Arq. Bras. Med. Vet. Zootec., **v.76, n.6, e13163, 2024** http://dx.doi.org/10.1590/1678-4162-13163
Case Report - Veterinary Medicine

Clinical, ultrasonographic and pathological aspects of iatrogenic thrombophlebitis in a mare – case report

[*Aspectos clínicos, ultrassonográficos e patológicos da tromboflebite iatrogênica em uma égua – relato de caso*]

A. *Serruya*, C.C. *Barbosa*, T.T.A. *Ferreira*, P.P.M. *Teixeira*, J.D. *Barbosa*

Universidade Federal do Pará, Castanhal, PA, Brasil

ABSTRACT

A 7-year-old quarter horse mare showed swelling of the tongue, head and neck region, dyspnea, and red urine after eight days of administration of intravenous medications by the animal's handler. The horse was referred to the University Veterinary Hospital of the Federal University of Pará and, at the clinical examination, showed apathy, edema in the head, neck, and tongue region, which was slightly cyanotic and with loss of epithelium in the dorsal region. The maxillary, linguofacial and external jugular veins were bilaterally engorged, firm to palpation and with cord-shaped appearance, with extension of the head to the entrance to the thoracic cavity. Ultrasound examination showed a thrombi with a hyperechoic and heterogeneous appearance that completely obstructed the vessel. The horse died five days after entering the Hospital and at necropsy it was observed: maxillary, linguofacial and external jugular veins bilaterally filled with firm, dark red to blackish thrombi; ulcerated areas in the final third of the esophagus and the stomach; lighter areas on the surface of the kidneys and dark areas at the corticomedullary junction. Based on clinical, ultrasonographic and necropsy findings, iatrogenic thrombophlebitis was diagnosed, associated with repeated injections of drugs administered intravenously.

Keywords: thrombi, equine, leukocitosis, jugular veins

RESUMO

Uma égua Quarto de Milha de sete anos apresentou aumento de volume da língua, da cabeça e da região do pescoço, dispneia e urina vermelha após oito dias de administração de medicamentos intravenosos pelo tratador do animal. O animal foi encaminhado para o Hospital Veterinário da Universidade Federal do Pará e, no exame clínico, apresentou apatia, edema na região da cabeça, do pescoço e da língua, que estava ligeiramente cianótica e com perda de epitélio na região dorsal. As veias maxilares, linguofaciais e jugulares externas estavam bilateralmente dilatadas, firmes ao toque e com aspecto de cordão, com extensão da cabeça até a entrada da cavidade torácica. O exame de ultrassom mostrou trombos com aparência hiperecoica e heterogênea que obstruíam completamente o vaso sanguíneo. O equino morreu cinco dias após entrar no hospital e, na necropsia, foi observado: veias maxilares, linguofaciais e jugulares externas bilateralmente preenchidas com trombos firmes, de cor vermelho escuro a negra; áreas ulceradas no terço final do esôfago e no estômago; áreas mais claras na superfície dos rins e áreas escuras na junção corticomedular. Com base nos achados clínicos, ultrassonográficos e na necropsia, foi diagnosticada tromboflebite iatrogênica, associada a injeções repetidas de medicamentos administrados por via intravenosa.

Palavra-chave: trombos, equino, ultrassonografia, flebite, leucocitose

INTRODUCTION

Thrombophlebitis is defined as venous inflammation and thrombosis secondary to vessel wall inflammation. It usually has an iatrogenic origin and is associated with intravenous injections, accidental perivascular injections, prolonged or inadequate catheterization, trauma (mechanical damage or chemical injury) to the vascular endothelium, and bacterial infection at the site of venipuncture Dornbusch *et al.*, 2000; Lankveld *et al.*, 2001; Müller and Gehlen, 2016;

Corresponding Author: analielserruya.as@gmail.com
Submitted: October 13, 2023. Accepted: February 6,2024

Assis *et al.*, 2021. The disease most commonly affects the jugular vein of horses, as it is the most used route for catheterization, medication administration and blood sample collection.

The clinical signs observed include engorgement of the vein, pain on palpation and increased skin temperature. The jugular veins are most often affected and is usually firm and cord-shaped appearance (Dornbusch *et al.*, 2000; Hussni *et al.*, 2012; Borghesan *et al.*, 2018). In cases of bilateral thrombophlebitis of the jugular veins, there is a decrease in venous drainage in the head region, causing swelling of the face, tongue, pharynx, larynx and parotid region. In addition, dysphagia and respiratory distress may occur (Dornbusch *et al.*, 2000; Borghesan *et al.*, 2018; Moreau and Lavoie, 2009). Ultrasonography is a widely used diagnostic method, as it is a non-invasive method that makes it possible to assess the extent of the thrombus in the vascular bed, blood flow and differentiate the structures involved (Dornbusch *et al.*, 2000).

Thrombophlebitis treatment seeks to alleviate inflammation of the vessel wall, prevent thrombus propagation, prevent or treat bacterial infections, and to restore blood flow. However, in severe cases, treatment becomes ineffective and unfeasible. Thus, the present study seeks to report a clinical case of bilateral jugular thrombophlebitis in a mare attended at the University Veterinary Hospital (HV - Sector of Production Animals) of the Federal University of Pará (UFPA), Brazil.

CASUISTRY

A seven-year-old Quarter Horse mare, weighing 475kg, with a history of edema of the face and difficulty breathing, was admitted on August 4, 2022 to the University Veterinary Hospital (Production Animal Sector) of the Federal University of Pará (UFPA), Castanhal, for clinical care.

According to the history provided by the owner, approximately 15 days ago the animal presented clinical signs like claudication, reluctance to move and increase respiratory, rate suggestive of laminitis due to an episode of colic caused by the ingestion of large amounts of easily digestible carbohydrate, the which made him administer 10ml of flunixin meglumine, intravenously (IV) for three days, however, without proper antisepsis care without obtaining clinical improvement. Therefore, a veterinarian was contacted, and an online consultation was requested, in which 4.4mg/kg of phenylbutazone, 0.2mg/kg of dexamethasone and 1mg/kg of flunixin meglumine were prescribed for eight days, via IV and penicillin (20,000IU/kg) intramuscularly (IM). Additionally, 70ml of calcium, four liters of glucose and antitoxic serum were administered intravenously (IV) and meloxicam (0.6mg/kg) in a single dose; all medications were administered by the animal's keeper. After five days of treatment, the patient began to show swelling of the tongue, head and neck region, dyspnea and red urine. Due to the difficulty breathing, another veterinary was requested, who performed an emergency tracheostomy and referred the mare to the University Veterinary Hospital of UFPA.

On clinical examination, the animal was standing, with its head down, apathetic, with edema in the head, tongue, and neck region (Fig. 1A); the tongue was slightly cyanotic and with loss of epithelium in the dorsal region (Fig. 1B). The maxillary, linguofacial and external jugular veins were bilaterally engorged, firm to palpation and with cord-shaped appearance. The lesions extended from the head to the entrance to the thoracic cavity (Fig. 2A-B). In addition, there was congested oral mucosa and presence of toxemic halo, severe dehydration characterized by decreased skin turgor and eyeball retraction, subcutaneous emphysema extending from the neck to the rump region, dyspnea, increased respiratory (36rpm) and heart rates (60bpm), pulmonary stridor, increased rectal temperature (39.1°C), greater sensitivity in the face region and decreased pupillary reflex. Furthermore, the animal lay down frequently and the digital pulse increased in all four limbs.

Blood samples were collected by cephalic venipuncture for blood count and urea and creatinine analysis. The leukogram revealed leukocytosis (29.8x103/µL) by lymphocytosis, monocytosis and neutrophilia with regenerative left shift and relative erythrocytosis (Globular Volume of 49% and total red blood cell count of 11.48x106) and normal platelets counts in horses, as well as the total plasmatic proteins. The serum biochemistry showed azotemia due to increases in creatinine (3.6mg/dL) and urea (205mg/dL).

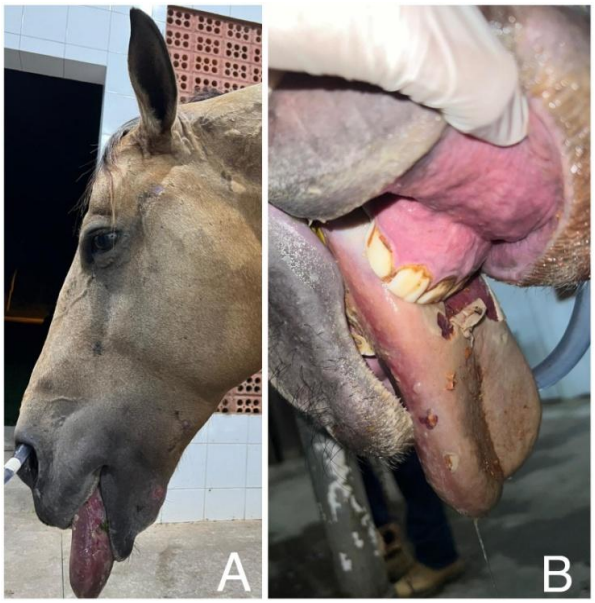

Figure 1. Iatrogenic thrombophlebitis in a mare. (A) Generalized edema in the region of the head and tongue. (B) Tongue edema with slightly cyanotic of the tongue and oral mucosa with loss of epithelium in the dorsal region of the tongue.

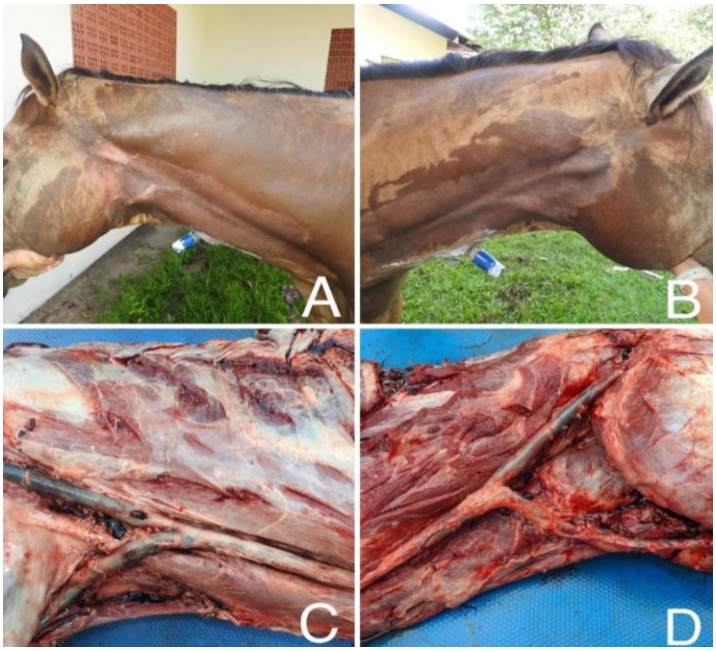

Figure 2. Iatrogenic thrombophlebitis in a mare. (A-B) The maxillary, linguofacial and external jugular veins were bilaterally engorged, firm to palpation and with cord-shaped appearance, with extension of the head to the entrance to the thoracic cavity. (C-D) Aspect of the veins after neck dissection at necropsy.

Ultrasound examination of the maxillary, linguofacial and jugular veins was performed using the Z5 Vet device (Mindray Bio-Medical Electronics Co. Ltd., Shenzhen China) with a linear probe operating at 7.5MHz at a depth of 5cm. The ultrasound imaging revealed a thrombus with a hyperechoic and heterogeneous appearance that obstructed the maxillary, linguofacial and bilateral external jugular veins, as well as the stagnant flow in the vessel (Fig. 3). The lesion extended to the entrance of the thorax, with anechoic areas and thickened vascular wall.

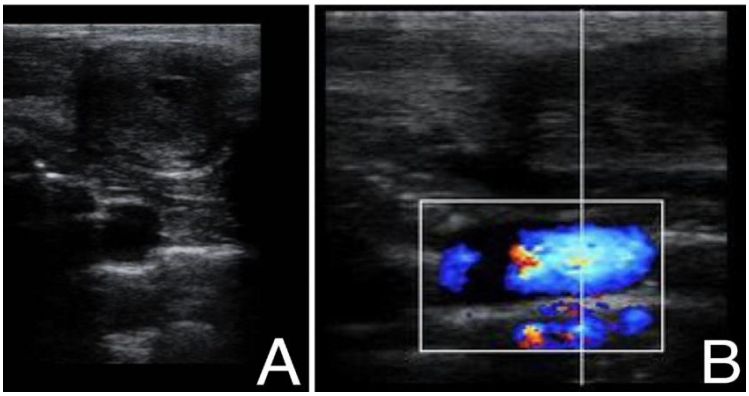

Figure 3. Iatrogenic thrombophlebitis in a mare. (A) Hyperechoic and heterogeneous appearance that completely obstructed the vessel, with the presence of anechoic areas and a thickened vascular wall in the B-mode ultrasonography. (B) Total occlusion of the vessel in Doppler ultrasonography.

Based on the history, clinical and ultrasonographic examinations, bilateral thrombophlebitis involving the maxillary, linguofacial and external jugular veins was diagnosed.

During the four days of hospitalization, the patient was treated with antibiotics (Ceftiofur 2.2mg/kg/IM, every 24 hours), non-steroidal anti-inflammatory drugs (flunixin meglumine 0.25mg/kg/IM, every 8 hours), pain control protocol [dipyrone 25mg/kg/IM every 8 hours; ketamine 0.2mg/kg, subcutaneously (SC), every 8 hours; and tramadol 2mg/kg/IM, every 8 hours)]. In addition to the permanent nasogastric intubation used for enteral hydration with water (8ml/kg/hour) and topical use of DM-Gel® in the neck region.

The mare died on the fifth day of hospitalization and necropsy was performed, which showed that the maxillary, linguofacial, external jugular, and rete mirabile veins were bilaterally filled with firm, dark red to blackish thrombi (Fig.2C-D, Fig. 4A-B). In the final third of the esophagus and in the glandular region of the stomach, there were intense reddish and ulcerated areas. The surface of the kidneys had lighter areas and on the cut surface there were dark areas at the corticomedullary junction.

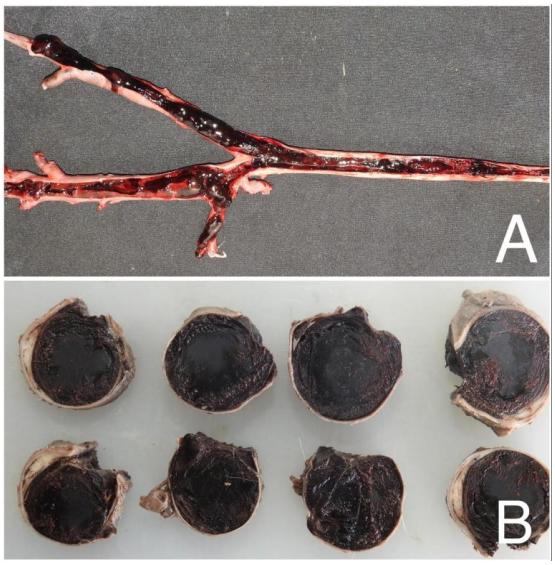

Figure 4. (A-B) Iatrogenic thrombophlebitis in a mare. Completely obstructed jugular vein by a firm and dark red to blackish thrombus.

DISCUSSION

The diagnosis of thrombophlebitis of the maxillary, linguofacial, and external jugular veins was based on history, clinical signs, ultrasonography, and necropsy findings. During the anamnesis, it was verified that there were repeated applications of different drugs intravenously by a person who was not qualified and without antisepsis care, which points to bilateral iatrogenic thrombophlebitis. This cause has already been mentioned in previous clinical studies, resulting from the complication of prolonged use of venous catheters or intravenous injections that cause mechanical or chemical damage to the vessel wall (Lankveld *et al.*, 2001; Müller & Gehlen, 2016; Assis *et al.*, 2021).

The clinical signs presented by the patient in our study, such as apathy, dyspnea, generalized edema in the head, neck and tongue region, engorged, firm to palpation and with cord-shaped appearance are clinical findings related to the type of thrombophlebitis in this species, and have already been pointed out in other publications (Dornbusch *et al.*, 2000; Hussni *et al.*, 2012; Borghesan *et al.*, 2018).

The severity of the clinical signs of this equine is due to the total and bilateral obstruction of the jugular veins, which differs from the unilateral impairment of the jugular vein presented by the experimentally evaluated animals (Hussni *et al.*, 2012; Borghesan *et al.*, 2018). The severe edema in the head, neck, tongue, pharynx, larynx, and parotid region demonstrated in the horse in this study is explained by the bilateral obstruction of the maxillary, linguofacial and external jugular veins, which implies a decrease in venous drainage in the head region (Dornbusch *et al.*, 2000; Borghesan *et al.*, 2018; Moreau *et al.*, 2009).

Dyspnea has been associated with edema in the laryngeal region (Dornbusch *et al.*, 2000; Borghesan *et al.*, 2018; Moreau and Lavoie, 2009), whereas nervous signs such as excitation, skin sensitivity in the face region, decreased pupillary reflex and the presence of thrombi in the rete mirabile justify the encephalic edema and venous stasis due to bilateral jugular obstruction (Dias *et al.*, 2013). The extensive subcutaneous emphysema evidenced in the animal can be explained by the surgical intervention performed in the trachea region (tracheostomy), for the insertion of a probe to facilitate breathing (Kim *et al.*, 2023)

The ultrasound examination carried out in the horse was easy, non-invasive, efficient, and enlightening to assess the thrombi extension and shape, which had a hyperechoic and heterogeneous aspect. The thrombi totally and bilaterally obstructed the maxillary, linguofacial and external jugular veins, and distorted the vessels anatomy of these vessels in cord-shaped appearance, which extended to the entrance of the thorax, with anechoic areas and thickened vascular wall, similar to the described in the literature (Borghesan *et al.*, 2018, Dias *et al.*, 2014). The ultrasound monitoring of the thrombi was important to establish a prognosis and evolution of the clinical case (Hussni *et al.*, 2012; Moreau and Lavoie, 2009).
The necropsy findings were another important data for the confirmation of thrombophlebitis, which confirmed the presence of a thrombi that totally obstructed the maxillary, linguofacial and external jugular veins.

The inflammatory leukogram shown in the present study was also reported by other authors (Meuten 2015, Moreau and Lavoie, 2009). Relative erythrocytosis can be explained by dehydration because of generalized edema in the cephalic region, which compromises the upper structures of the digestive tract, such as lips and tongue, making it impossible to drink water. Total plasma protein was observed within the reference values, however, its real value is probably close to the lower limit, as dehydration causes a misleading increase. Platelets are within the reference values, however, close to the lower limit and this can be explained by the participation of platelets in the local inflammatory process, which leads to increased consumption. In addition, platelets may also have decreased due to the formation of thrombi that were obstructing the vessels.

The increase in serum levels of creatinine and urea, associated with the findings of dehydration, leads us to infer the presence of pre-renal azotemia (Meuten, 2015). However, renal azotemia may also have occurred due to the use of non-steroidal anti-inflammatory drugs and the presence of macroscopic lesions in the kidneys, observed during necropsy.

This case is notable for the bilateral involvement of the jugular veins, as well as the gravity of the lesions identified during necropsy. The severity of the case was underscored by the inefficacy of the treatment with antibiotics and anti-inflammatories, which can be explained by the extension and severity of the lesions that culminated in the animal's death.

It is necessary to perform a differential diagnosis with diseases exhibiting similar clinical signs, such as ophidian envenomation (*Bothrops* sp.), followed by neoplasms at the entrance of the thoracic cavity and right congestive heart failure (CHF). Ophidian envenomation was ruled out due to the absence of snakebite marks, as well as the absence of thrombocytopenia, extensive areas of subcutaneous tissue hemorrhage, and blood incoagulability. Both neoplasms at the entrance of the thoracic cavity and right CHF were excluded during the necropsy.

CONCLUSIONS

The diagnosis of iatrogenic thrombophlebitis in a mare was based on clinical, ultrasonographic and pathological aspects. Clinical and ultrasonographic evaluation were essential to establish the extension of the lesions. The thrombophlebitis presented by the animal in the present study was associated with repeated injections of drugs administered intravenously. Thus, the aforementioned study demonstrated the significance of rigorously practicing antisepsis, as well as the necessity of having duly qualified professionals for the administration of intravenous medications. Furthermore, adhering to the prescribed dosage of medications is a crucial factor in preventing potential complications associated with their improper use.

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