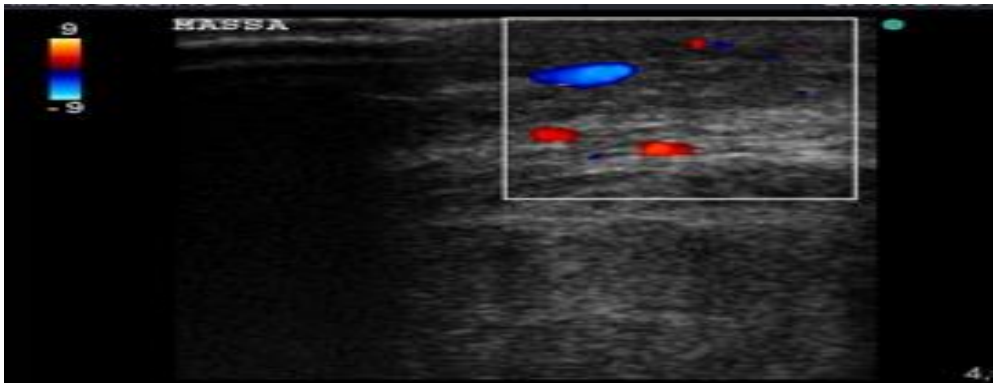
Source: own authorship.

Figure 2. (A) shows a radiological image of maxillary incisor region, ventro-dorsal incidence, with images indicating absence of right maxillary incisor bone (white arrow), radiolucent areas in bone marrow bilateral incisors (yellow arrows) and dense mass in the region of incisors and in the right nostril (yellow rectangle). (B): Radiological image of maxillary incisor region, latero-lateral incidence, with images indicating absence of maxillary incisor bone and alveoli of right-sided incisor teeth.

It was detected a bone demineralization in the mandibular branches and in the dental alveoli besides an increase of soft tissue adjacent to the described lesion. A soft tissue augmentation was revealed at the ultrasound, being possible to distinguish two regions, the first one was superficial, with depth of approximately 1.7 cm showed mixed echogenicity and heterogeneous ecotexture, the second one was deeper and closely bonded to the previous one, with a homogeneous texture, with predominantly hypoechoic echogenicity, some anechogenic regions (presence of liquid) and hyperechogenic points suggesting the presence of bone fragments or mineralized tissue.

The region evaluation using Doppler revealed a positive signal in the most superficial region. The ultrasonographic images of the deeper region suggested an abscess, due to the presence of well-defined hypoechogenic and anechogenic spots, and irregular edges of the lesion (Figure 3).

Figure 3. Ultrasonographic images.



Source: own authorship

Figure 3. Doppler evaluation of the region revealed a positive signal at the most superficial region where the presence of vascularization of the nodual formation was indicated.

No conclusive diagnosis was obtained, despite of the former exams. With the owner's authorization, a temporary tracheostomy with the introduction of a tracheotube to improve the mare's breathing and a oral biopsy were performed with sedation using xylazine 1.0 mg / kg / IV and maxillary nerve perineural block, as described by Escodro et. al. (2016). Through the McPhearson speculum, three fragments were removed in the caudal region to the teeth 102 and 103. The mare survived for three days after the procedure. As results of the histopathological analysis an exorbitance of reactive fibroblasts and desquamative cells without nuclear or cellular atypia were characterized, as well as neutrophilic inflammatory and red blood cells.

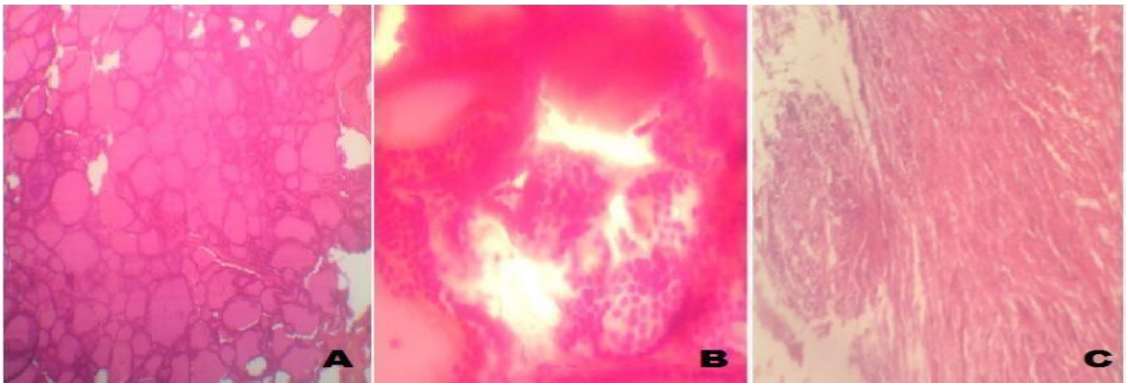
The therapeutic protocol used on the animal was immediate weaning of the foal and intravenous infusion of 0.5 ml/kg of 20% Calcium Gluconate diluted in 1 liter of saline 0.9%, every 5 days, totaling 10 administrations. Associated with the drug therapy, the foal was fed with 4 kg/day of 15% CP ration and 3% Ethereal Extract, 6 kg per day of *Tifton sp.* hay, supplementation of mineral salt for *ad-libitum* equines and 50 g/day of oral calcium carbonate.

With the objective of the nodule cytoreduction, a protocol with cisplatin (1 mg/kg diluted in 500 ml of 0.9% saline solution) described by Barros et al. (2016) was used and two applications with a 15-day time interval were administered. There was discrete apparent cytoreduction, with treatment been considered ineffective.

In necropsy analysis, the animal was evidenced a brownish tumor mass with approximately 7.5 cm in diameter, fibrosis from the facial bones to the incisor teeth region, swollen retropharyngeal lymph nodes, hypertrophy of the thyroid and parathyroid glands, with the presence of a cystic lobular mass subsequent to the glands, near the trachea, with no macroscopic pathological alterations on the animal's other systems.

The fragments removed from the incisors, thyroid, parathyroid and lung revealed, by microscopic analysis, facial and palate lesions, with fibrous tissue proliferation associated with neovascularization and multifocal areas of osteoclastic material presenting osteoclasts and mucosal epithelial hyperplasia. Evident hyperplasia in the parathyroid, with proliferation of acinar structures of typical histological appearance and glandular hypersecretion were observed. The simple cuboidal epithelium did not present cellular or nuclear atypia, and the lungs presented only a slight inflammatory infiltrate (Figure 4).

Figure 4. Histological finding.



Source: own authorship

Figure 4 represent histological slides where (A) indicates thyroid with hypersecretion. (B) indicates hyperplasic parathyroid and (C) indicates histology of the main mass characterizing osteodystrophy.

3. Discussion

The absence of an iatrogenic factor in hyperparathyroidism and fibrous osteodystrophy in the mare required many complementary and specific exams. Increased focal and nodular volume with decreased bone density in the incisive and unilateral maxillary bones directed a clinical suspicion of osteosarcoma, strengthened by radiographic images through absence of

the incisive bone and osteolysis of the right mandible, diverging from the classic lesion characteristics (Little et al., 2000; Toribio et al., 2011).

The discrepant disclosure of unilateral tissue density increase in this animal in the maxillary and mandibular regions refuted the pathognomonic findings of fibrous osteodystrophy considered by the generality of facial bone mineral deposition, airway obstruction, dyspnea, abnormal chewing and dysphagia (Curcio et. al., 2010).

The consumption of forages such as *Pennisetum purpureum, Panicum maximum, Cenchrus ciliaris, Brachiaria humidicola* among others, have high levels of oxalate and low levels of calcium, in Brazil, favors these cases incidence, especially in foals up to three years old, being uncommon in mares during the lactation period. However, those animals nutritional requirement to nourish the foals may have promoted the bone calcium mobilization, thus progressing to fibrous osteodystrophy (Curcio *Ibid* et. al., 2010; Rezende et al., 2015). Ospina et al. (2014) reported the same cell proliferations, increase in volume and histopathological findings in a pregnant mare after consumption of *Pennisetum purpureum*, predominantly bilateral, requiring the rare concentration of this report by the unilateral regionalization of the clinical findings.

The performed tracheostomy provided a clinical improvement to the animal's life quality, unblocking the airways and allowing air circulation to the lungs. Del Rio et al. (2017) used the same technique for the tracheal clearing of an animal with a wide extension mass at the trachea's entrance.

The final diagnosis obtained from the histopathological examinations, totally discarded neoplasia due to the mischaracterization of neoplastic cells for the osteosarcoma diagnosis in cytology and histology, due to the absence of inflammatory infiltrate (an abundance of fibrous tissue was found), being characteristic of fibrous osteodystrophy. As was seen in the typical histopathological glandular thyroid tissue, the hyperplasia was justified by the presence of a cyst, ruling out any presence of adenoma or carcinoma (Chavarria et al., 2006).

The reported case was different from those found in the literature, where the volume increase is bilateral and the findings are pathognomonic, leading clinicians to the initial suspicion of neoplasia. Cases like these should be considered in tropical climatic conditions of vegetation rich in calcium oxalate and diets with calcium and phosphorus imbalances.

4. Conlusion and Sugestions.

This paper presented an atypical case of hyperparathyroidism and fibrous osteodystrophy in a lactating *Mangalarga Marchador* mare, whose face enlargement was focal and nodular, with right nostrils and incisors compromising.

The radiological, ultrasonographic and histopathological exams weren't conclusive, as well as the treatment with calcium and cisplatin, so that the animal's condition evolved to death

Therefore, secondary nutritional hyperparathyroidism and fibrous osteodystrophy may not typically present with increased generalized bone density of the face, and may occur as a neoplastic-like focal lesion. Also, a possible primary hyperparathyroidism caused by a cyst near the parathyroid glands, rare in equines, was not confirmed.

Based on this case report, there is a need for exploratory research on atypical forms of fibrous osteodystrophy in horses under breeding conditions with forages with a high oxalate index, especially lactating and gestating mares.

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