UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
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PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS VETERINÁRIAS

NEUROTOXICOSE POR INGESTÃO DE *Trema micrantha* EM EQUINOS

MARINA PAULA LORENZETT

PORTO ALEGRE
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Dissertação apresentada como requisito para a obtenção do grau de Mestre em Ciências Veterinárias na área de concentração em Cirurgia, Morfologia e Patologia Animal, da Universidade Federal do Rio Grande do Sul.

Orientador: Prof. Dr. David Driemeier

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MARINA PAULA LORENZETT

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Aprovada em 22 de fevereiro de 2017.

APROVADA POR:

_____

Prof. Dr. David Driemeier

Orientador e Presidente da Comissão

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Prof. Dra. Ana Lucia Schild

Membro da Comissão

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Prof. Dra. Luciana Sonne

Membro da Comissão

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Prof. Dr. Saulo Petinatti Pavarini

Membro da Comissão

DEDICATÓRIA

Momentos

Victor & Leo

Compositor: Victor Chaves

Há momentos inevitáveis
Que o coração da gente pede respostas
É nessa hora
Que a gente diz que não entende a vida e chora

Se a gente soubesse
O quanto merece cada um
O que cada um tem
A gente nada pediria
Simplesmente o bem faria
Para merecer o bem

Eu, que sempre tive o que dizer
Hoje, ouço em silêncio
Levei tempo pra entender
Que só o tempo
Apenas o tempo nos ensina a viver

A minha família.

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RESUMO

NEUROTOXICOSE POR INGESTÃO DE *Trema micrantha* EM EQUINOS

Trema micrantha, uma árvore amplamente distribuída no continente Americano, produz folhas altamente palatáveis que têm sido relacionadas a intoxicações naturais e/ou experimentais em caprinos, equídeos, coelhos, ovinos e bovinos, com desenvolvimento de necrose hepática e alterações neurológicas por encefalopatia hepática. Casos de intoxicação espontânea em ovinos indicaram quadro clínico e patológico respiratório na maioria dos casos. Esse trabalho descreve malacia e hemorragia no sistema nervoso central em equinos desencadeado pelo consumo de *Trema micrantha*, em que as lesões hepáticas foram mínimas a ausentes, e as principias lesões eram restritas ao sistema nervoso central. Quatorze equinos apresentaram sinais neurológicos de ataxia, sialorreia intensa, movimentos de pedalagem, decúbito esternal com evolução para lateral e morte em um curso clínico que variou de 24h a nove dias. Previamente ao início dos sinais clínicos, todos os equinos haviam consumido espontaneamente, doses potencialmente tóxicas de folhas de *T. micrantha*. Todos os 14 cérebros apresentaram coloração amarelada difusa afetando o rombencéfalo, mesencéfalo, diencéfalo, telencéfalo e corpo estriado. Em todos os casos, as lesões mais graves foram observadas na região de ponte. Lesões na medula espinhal foram obervadas afetando a intumescência lombar, que apresentava-se edemaciada com áreas enegrecidas e deprimidas nos cornos dorsais e ventrais, e na região sacral, a superfície de corte exibia material friável e amarelado acinzentado. As lesões observadas macroscopicamente no cérebro e na medula espinhal consistiram microscopicamente em vasculite severa e necrose liquefativa da substância branca e cinzenta do tronco encefálico, cerebelo e medula espinhal. Estes resultados indicam que a intoxicação por essa planta deve ser considerada no diagnóstico diferencial em casos de doença do sistema nervoso central de equinos.

Palavras chaves: equino, intoxicação por planta, doenças de equinos, neuropatologia, Cannabaceae; malacia.

ABSTRACT

NEUROTOXICOSIS IN HORSES ASSOCIATED WITH CONSUMPTION OF Trema micrantha

Trema micrantha is a tree widely distributed in the American continent, produces highly palatable leaves that have been related to natural and / or experimental poisoning in goats, equines, rabbits, sheep and cattle, with development of hepatic necrosis and neurological signs due to hepatic encephalopathy. Spontaneous poisoning occurred in sheep in which respiratory clinical signs and pathological findings where observed in most cases. This study describes malacic and hemorrhagic lesions in the central nervous system in horses due to T. micrantha consumption, with minimal to absent hepatic lesions, and the main lesions were restricted to the central nervous system. All 14 horses had neurological signs of ataxia, severe sialorrhoea, involuntary running movements, sternal decubitus which progressed to lateral recumbency, and death after a clinical course that lasted from 24 h to 9 days. For a few days prior to the onset of clinical signs, all horses had spontaneously consumed,potentially toxic doses of T. micrantha leaves. All 14 brains had diffuse yellowish discoloration affecting the rhombencephalon, mesencephalon, diencephalon, telencephalon and corpus striatum. In all cases, the most severe lesions were observed in the pons. Spinal cord lesions were observed affecting the lumbar intumescence, which was swollen with darken and depressed areas at the dorsal and ventral horns, and at the sacral level, which on cut surface displayed a friable and yellowish grey matter. The lesions observed grossly in brain and spinal cord consisted microscopically of severe vasculitis and liquefactive necrosis of white and grey matter of the brainstem, cerebellum and spinal cord. T. micrantha poisoning should be included in the differential diagnosis of neurological diseases affecting horses.

Key words: horse; plant poisoning; diseases of horses; neuropathology; Cannabaceae; malacia

LISTA DE ILUSTRAÇÕES

SUMÁRIO

1 INTRODUÇÃO

Trema micrantha é uma espécie arbórea pertencente a família Cannabaceae, que ocorre nas zonas tropicais e subtropicais na América do Sul, Central e do Norte. No Brasil ela é amplamente distribuída em todas as regiões. A planta é conhecida popularmente como grandiúva, crindiúva, pau-pólvora, periquiteira, orindeúva, coatidiba, orinduíba, orindiba, gurindiba, candiúba, taleira, motamba e seriúva. É uma espécie arbórea perene, ereta, ramificada, copa alargada e crescimento rápido, que atinge até 20m de altura (Figura 1). O tronco é ereto, de casca inteira ou com leves fissuras, madeira mole e pouco resistente. As folhas são alternas, margens serruladas, base arredondada e ápice agudo com até 12 cm de comprimento e cinco cm de largura (Figura 2). Suas flores são pequenas e de coloração creme. Os frutos são de coloração amarelada, avermelhada ou roxa na maturação e se apresentam na forma de drupas globosas com 2-3 mm de diâmetro (KISSMANN, 2000; LORENZI, 2008).

Trema micrantha é uma árvore nativa do Brasil, de surgimento natural após desmatamentos e encontrada como vegetação secundária ou na recuperação de áreas degradadas de preservação permanente, ou após queimadas. A planta desenvolve-se em diversas condições ecológicas, exceto em áreas muito úmidas. Floresce nos meses de abril e maio, preferencialmente, em solos porosos e férteis. É considerada infestante agressiva em campos de pastagem nativa e áreas desocupadas (VASQUEZ, 1998; KISSMANN, 2000; LORENZI, 2008).

A planta é considerada palatável para animais, e suas folhas são consumidas por herbívoros, especialmente, em tempos de escassez de alimentos (TRAVERSO et al., 2004). Em pequenas propriedades rurais a planta é utilizada como forrageira e fornecida na alimentação de bovinos e caprinos, em épocas de escassez de forragem (WOUTERS et al., 2013). Outro importante fator de risco associado a intoxicação são as derrubadas de árvores por ação de podas ou vento (BANDARRA et al., 2010).

Intoxicações por plantas do gênero *Trema* em animais são descritas na Austrália desde 1942, pela espécie *Trema tomentosa* (MULHEARN, 1942), e no Brasil pela espécie *Trema micrantha* desde 2000, com diagnóstico nos estados do Rio Grande do Sul e em Santa Catarina (TRAVERSO et al., 2003, TRAVERSO et al., 2005, GAVA et al., 2010).

Na Austrália, um surto de intoxicação por *Trema tomentosa* foi observado em quatro equinos que morreram após consumirem a planta e apresentarem quadro clínico semelhante ao de cólica aguda, com rigidez e relutância ao movimentar-se, dispneia, poliúria e taquicardia. Os achados macroscópicos restringiram-se ao fígado, que apresentava-se friável e com aspecto moteado. Microscopicamente no fígado dos três equinos mais afetados, havia necrose de coagulação centrolobular e hemorragia, e no equino menos afetado havia discreta necrose e tumefação centrolobular e proliferação de ductos biliares (HILL et al., 1985).

A intoxicação foi observada também em camelos, que consumiram a planta após serem colocados em um parque na Austrália. A manifestação clínica foi de anorexia, fraqueza, diarreia e consequente morte. As lesões de necropsia consistiram em hemorragias no tecido subcutâneo, rúmen, abomaso, duodeno e fígado. Lesões hepáticas foram observadas no fígado de um camelo analisado, no qual havia intensa necrose de coagulação aguda com hemorragia severa (TRUEMAN; POWELL, 1991).

Intoxicações experimentais, pela administração de *T. tomentosa*, foram realizadas em bovinos, caprinos e ovinos (MULHEARN 1942), e em animais de laboratório pela ingestão do princípio tóxico extraído das folhas de *T. tomentosa*, a trematoxina (OELRICHS, 1986).

No Brasil, há descrições de intoxicações naturais por *Trema micrantha* em caprinos (TRAVERSO et al., 2003; TRAVERSO et al., 2005; GAVA et al., 2010), equídeos (BANDARRA et al., 2010; PAVARINI et al., 2013) e ovinos (WOUTERS et al., 2013) e reproduções experimentais demonstraram toxicidade para bovinos (TRAVERSO et al., 2004), coelhos (TRAVERSO; DRIEMEIER, 2000), equinos (BANDARRA et al., 2011), caprinos (TRAVERSO et al., 2002) e ovinos (WOUTERS et al., 2013).

Nas intoxicações naturais e experimentais, o quadro clínico-patológico é caracterizado por insuficiência hepática aguda com necrose centrolobular acentuada de hepatócitos (TRAVERSO et al., 2003, TRAVERSO et al., 2005, BANDARRA et al., 2010, GAVA et al., 2010), que por consequência pode levar a sinais neurológicos por encefalopatia hepática (BANDARRA et al., 2010; BANDARRA et al., 2011; PAVARINI et al., 2013). Além disso, quadros respiratórios foram observados em ovinos após ingestão de sucessivas doses da planta (WOUTERS et al., 2013).

Esse trabalho tem por objetivo descrever os aspectos epidemiológicos e clínico-patológicos da intoxicação natural por *T. micrantha* em equinos, com ênfase em lesões no sistema nervoso central.

Figura 1: Aspecto de uma árvore jovem de *Trema micrantha* em período vegetativo.

Figura 2: Detalhe de um ramo da planta com frutos imaturos e maduros.

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Neurotoxicosis in horses associated with consumption of *Trema micrantha*

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Summary

Background: *Trema micrantha* is a tree widely distributed throughout the Americas. The tree produces highly palatable leaves that have been associated with natural poisoning in goats, sheep and horses, in which hepatic necrosis and hepatic encephalopathy have been observed.
Objectives: This study describes malacia and haemorrhage in the central nervous system (CNS) due to *T. micrantha* consumption, with minimal to absent hepatic lesions.
Study design: Retrospective case series.
Methods: A total of 14 horses with a history of neurological signs and spontaneous consumption of *T. micrantha* leaves were submitted to necropsy and multiple samples were collected for histopathology. Details of clinical history and signs of the horses were obtained through inquiries to the owners and attending veterinarians.
Results: All the 14 horses had neurological signs of ataxia, severe sialorrhoea, involuntary running movements, sternal and lateral recumbency, and death after a clinical course that lasted from 24 h to 9 days. For a few days prior to onset of clinical signs, all horses had spontaneously consumed, potentially toxic doses of *T. micrantha* leaves. All 14 brains had diffuse yellowish discoloration affecting the rhombencephalon, mesencephalon, diencephalon, telencephalon and corpus striatum. In all cases, the most severe lesions were observed in the pons. Spinal cord lesions were observed affecting the lumbar intumescence, which was swollen with darken and depressed areas at the dorsal and ventral horns, and at the sacral level, which on cut surface displayed a friable and yellowish grey matter. The lesions observed grossly in brain and spinal cord consisted microscopically of severe vasculitis and liquefactive necrosis of white and grey matter of the brainstem, cerebellum and spinal cord.
Main limitations: This is a small retrospective series relying on clinical observations reported by owners and attending veterinarians. The mechanism of action of the plant toxin in the CNS is still unidentified.
Conclusion: *T. micrantha* poisoning in horses causes predominantly a neurological disease, with minimal to absent hepatic lesions.

Keywords: horse; plant poisoning; diseases of horses; neuropathology; Cannabaceae; malacia

Introduction

Trema micrantha is an arboreal species widely distributed in Brazil, within the Cannabaceae family, occurring in tropical and subtropical areas in almost all South and Central American countries [1,2], and in the southern counties of Florida (USA) (Fig 1) [3]. This plant is palatable [4] and the leaves are consumed by herbivores, especially when there is food shortage [5] or when branches with green leaves fall to the ground, either due to pruning or windstorms, becoming readily available for consumption [6]. Spontaneous poisonings by *T. micrantha* have been reported in goats [7–9], horses and donkeys [6,10] and sheep [5], and the toxicosis has been experimentally produced in cattle [4], rabbits [11] and horses [12]. The poisoning has been characterised by an acute liver insufficiency with centrilobular necrosis of hepatocytes [8], leading to hepatic encephalopathy [6,10,12]. Additionally, toxicosis has been associated with respiratory signs in sheep [5].

Our aim is to describe the clinical history, signs and pathological findings in a group of horses with naturally occurring *T. micrantha* poisoning in which hepatic lesions were minimal to absent, and lesions were mainly restricted to the central nervous system (CNS).

Materials and methods

Between July 2014 and June 2016, 14 horses with a history of neurological signs and spontaneous consumption of *T. micrantha* leaves were submitted to necropsy. Details of clinical history and signs were obtained through inquiries to the owners and attending veterinarians. Multiple tissue samples were collected during necropsy immediately after death in six horses (horses 1, 3, 5, 6–8), which were subjected to euthanasia, and within 12 h after death in the remaining. These samples included whole brain and full-length spinal cord, that were fixed in 10% buffered formalin for 24–48 h, trimmed, routinely processed for histology, embedded in paraffin and cut at 3 μm. Tissue sections were stained with haematoxylin and eosin (HE) and periodic acid-Schiff (PAS). A complete histopathological analysis was performed in liver sections of all horses. Fragments of the cerebrum, cerebellum and spinal cord were refrigerated and tested by direct fluorescent antibody test (DFAT) for *Rabies virus* (RABV) in a certified laboratory, following OIE recommendations.

Results

History and clinical features

Horses were derived from properties located nearby Porto Alegre (30°1′58″S, 51°13′48″W), Brazil, from July 2014 to June 2016. The age ranged from 5 to 25 years, and the study consisted of 14 horses (eight males and six females; eight Criollo, four mixed breed, one Thoroughbred and one American Quarterhorse). All 14 horses had neurological signs of ataxia, severe sialorrhoea, involuntary running movements, sternal and lateral recumbency and died after a clinical course that lasted from 24 h to 4 days in 13 horses, while horse 7 had 9 days of clinical signs. For a few days prior to onset of clinical signs, all horses had spontaneously

Fig 1: Neurotoxicosis associated with consumption of *Trema micrantha*, tree. Young *T. micrantha* tree with 5 m height occurring in highly degraded area. Green leaves were readily available for herbivores consumption. Inset: green leaves and fruits from *T. micrantha*.

consumed potentially toxic doses of *T. micrantha* leaves which were available to the horses after pruning or falling of branches with green leaves in four horses and or direct consumption of low parts of young trees due to food shortage in 10 horses (Fig 1). Pathologists attending the affected properties to undertake necropsies observed evidence of food shortage in all 10 of the latter group. Duration of clinical signs ranged from 24 h to 9 days. However, most of the horses had a clinical course of 24 h to 4 days (13 horses), while only horse 7 survived for longer. Data regarding the breed, sex, age, duration of clinical signs, source of plant access and lesions distributions are shown in Supplementary Item 1.

Necropsy findings

Thirteen horses were in average to good body condition, while one was in poor body condition (horse 5). The brain of the 14 horses was diffusely yellow with greyish to dark-red multifocal to coalescent friable foci (Fig 2a). The rhombencephalon was affected in 13 horses, diencephalon in 9 horses, telencephalon in 7 horses, mesencephalon in 9 horses, and corpus striatum in 2 horses. Lesion distribution for each animal affected is shown in Supplementary Item 1. In all cases, the most severe lesions were observed in pons (Fig 2b–c). Spinal cord lesions were observed in three horses (horses 7, 8 and 9), affecting the lumbar intumescence, which was swollen with darken and depressed areas at the dorsal and ventral horns, and at the sacral level, which on cut surface had a friable and yellowish grey matter (Fig 2d). Duration of clinical signs in these horses was longer than that of horses with only brain lesions, and ranged from 3 to 9 days. Hepatic changes were observed in only four horses (1, 2, 4 and 6), and were characterised by mild enlargement and moderate enhanced lobular pattern, better demonstrable on cut surface.

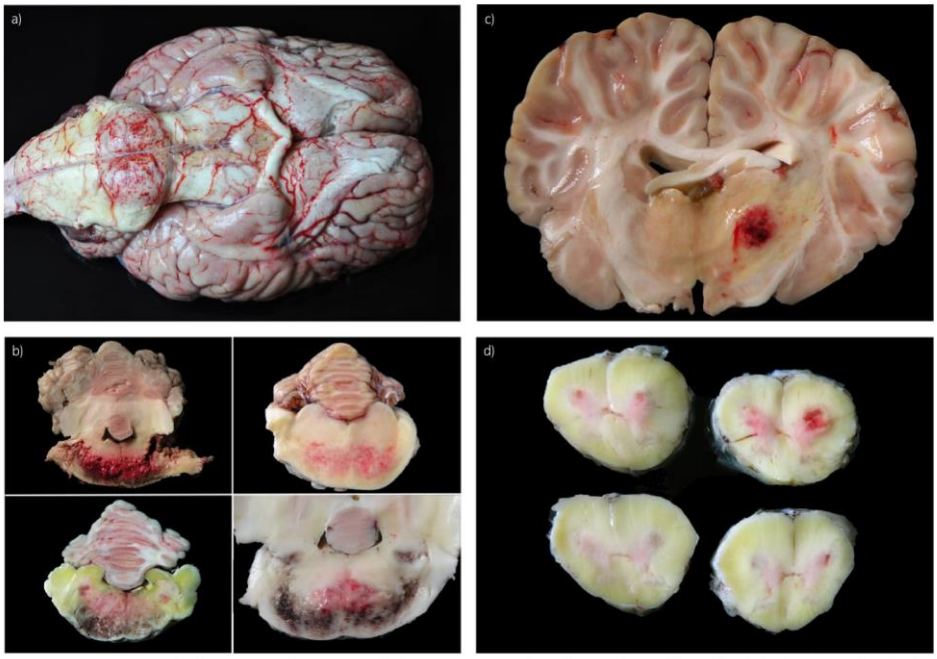

Fig 2: Neurotoxicosis associated with consumption of *Trema micrantha*, horses. a) Brain, ventral view, horse 7. There is diffuse yellowish discoloration, mainly in the basal portion of the brainstem. The region of the pons has marked hyperaemia and is greyish. b) Brainstem and cerebellum. Clockwise, horses 9, 5, 7, and 8. In the different brainstem coronal sections, there is a diffuse yellowish discoloration (oedema) interspersed by grey areas and pinpoint multifocal haemorrhage in the pons. c) Brain, coronal section at the level of thalamus, horse 5. Focal foci of haemorrhage in thalamus with marked yellow discoloration of adjacent tissue (oedema). d) Spinal cord, horse 7. In the lumbar intumescence (above), there are darkened and depressed areas at the dorsal and ventral horns. At the sacral level (below) the grey matter is softened and yellowish.

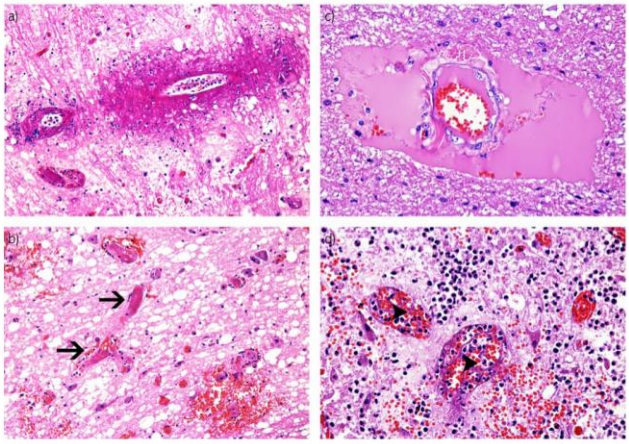

Fig 3: Neurotoxicosis associated with consumption of *Trema micrantha*, horses. a) Brain, horse 7. Multifocal transmural fibrinoid degeneration of blood vessels with loose oedematous surrounding neuropil. HE, 200×. b) Brain, horse 7. Severe vacuolation of the neuropil with perivascular haemorrhage and multifocal thrombosis (arrows). HE, 200×. c) Brain, horse 6. Severe perivascular oedema. Haematoxylin and eosin (HE), 400×. d) Brain, horse 7. Vasculitis (lumen of blood vessels are indicated by arrowheads), haemorrhage and marked multifocal thrombosis, associated with marked diffuse neutrophilic infiltrate, with occasional lymphocytes, plasma cells and macrophages. HE, 400×.

Histopathological findings

The lesions observed grossly in the brain (horses 1–14) and spinal cord (horses 7, 8 and 9) consisted microscopically of severe vasculitis and liquefactive necrosis of white and grey matter of the brainstem, cerebellum and spinal cord. These were characterised by multifocal transmural fibrinoid necrosis of blood vessels (Fig 3a), which sometimes were occluded by thrombosis and associated with perivascular haemorrhage, in addition to severe vacuolation of myelin (suggestive of intramyelinic oedema) (Fig 3b) and perivascular oedema, occasionally extending to adjacent neuropil, were observed (Fig 3c). Severe multifocal perivascular inflammatory infiltrate consisting predominantly of neutrophils with few lymphocytes and plasma cells (horses 1–4, 7 and 8). At the periphery of the areas with necrosis of blood vessels, numerous Gitter cells, Wallerian degeneration and multiple axonal spheroids associate to occasional necrotic neurons were observed in four horses (horses 2 and 6–8) (Fig 3d). In the telencephalic cortex from horses 3–5, hypertrophied astrocytes with scant cytoplasm, vesicular nucleus, marginated chromatin were observed frequently in pairs (Alzheimer type II astrocytes).

Hepatic lesions were found in five horses (horses 1–4, and 6) and were characterised by multifocal and mild necrosis of centrilobular hepatocytes. The remaining horses had no microscopic hepatic lesions.

Discussion

The toxic compounds of *T. micrantha* are yet unknown [13], although a toxic compound named trematoxin and obtained from *Trema tomentosa* is described in Australia [14]. This is a hepatotoxic glycoside associated with centrilobular necrosis in cattle, sheep, goats, horses and camels [15,16]. *T. micrantha* poisoning frequently occurs in herbivores through voluntary ingestion of leaves. The degree of susceptibility depends on the species affected, the toxic dose and the type of access to the plant. Among these, pruning or falling of the branches after windstorms and supplying leaves as an animal feed supplement are highlighted [6,8,10]. In the current study, owners reported that the plant consumption occurred either by direct consumption of the leaves due to food shortage and by access to the leaves in pruned branches of *T. micrantha*. *T. micrantha* appears to be a highly palatable plant to horses [12], thus prevention must be based in restricting access to the plant.

T. micrantha poisoning causes an acute toxic hepatic necrosis in horses [6,10], goats [7–9] and sheep [5]. Neurological abnormalities have previously been related to hepatic encephalopathy, with Alzheimer type II astrocytes and perivascular oedema on histopathology of the CNS from the affected animals [6,12]. In the current study, the main histopathological lesions were in the CNS and were characterised by malacia, severe fibrinoid degeneration of blood vessels, thrombosis, haemorrhage and marked infiltrate of neutrophils adjacent to the malacic areas. These are lesions not usually related to hepatic encephalopathy and hepatic lesions of the current horses were mild or absent. Focal areas of malacia have been previously described in the brain of equids poisoned by *T. micrantha* [10]. The cause of these lesions is unknown; however, it is speculated that there may be an intermediary metabolite formed immediately after *T. micrantha* consumption in equines [10]. In agreement with that, there may be species differences, as in fatal lung lesions resulting from *T. micrantha* ingestion have been described in sheep [5].

Differing from the previously described cases of *T. micrantha* toxicity in horses [6,12], histological abnormalities in the current study were virtually restricted to the brain and spinal cord, mainly the pons and lumbar intumescence. The massive necrosis of the brain and spinal cord parenchyma may relate to ischaemia secondary to the fibrinoid necrosis of blood vessels, which resulted in extensive areas of haemorrhage and thrombosis and, consequently, areas of liquefactive necrosis, as previously described [10]. The clinical course of the horses that had spinal cord lesions was longer than that from horses with only brain lesions. Ischaemia affected mainly the dorsal and ventral horns of the lumbar intumescence where there are large amount of neuronal bodies. We speculate this may be a response to severe energy deficit, suggesting energy deprivation may be a component of the pathogenesis of *T. micrantha* poisoning as a similar distribution is recognised in selenium toxicosis [17,18].

Oedema and liquefactive necrosis of the white and grey matter of the brain and spinal cord in horses has also been related to parasitic infection by *Trypanosoma evansi* [19], and leukoencephalomalacia due to the prolonged ingestion of corn contaminated with *Fusarium verticillioides*

[20,21]. However, the current horses had no history of access to contaminated corn, and lesions differed from that condition due to the involvement of both grey and white matter. Lesions caused by *T. evansi* in horses are characterised by a nonsuppurative encephalitis and oedema [19,20], which were not observed in the horses of the current study. All horses were negative for RABV infection, and, histologically, there were neither encephalitis nor Negri bodies in neuronal cytoplasm, which are hallmark lesions of Rabies [22].

This study is limited by the small number of cases and its retrospective nature, relying on clinical observations reported by owners and attending veterinarians. Nevertheless, we conclude that *T. micrantha* poisoning in horses may cause predominantly a neurological disease, with minimal to absent hepatic lesions. Thus, the neurotoxicosis associated with consumption of this plant should be considered in the differential diagnosis of neurological disorders in horses.

Authors' declaration of interests

No competing interests have been declared.

Ethical animal research

Research ethics committee oversight not required by this journal: retrospective study of clinical records. Explicit owner informed consent for inclusion of animals in this study was not stated.

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Authorship

M.P. Lorenzett, P.R. Pereira, D.M. Bassuino, G. Konradt, W. Panziera, M.V. Bianchi, F.F. Argenta, M.E. Hammerschmitt, R.A. Caprioli, S.P. Pavarini and D. Driemeier contributed to the collection of the samples, made substantial contribution to gross and histopathological analysis, drafted and revised the manuscript and its final version. C.S.L. Barros revised the manuscript, the English language and approved the final version.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Supplementary Item 1: Breed, sex, age, duration of clinical signs, source of plant access and lesion distribution in 14 horses naturally poisoned by *Trema micrantha*.

Equine Veterinary Journal

Supplementary Item 1: Breed, sex, age, duration of clinical signs, source of plant access and lesion distribution in 14 horses naturally poisoned by *Trema micrantha*.

Nº	Breed	Sex	Age (years)	Duration of signs (days)	Source of plant access	Lesions distribution
1	Mixed breed	Female	10	2	Direct consumption of leaves	Rh, Te
2	Mixed breed	Male	12	2	Direct consumption of leaves	Rh, Te
3	AQH	Male	8	1	Direct consumption of leaves	Rh, Te
4	Thoroughbred	Female	13	2	Pruned or falling branches	Rh, Di, Te
5	Criollo	Male	10	1	Direct consumption of leaves	Rh, Di, Te
6	Mixed breed	Female	5	3	Direct consumption of leaves	Me, Di
7	Criollo	Male	6	9	Pruned or falling branches	Rh, Me, Di, Sp
8	Criollo	Male	12	1	Pruned or falling branches	Rh, Me, Di, Sp
9	Criollo	Male	10	3	Pruned or falling branches	Rh, Me, Di, Sp
10	Criollo	Female	6	4	Direct consumption of leaves	Rh, Me, Di,
11	Criollo	Female	10	4	Direct consumption of leaves	Rh, Me, Di, Cs
12	Mixed breed	Female	25	4	Direct consumption of leaves	Rh, Me, Di, Cs
13	Criollo	Male	12	4	Direct consumption of leaves	Rh, Me, Di, Te
14	Criollo	Male	12	4	Direct consumption of leaves	Rh, Me, Di, Te

AQH: American Quarter Horse; Rh: rhombencephalon; Te: telencephalon; Di: diencephalon; Me: mesencephalon; Cs: corpus striatum; Sp: spinal cord.

2 CONCLUSÕES

As alterações clínico-patológicas associadas à ingestão espontânea de *Trema micrantha* em equinos foram caracterizadas, predominantemente, por manifestações neurológicas, com lesões hepáticas mínimas a ausentes.

O curso clínico da intoxicação variou de 24 horas a nove dias com sinais clínicos caracterizados por apatia, sialorreia intensa, movimentos de pedalegem, decúbito esternal com evolução para lateral e morte.

Os achados de necropsia restringiram-se ao encéfalo, que se apresentava friável, com coloração amarelada difusa e áreas multifocais a coalescentes de hemorragia mais acentuadas em região de ponte. Nos equinos com quadro clínico prolongado, as lesões estenderam-se a medula espinhal.

Os achados histopatológicos consistiram em edema, degeneração fibrinoide vascular e necrose liquefativa na substância branca e cinzenta de tronco cerebral, cerebelo e medula espinhal.

A intoxicação por *Trema micrantha* na espécie equina causa predominantemente uma doença neurológica, com lesões hepáticas mínimas ou ausentes, e deve ser considerada no diagnóstico diferencial em quadros de doenças agudas do sistema nervoso central de equinos, dentre elas leucoencefalomalacia, tripanossomíase e raiva.