

Anatomopathological and immunohistochemical characterization of a case of granulomatous meningoencephalitis in a bovine with systemic tuberculosis

Caracterização anatomopatológica e imuno-histoquímica de um caso de meningite granulomatosa em bovino com tuberculose sistêmica

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Renan Lazzaretti

Mestrando em Ciências Veterinárias pelo Programa de Pós-Graduação em Bioexperimentação

Instituição: Universidade de Passo Fundo - UPF

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: 156147@upf.br

Ezequiel Davi dos Santos

Mestre em Ciências Veterinárias

Instituição: Universidade de Passo Fundo

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: 68991@upf.br

Diorges Henrique Setim

Doutorando em Ciências Veterinárias pelo Programa de Pós-Graduação em Bioexperimentação

Instituição: Universidade de Passo Fundo - UPF

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: setimdiorges@gmail.com

Tanise Policarpo Machado

Mestre em Ciências Veterinárias

Instituição: Universidade de Passo Fundo

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: tanisemachado@upf.br

Renata Seibel

Graduanda em Medicina Veterinária

Instituição: Universidade de Passo Fundo - UPF

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: 171180@upf.br

Carlos Bondan

Doutor

Instituição: Universidade de Passo Fundo - UPF

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: cbondan@upf.br

Ricardo Zanella

Doutor

Instituição: Universidade de Passo Fundo - UPF

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: ricardozanella@upf.br

Giseli Aparecida Ritterbusch

Doutora

Instituição: Universidade de Passo Fundo - UPF

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: giseliritter@upf.br

Adriana Costa da Motta

Doutora pelo Programa de Pós-Graduação em Bioexperimentação

Instituição: Universidade de Passo Fundo - UPF

Endereço: BR 285, Km 292,7, São José s/n, Passo Fundo - RS, Brasil

E-mail: acmotta@upf.br *autor para correspondência

ABSTRACT

A two-year-old male bovine of Aberdeen Angus breed with anorexia, weight loss, and apathy was reported for necropsy, being diagnosed with systemic tuberculosis and tuberculoid meningitis lesions. Bovine tuberculosis was observed and confirmed through the necropsy of granulomatous lesions, mainly in the lungs and regional lymph nodes; specific staining for alcohol-acid resistant bacilli and immunohistochemistry were also performed. It should be noted that bovine tuberculosis is a zoonotic disease, with mandatory notification, caused by *Mycobacterium bovis*. In most cases, it has nonspecific clinical symptoms, such as respiratory signs, weight loss, and lymphadenopathy. In rare cases, alterations in the central nervous system occur. Therefore, this study aimed to report a case of granulomatous meningitis in a bovine with systemic tuberculosis through the characterization of its anatomicopathological and immunohistochemical aspects.

Keywords: meningitis, tuberculosis, zoonosis, bovine, immunohistochemistry.

RESUMO

Um bovino macho, com dois anos de idade, raça Aberdeen Angus, apresentando anorexia, emagrecimento e apatia foi encaminhado para necropsia, sendo diagnosticado com tuberculose sistêmica e lesões de meningite tuberculoide. A tuberculose bovina foi evidenciada e confirmada através do exame de necropsia, das lesões granulomatosas encontradas, sobretudo nos pulmões e linfonodos regionais, e pelo emprego de coloração especial para bacilos álcool-ácido resistentes e imuno-histoquímica. Salienta-se que a tuberculose bovina é uma doença de caráter zoonótico e de notificação obrigatória, causada por *Mycobacterium bovis*. Na maioria dos casos apresenta-se com sinais clínicos inespecíficos, como sinais respiratórios, emagrecimento e linfadenopatia. Em casos raros ocorre o comprometimento do sistema nervoso central. Este trabalho tem por objetivo relatar um caso de meningite granulomatosa em bovino com tuberculose sistêmica, caracterizando seus aspectos anatomopatológicos e imuno-histoquímicos.

Palavras-chave: meningite, tuberculose, zoonose, bovino, imuno-histoquímica.

1 INTRODUCTION

Tuberculosis is a chronic infectious-contagious and zoonotic disease to which any detected case needs mandatory notification since it causes serious economic losses in livestock production (TODESCHINI et al., 2018; DAMETTO et al., 2020). These economic losses are mainly related to decreasing milk and meat production, carcass condemnation by the food safety and inspection services, and the mandatory disposal of animals with a positive disease diagnosis (DAMETTO et al., 2020). In addition to domestic herbivores, other species are also affected, such as domestic felines and canines (ALVES et al., 2017; ROCHA et al., 2017; SOUSA et al., 2018), as well as wild animals (RIBEIRO et al., 2017). Regarding humans, most cases of tuberculosis present challenging clinical manifestations and lesions, especially when the patient has comorbidities (ALEIXO et al., 2020). In immunocompromised individuals, cases of tuberculous meningitis have already been described (LAN et al., 2001; GARG, 2010; SOUZA et al., 2014).

The disease is caused by *Mycobacterium bovis* and less frequently by *Mycobacterium tuberculosis* in cattle. The infectious agent is a resistant acid-alcohol bacillus, mainly infecting the respiratory system. The primary infection affects the lungs and bronchial and mediastinal lymph nodes. Although the disease usually presents subclinical manifestation, a chronic picture of tuberculosis is already established when respiratory signs, weight loss, and lymphadenopathy are observed (HEADLEY, 2002; QUADRI et al., 2021). In cattle with central nervous system (CNS) impairment, the symptoms may vary according to the location of the granulomas, ranging from motor incoordination or blindness to severe paresis (BARROS et al., 2006; DEL FAVA et al., 2020; KONRADT et al., 2016). However, early-stage tuberculoid granulomas may not present noticeable nervous symptoms, regardless of their location.

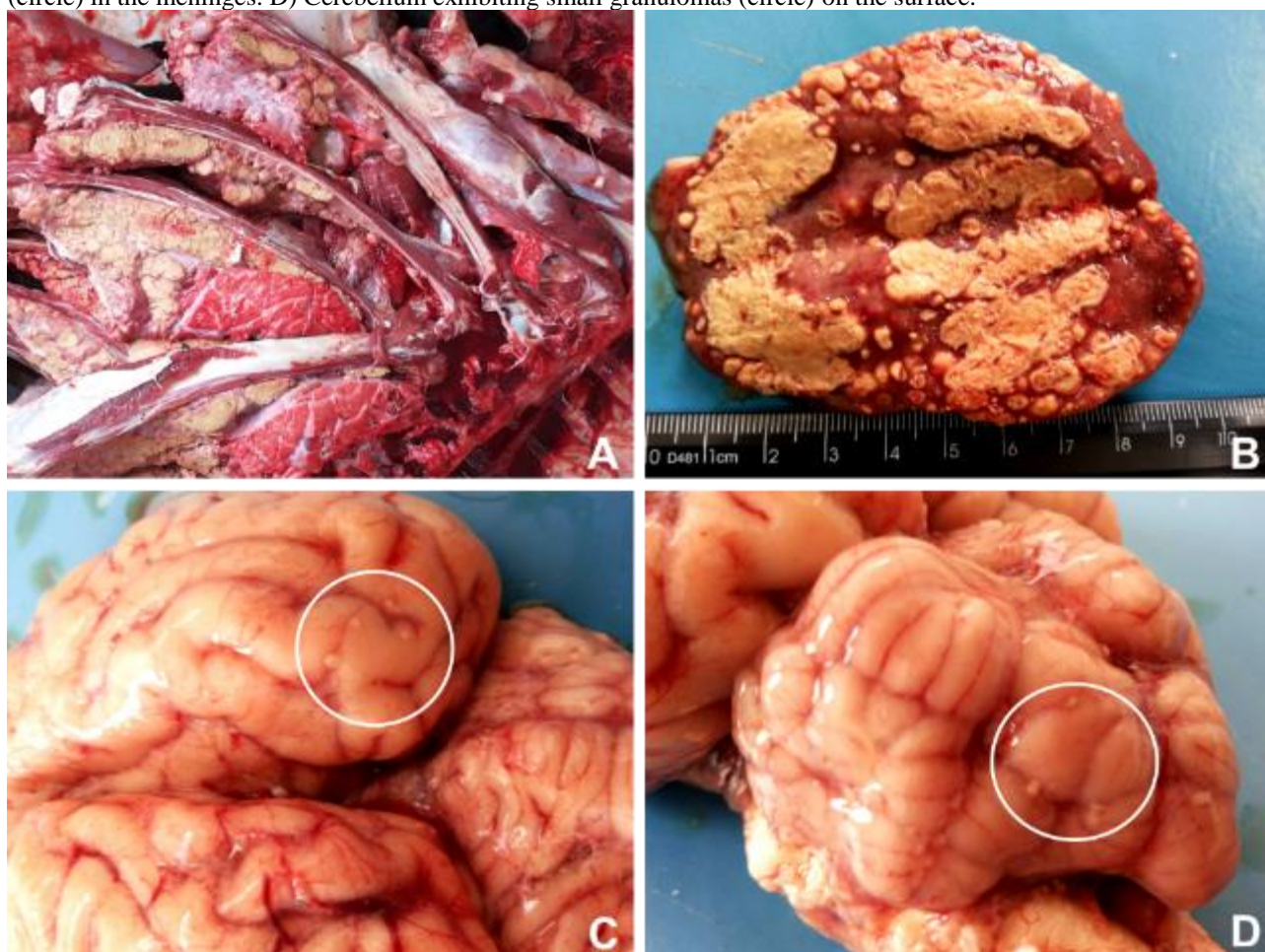
We report a case of granulomatous meningoencephalitis in cattle with systemic tuberculosis through the characterization of its anatomicopathological and immunohistochemical aspects.

2 CASE REPORT

The case was observed in a 2-year-old male Aberdeen Angus cattle presenting anorexia, weight loss, and apathy before death. The animal was subsequently referred to necropsy.

Accentuated emaciation was detected during external examination. The main findings after internal examination were observed in the thoracic cavity, with pulmonary adhesion to the parietal pleura (Figure 1 A), as well as diaphragm and mediastinal, submandibular, and retropharyngeal lymph nodes with granulomatous nodules with sandy consistency when cut (Figure 1 B). Adhesion of the parietal pleura with the pericardium was also observed, accompanied by numerous small granulomatous nodules. Nodules similar to those described above were also present in the heart. The brain and cerebellum also had small granulomas in the meninges (Figure 1 C-D).

FIGURE 1. Granulomatous meningitis in cattle with systemic tuberculosis. A) Chest cavity showing numerous tuberculoid granulomas causing adhesion between visceral and parietal pleurae. B) Mediastinal lymph node, cutting surface showing tuberculoid granulomas. C) Brain displaying small granulomas (circle) in the meninges. D) Cerebellum exhibiting small granulomas (circle) on the surface.



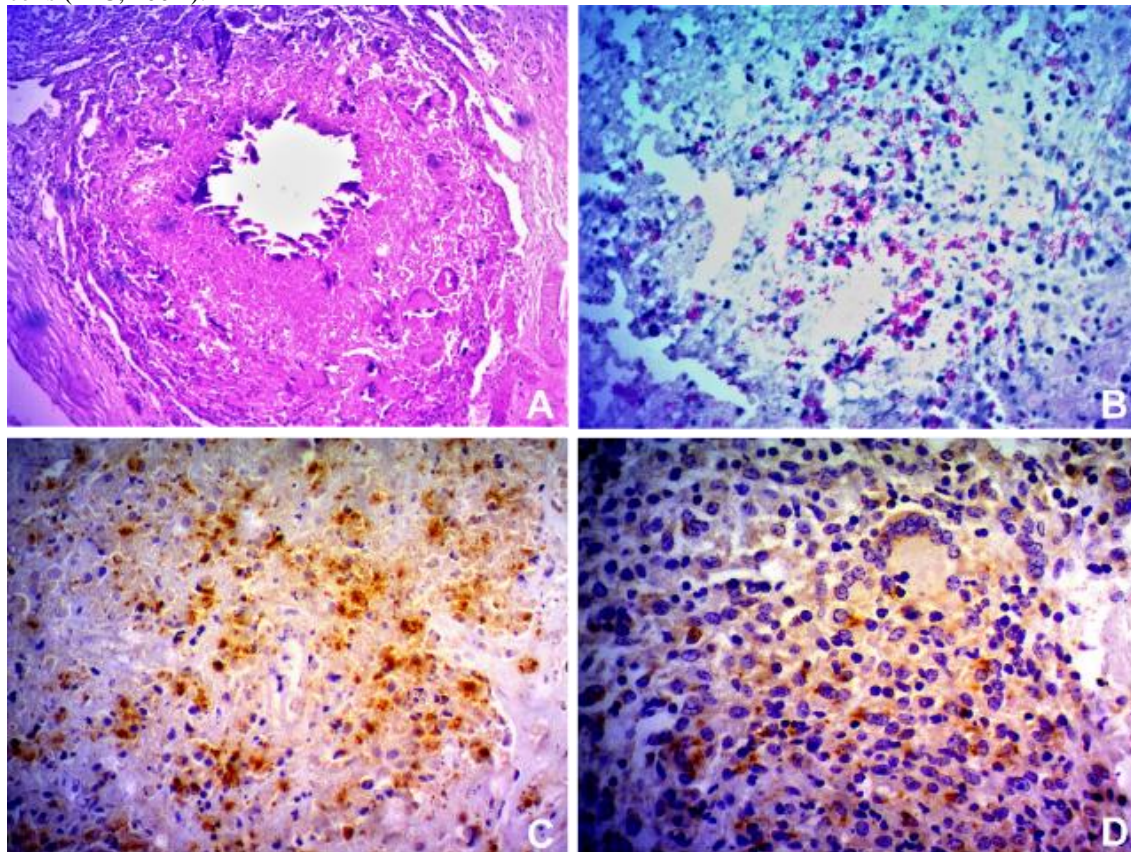
Samples from all organs were collected and fixed in 10% buffered formalin, processed by conventional histochemical methods, and stained with hematoxylin and eosin (HE). Lung sections were subjected to Ziehl–Neelsen staining to verify the presence

of acid-fast bacilli (AFB). In addition, immunohistochemistry (IHC) was performed using polyclonal anti-*Mycobacterium tuberculosis* antibody at a dilution of 1:200, applying the streptavidin-biotin-peroxidase technique on sections of the mediastinum lymph node and brain.

Histopathological findings in the lung consisted of numerous granulomas with central mineralization (Figure 2 A). Multiple areas of mineralization of interalveolar septa and granulomatous bronchopneumonia were also detected. The lymph nodes showed marked granulomatous lymphadenitis. The kidneys had marked granulomatous interstitial nephritis and moderate chronic pyelonephritis. Significant calcification was observed in the endocardium, associated with mononuclear cells and epithelioid macrophages. The brain, cerebellum, and spinal cord had moderate multifocal granulomatous meningitis.

Numerous AFB were found in the cytoplasm of macrophages in lung sections submitted to Ziehl–Neelsen staining (Figure 2B). Through IHC, immunostaining for *Mycobacterium* spp. was verified in the cytoplasm of epithelioid macrophages of the mediastinal lymph node (Figure 2C) and macrophages and giant cells of the cerebral meninges (Figure 2D).

FIGURE 2. Granulomatous meningitis in cattle with systemic tuberculosis. A) Lung: Formation of tuberculoid granuloma with a mineralized central area (HE, 100X). B) Lung: Granulomatous lesion with the presence of AFB (Ziehl–Neelsen, 400X). C) Mediastinal lymph node: Granulomatous lesion showing positive immunostaining for *Mycobacterium* spp. in a caseous necrosis area, cytoplasm of macrophages, and epithelioid macrophages (IHC, 400X). D) Brain meninges: Granulomatous lesion showing positive immunostaining for *Mycobacterium* spp. in cytoplasm of macrophages, epithelioid macrophages, and giant cells (IHC, 400X).



3 DISCUSSION

In the reported case, bovine tuberculosis was characterized by severe alterations in the respiratory system and regional lymph nodes, as well as by the dissemination and multisystem affections, as detected in previous studies (Headley, 2002; Andreazza et al., 2015; Quadri et al., 2021). The systemic dissemination was undoubtedly influenced and aggravated by the marked tuberculoid lesions observed in the thoracic cavity and lung parenchyma. The bacteria possibly reached the bloodstream and the other affected organs through these lesions. Anorexia, apathy, and weight loss observed in the analyzed bovine may have originated from strenuous breathing associated with lymphadenopathy of the lymph nodes of the thoracic cavity and cervical region, which caused discomfort in ingesting food.

Although rare, the infectious agent can also cause damage to the nervous system, with clinical manifestations varying according to the magnitude and location of the

damage (ROELS et al., 2003; BARROS et al., 2006; KONRADT et al., 2016). Macroscopically, multiple small granulomas were observed in the meninges of the brain and cerebellum. However, when alive, the bovine did not present noticeable nervous symptoms. This fact may have occurred due to the size and/or initial stage of tuberculoid granulomas since they were not compressing any sensitive area of the CNS.

Microscopically, the numerous granulomas with central mineralization found in the lung, the multiple lymph nodes with granulomatous lymphadenitis, granulomatous interstitial nephritis, and marked granulomatous endocarditis are part of the histological lesions presented in the literature for cattle with systemic tuberculosis (HEADLEY, 2002; LIEBANA et al., 2008; DOMINGO, 2014; ANDREAZZA et al., 2015) and also for cattle with central nervous system tuberculosis (ROELS et al., 2003; BARROS et al., 2006; KONRADT et al., 2016; DEL FAVA et al., 2020; FAVILA-HUMARA et al., 2021). There are few studies describing cases of bovine with tuberculoid meningitis in the brain, cerebellum, and spinal cord through the application of various diagnostic tools, highlighting the importance of the present report.

The use of technics such as Ziehl–Neelsen staining to verify the presence of AFB and antigen detection by IHC was essential for the definitive diagnosis of the present case, in particular, to confirm the anatomicopathological picture of tuberculoid meningitis. The use of different diagnostic alternatives for bovine tuberculosis has been previously proposed and used (KONRADT et al., 2016; ANDREAZZA et al., 2015; SOUZA et al., 2016; DAMETTO et al., 2020; SANTOS et al., 2021), evidencing the importance of diagnostic improvement regarding the use of increasingly accurate methods.

The present case, which involved necropsy and histopathological study of all organs and the CNS, shows that the association of diagnostic techniques is an excellent alternative for detecting bovine tuberculosis. This approach increases the accuracy in identifying the disease, particularly for central nervous system tuberculosis. However, it is essential to emphasize that the control of the disease in bovine herds occurs through the tuberculin test, which is the technique recommended for diagnosis and control of the disease worldwide.

4 FINAL CONSIDERATIONS:

It is noteworthy the importance of performing necropsy, histopathology exams, and, especially, using accurate methods to elucidate diagnoses of infectious diseases, such as tuberculosis. In addition, an accurate diagnosis, like the one performed in the present

case, contributes to alerting the rural properties and their surrounding regions to the presence of the tuberculosis agent. This practice can also alter livestock farmworkers to seek public health services for advice and possible examinations.

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