

Multicentric lymphoma in a Brazilian Warmblood Horse - Case report*

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ABSTRACT. da Silva L.A.F., Guttmann P.de M., de Carvalho e Suzano S.M., Lessa D.A.B. & Alencar N.X. **Multicentric lymphoma in a Brazilian Warmblood Horse - Case report.** [Linfoma multicêntrico em um cavalo da raça Brasileiro de Hipismo - Relato de caso.] *Revista Brasileira de Medicina Veterinária*, 38(4):393-396, 2016. Faculdade de Veterinária, Universidade Federal Fluminense, Rua Vital Brasil Filho, 64, Santa Rosa, Niterói, RJ 24230-340, Brasil. E-mail: luaaf@hotmail.com

Lymphoma is a malignant neoplasia and the multicentric form is the most common presentation in horses. This paper describes the clinical and pathological findings of a multicentric lymphoma in a horse, emphasizing the laboratorial findings. A 13-year-old Brazilian Warmblood horse presented with a previous ultrasonography diagnosis of spleen neoplasia. The horse had muscle mass loss, polyuria and polydipsia, pitting lower limb edema, irregular thermoregulation, abdominal discomfort and selective appetite. Laboratory exams revealed occasional anemia, absolute lymphopenia, hyperproteinemia with hyperglobulinemia and alpha portion increase, as well as increase in AST, GGT, triglycerides, cholesterol and bilirubin. Glycaemia was constantly low. The horse was humanely euthanized after clinical deterioration at the end of a 60-day period. At necropsy, the spleen was increased in size, and had multiple nodules. Microscopic analysis of the nodules characterized large cell lymphoma. Since neoplasias are not frequent in this species, case reports help reaching a diagnosis. Laboratory exams during the disease are useful to monitor progression and in clinical decision-making.

KEY WORDS. Lymphoma, neoplasia, horse.

RESUMO. O linfoma é considerado uma neoplasia maligna, sua forma multicêntrica é a mais observada em equinos. O objetivo deste trabalho foi descrever os achados clínicos e patológicos de um caso de linfoma multicêntrico em equino, com focos achados laboratoriais. Um cavalo da raça Brasileiro de Hipismo, de 13 anos, foi atendido com diagnóstico prévio ultrassonográfico de neoplasia em baço. Os sinais clínicos incluíram perda de mas-

sa muscular, poliúria e polidipsia, edema difuso de membros, dificuldade de termorregulação, desconforto abdominal e apetite seletivo. Os exames laboratoriais mostraram, em alguns momentos, anemia e linfopenia absoluta. Hiperproteinemia, com hiperglobulinemia e aumento da fração alfa. Aumento de AST, GGT, triglicérides, colesterol e bilirrubina. Hipoglicemia foi observada durante todo o período. Ao final de 60 dias de acompanha-

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mento foi decidida a eutanásia pós piora clínica. A necropsia destacou esplenomegalia e nódulos no baço. A análise microscópica dos nódulos caracterizou linfoma de células grandes. Como as neoplasias não são enfermidades de grande ocorrência na espécie os relatos de caso auxiliam no momento do diagnóstico. A realização de exames laboratoriais durante o curso da doença permite observar a progressão, acrescenta informações sobre a doença e auxilia nas decisões clínicas.

PALAVRAS-CHAVE. Linfoma, neoplasia, equino.

INTRODUCTION

Neoplasia is one of the less frequent disease in horses and is rarely diagnosed (Buechner-Maxwell 2009). Lymphoma is the main hematopoietic neoplasia in many species and corresponds to 3-4% of histopathologic diagnosis in horses (Ramos et al. 2008, Baccarin et al. 2011), and the multicentric form is the most common (Durham et al. 2012).

Lymphomas are classified as malignant neoplasias and clinical signs may be non-specific depending on the affected organs until the end of the disease, which leads to a bad prognosis (Meyer et al. 2006, Durham et al. 2012). Multicentric lymphoma is a neoplasia that can affect lymphatic organs such as peripheral and deep lymph nodes; abdominal cavity organs, such as liver, spleen and small intestine and the thoracic cavity. Cases of isolated tumors in the abdominal cavity and subcutaneous tissues have been described (Meyer et al. 2006). Ocular, nasal, central nervous system, bone marrow and heart lymphomas have also been reported (Durham et al. 2012). Histopathology and clinical staging are determinant for prognosis, and advanced cases usually result in death (Taintor & Schleis 2011).

This paper reports a *post-mortem* diagnosed multicentric lymphoma in a horse, emphasizing clinical-laboratorial findings of the neoplasia.

HISTORY

A 13-year-old Brazilian warmblood gelding presenting with a splenic neoplasia diagnosed by ultrasound was monitored for 60 days before euthanasia. Clinically, the horse had great muscle mass loss, polyuria and polydipsia, pitting limb edema and irregular thermoregulation. The left body wall was increased on contour. Sporadic abdominal discomfort episodes were treated with flunixin meglumine (1.1mg/kg IV). Transabdominal ultrasonography exam showed an irregular eco texture and increase of the size of the spleen. Despite of the selective appetite, the horse was bright and alert most of the time.

During this period, multiple laboratory exams were performed. Anemia was observed when the animal deteriorated, at the end of two months (hematocrit 28%, reference range 32 - 52%). White blood cell count remained within the normal limits (varied from 8,600 to 10,400 cells/ μ L; reference range 6,000 a 12,500 cells/ μ L). There was absolute lymphopenia (768 to 1,806 cells/ μ L, reference range 1,750 a 9,800 cells/ μ L) that started 30 days after the observation period until the end. Fibrinogen was within the normal limits all the time (100-200 mg/dL, reference range 100-400 mg/dL).

There was hyperproteinemia (7.9 - 9.8 g/dL, reference range 5.20 - 7.90 g/dL), with hyperglobulinemia (5.2 - 6.5g/dL; reference range 2.6 -5.0g/dL) and decreased albumin/globulin ratio (0.46 a 0.52; refence range 0.60 a 1.40) during the entire period. Electrophoretic fractionation of total protein at the beginning of the observation period detected increase in the alpha fraction (alpha 1: 1.18g/dL; reference range 0.10 a 0.70g/dL e alpha 2: 1.73g/dL; reference range 0.10 a 0.70g/dL).

AST was increased in the first exam (453 U/L), and was within normal limits in the following exams (276 - 358; reference range 226 - 366 U/L). GGT was increased in the first exams (112 U/L, reference range 12 - 105 U/L), decreased to 93 U/L after one month, and increased to 107 U/L ten days later, remaining high until the end of the period (145 U/L). There was hyperlipidemia with constant hypertriglyceridemia (1,500 - 2,180 mg/dL, reference range 20 - 150 mg/dL) and hypercholesterolemia (482 - 576 mg/dL, reference range 46 - 177 mg/dL) in successive exams performed at days 15 and 45 of the observation period.

Bilirubin increased gradually over the period (2.3 - 4.2 mg/dL, reference range 0 - 2,2 mg/dL), and was 3,5 mg/dL at the end of the observation period. Hypoglycemia was observed throughout the period (21 - 54 mg/dL, reference range 75 - 115 mg/dl). Urea (27 - 41mg/dL; reference range 22 - 58mg/dL) and creatinine (0.6 a 0.8mg/dL; reference range 0.60 a 1.8mg/dL) were within normal limits during all the observation period.

At the end of 60 days, the horse deteriorated and could not stand anymore, so it was humanely euthanized.

At necropsy, there was splenomegaly and multiple diffuse nodules all over the spleen. Liver, kidneys and lung were grossly normal in appearance. Fragments of the spleen were collected and kept in 10 % formalin for histopathologic evaluation. At microscopy, there was diffuse proliferation of round cells, with round nucleus, coarse chromatin, evident nucleoli and scant cytoplasm. The neoplasia was surrounded by either delicate stroma or by extensive proliferation of fibrous tissue (Figure 1), which characterized large cell lymphoma.

DISCUSSION

Lymphoma is a neoplasia that can present different clinical signs, which are generally non-specific. Progressive weight loss, fever and edema are among the most common clinical signs (Lawn 2005,

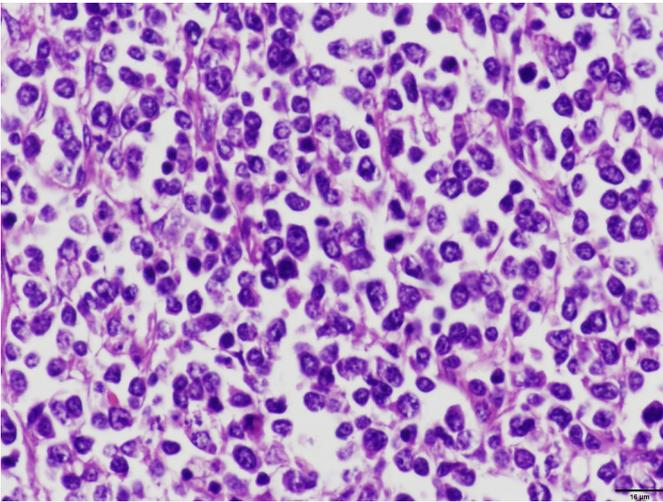


Figure 1. Horse spleen. Diffuse large-cell lymphoma. Proliferation of round cells, gross chromatin, prominent nucleoli and scant cytoplasm. HE. Obj. 40X.

Smith 2006, Sanz et al. 2010). Polyuria, polydipsia, abdominal discomfort, irregular thermoregulation and selective appetite, which were other clinical signs presented at this case report, can lead to renal failure suspicion (Taylor & Hillyer 1997). However, the splenomegaly observed can cause abdominal discomfort. Urea and creatinine results within normal limits rule out chronic renal failure.

Anemia is one of the most reported paraneoplastic syndromes in animals and humans with lymphoma (Madewell & Feldman 1980), which can happen by direct effect of the tumor on the organs (Kruth & Carter 1990). Patients with lymphoma frequently develop mild anemia due to erythropoiesis depression by neoplastic factors (Figuera & Barros 2002). Anemia was observed at the final phase of the disease in this case. Other causes of anemia in these situations can be related to chronic disease, immune-mediated processes or blood loss (Bergman 2007).

Other authors (Silva et al. 2012) described Lymphopenia, such as presented in this case, as a common feature in animals with lymphoma (Stockham & Scott 2011). Neoplasia can block lymphatic flow leading to reduction in recirculating lymphocytic population, which causes lymphopenia (Latimer 1997). The processes that obstruct normal lymphocytic circulating pattern remove these cells from the blood and keep them in neoplastic lymph nodes or chylous effusion and this leads to lymphocyte sequestration to body cavities (Rebar 1998). This may justify the pitting edema observed, since there was no hypoalbuminemia, which could be other cause of edema.

Hyperproteinemia was a constant finding in

this case. Selective hyperproteinemia, when certain protein fractions are increased, can be result of B lymphocyte neoplasia (Stockham & Scott 2011). Hypergammaglobulinemia is a paraneoplastic syndrome that increases blood viscosity and has been described in other lymphoma cases (Dorfman & Dimski 1992). An increase in gamma fraction would be expected in an animal with lymphoma, and not an increase in alpha fraction, as observed in this case. Dogs presenting with neoplasia show high peaks of alpha globulin, which may be related to an acute phase reaction. Acute inflammation, fever and tissue injury are responsible for this increase, in fractions such as haptoglobin, together with beta globins, such as fibrinogen (Thomas 2000). In this case report, increase in alpha globulin happened together with normal fibrinogen levels.

Since lymphomas have non-specific clinical signs, blood count and biochemistry results may not be useful for diagnosis, however, when there is no evidence of inflammatory disease, anemia and hyperproteinemia can place lymphoma within the differential diagnosis (Taintor & Schleis 2011). Hyperfibrinogenemia (Smith 2006) and hypoalbuminemia (Smith 2006, Mair et al. 2011) can be observed. Although within the normal limits, albumin values in this case were always close to the lower reference range. Recurrent hypoalbuminemia can result from protein losing enteropathy, especially in horses with alimentary lymphoma Mair & Hillyer 1997, Meyer et al. 2006, Taylor et al. 2006).

Extremely elevated values for cholesterol and triglycerides characterize hyperlipidemic syndrome. Triglycerides above 500 mg/dL, together with non-specific signs such as rapid loss of body condition and fever, indicate the syndrome (Lewis 2000, Stockham & Scott 2011). This syndrome can cause lipidosis and damage to hepatocytes. Hypoglycemia is an aggravating factor, since it stimulates glucagon release and subsequent fatty acid release (Stockham & Scott 2011). Hypoglycemia in paraneoplastic syndromes is common in insulinoma, but can also be present in lymphoma (Bergman 2007), in which case, it could be a higher glucose consumption by the tumor, hepatic gluconeogenesis or increase in insulin release. Fasting equine use glucose to conjugate bilirubin. Therefore, bilirubin increase can be due to a reduced glucose level at hepatocytes (Stockham & Scott 2011). The horse at this case report probably presents hypoglycemia due to glucose consumption by the tumor and to the selective appetite.

Increase in GGT relates to biliary obstructive disorders (Stockham & Scott 2011). This hypothesis is confirmed in this case since GGT variates according to bilirubin variation.

Hepatocyte injury and the lymphoma can cause increase in AST (Stockham & Scott 2011). In this case, there was an increase in the initial phase of the observation period, which indicates that there was no permanent injury to hepatocytes.

The clinical course of the multicentric lymphoma, such as observed in this case, tends to worsen rapidly, and euthanasia is a common choice (Smith 2006).

The diagnosis was concluded after death with histopathologic exam, considered as the standard in these cases (Morris & Dobson 2001).

Although frequent in company animals, this disease is rarely reported in large animals, and individual reports or retrospective studies are scarce in horses (Baccarin et al. 2011, Durham et al. 2012). This fact contributes to the lack of understanding of many aspects of some types of tumors (Dixon & Reed 1999) and justifies the importance of case reports.

CONCLUSION

The clinical laboratorial monitoring of disease progression, the consequent disorders and paraneoplastic syndrome observed in this case contributes to the understanding of multicentric lymphomas in horses. This can help to lengthen the animal's life with better quality or in the decision making as to the moment of euthanasia in order to finish suffering.

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