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Case Report

Asteroid Bodies Associated with Granulomatous Meningoencephalitis in a Female Dog

Juneo F. Silva[1], Rogéria Serakides[1], Matheus V. L. Moreira[1], Natália M. Ocarino[1*]

[1]Departamento de Clínica e Cirurgia Veterinárias, Escola de Veterinária, Universidade Federal de Minas Gerais, Brazil.
*** Corresponding Author:** Natalia M. Ocarino, Departamento de Clínica e Cirurgia Veterinárias, Escola de Veterinária, UFMG, Universidade Federal de Minas Gerais, Av. Presidente Antônio Carlos, 6627 – CEP: 30.161-970, Belo Horizonte, MG, Brazil. E-mail: nataliaocarino@gmail.com

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Abstract

A case of asteroid bodies associated with granulomatous meningoencephalitis is reported in a 4-year-old female dachshund that showed intermittent tremors and blindness. Necropsy revealed leptomeninges moderately hyperemic and from the parietal cortex extending into the temporal and frontal cortex, thalamus and midbrain flattening of the gyri and a grayish and friable focally extensive area. Microscopically intense and extensive perivascular inflammatory infiltrates of lymphocytes, plasma cells, macrophages and giant cells were observed. In the cytoplasm of the giant cells, neuropil stellate structures ranging from 20 to 80 μm in diameter with a central dense and homogenous zone and with amphophilic and vacuolated cytoplasm consistent with asteroid bodies were present. Special staining and transmission electron microscopy permitted the diagnosis of asteroid bodies associated with granulomatous meningoencephalitis.

Key words: nervous system, cytoplasmic inclusion, inflammation, dog.

Introduction

Giant-cell asteroid bodies are stellate acidophilic cytoplasmic inclusions formed during the process of macrophage fusion to become giant cells (9, 14). In humans, asteroid bodies (AB) have been described in association with granulomatous reactions such as sarcoidosis, cryptococcosis, sporotrichosis, lobomucosis, mycobacteriosis, schistosomiasis, foreign body and xanthogranuloma (6, 11, 14). Although granulomatous reactions are frequently identified in veterinary medicine, the occurrence of asteroid bodies is extremely rare, with only one case described in the literature (12). The origin, formation and constitution of AB are controversial, and several theories have been postulated (9, 10). Histologically, AB are characterized by star-shaped intracellular structures (7). The main differential diagnoses for AB are other cytoplasmic inclusions. This report describes a case of asteroid bodies associated with granulomatous meningoencephalitis in a female dog. This paper reports the occurrence of asteroid bodies and their differential diagnosis, but does not aim to characterize their constitution.

Case report

A 4-year-old female dachshund was submitted for necropsy at the Pathology Department of the Veterinary Hospital at the Escola de Veterinária – UFMG, Brazil. According to the owner, the dog showed intermittent tremors and blindness. Necropsy revealed intensely hyperemic mucous membranes and skeletal muscles. The leptomeninges were moderately hyperemic, and from the parietal cortex extending into the temporal and frontal cortex, thalamus and midbrain were observed flattening of the gyri and a grayish and friable focally extensive area (Fig. 1). The organs of the abdominal and thoracic cavities showed moderate hyperemia. Fragments of the brain,

spinal cord, and organs of the abdominal and thoracic cavities were collected and fixed in 10% neutral phosphate-buffered formalin, embedded in paraffin, and cut into 5 µm sections.

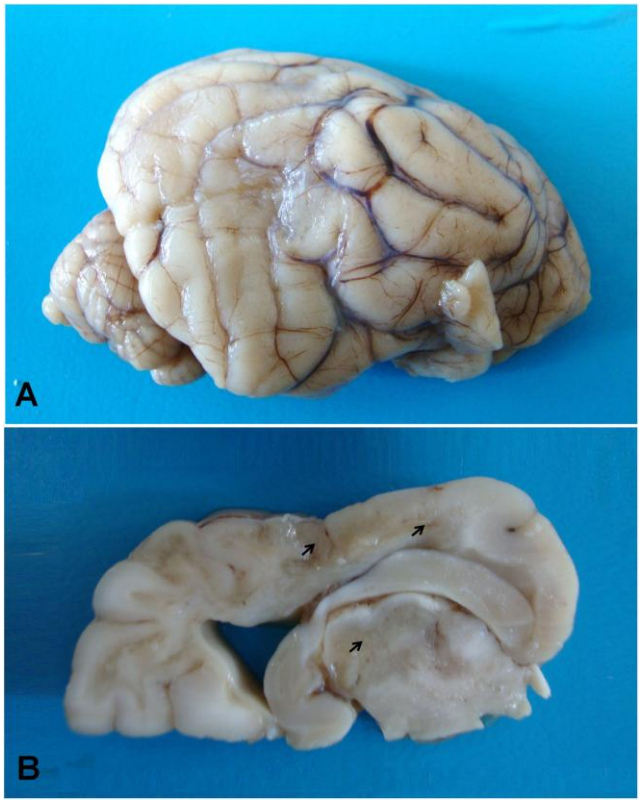

Figure 1. A and B Parietal cortex extending into the temporal and frontal cortex, thalamus and midbrain with flattening of gyri and a grayish and friable focally extensive area (arrows).

The sections were stained with hematoxylin and eosin, Periodic acid-Schiff (PAS), Alcian Blue pH 1 and 2.5, Goodpasture, Warthin–Starry, Giemsa, Ziehl–Neelsen, Congo red, Von Kossa, Masson trichrome and Luxol. Immunohistochemistry for vimentin (1:100) (V9, Dako, CA, USA) was also performed using the streptavidin-biotin-peroxidase technique (Streptavidin Peroxidase, Lab Vision Corp., Fremont, CA, USA). Histological section was incubated overnight in a humid chamber with primary antibody and was incubated during the steps of blocking endogenous peroxidase, blocking serum (Ultra Vision Block, Lab Vision Corp., Fremont, CA, USA) and streptavidin peroxidase for 30 minutes. Incubation with the secondary antibody (goat biotin, Lab Vision Corp., Fremont, CA. USA) was performed for 45 minutes. The chromogen utilised was diaminobenzidine (DAB substrate system, Lab Vision Corp., Fremont, CA. USA). Sections were counterstained with Harris hematoxylin. A negative control was obtained by replacing the primary antibodies with IgG. Fragments of the brain were also processed and embedded in epoxy. Thin sections were obtained in resin and stained with toluidine blue. Subsequently, ultrathin sections were cut for evaluation by transmission electron microscopy.

Microscopically, the brain areas of the parietal, temporal, frontal and occipital cortex, diencephalon, midbrain and pons showed intense and extensive perivascular inflammatory infiltrates of lymphocytes, plasma cells, macrophages and giant cells, mainly in the white matter of the midbrain and occipital cortex and extending into the gray matter. In the cytoplasm of the giant cells, neuropil stellate structures ranging from 20 to 80 µm in diameter with a central dense and homogenous zone and with amphophilic and vacuolated cytoplasm consistent with asteroid bodies were observed (Fig. 2). Intense and extensive vacuolation with necrosis, loss of neuropil, hemorrhage and gliosis were also observed.

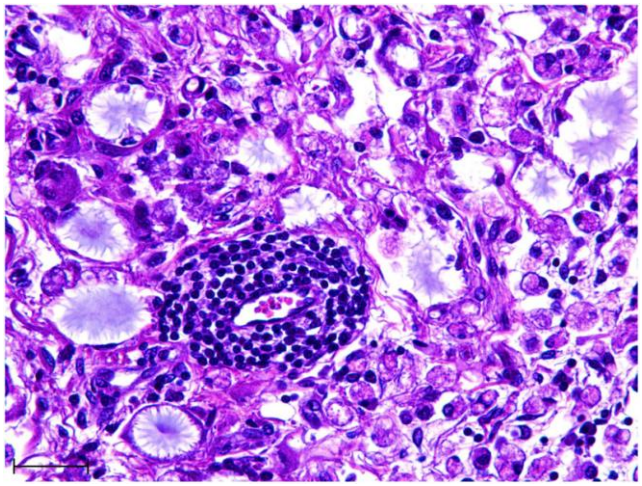

Figure 2. Midbrain with perivascular cuffing and surrounding inflammatory infiltrates of lymphocytes, plasma cells, macrophages, giant cells, and structures ranging from 20 to 80 µm in diameter with a central dense and homogenous zone and with amphophilic and vacuolated cytoplasm, consistent with asteroid bodies. HE. Bar, 42 µm

The asteroid bodies were strongly stained with Alcian Blue pH 1 and 2.5 (Fig. 3) and were negative for PAS, Goodpasture, Warthin-Starry, Giemsa, Ziehl-Neelsen, Von Kossa, Congo red, and Luxol (Fig. 3 detail) staining. The asteroid bodies were also negative for vimentin immunostaining. Transmission electron microscopy revealed dense osmiophilic lamellar concentric structures within the macrophage cytoplasm that sometimes showed aspects of myelin (Fig. 4). The structures within the macrophages were also strongly positive for Luxol (Fig. 4 detail). No viral, bacterial, protozoan or fungal agents associated with the granulomatous lesion were observed. Moderate hyperemia was confirmed in the thoracic and abdominal organs.

Giant cell asteroid bodies are cytoplasmic inclusions of uncertain origin (14). The constitution of AB is controversial. Electron microscopy and cytochemical

and immunohistochemical studies have yielded conflicting results (4, 5, 9, 10, 14). These studies suggest three possibilities for the formation of AB: 1) formation by collagenous fibers, 2) formation by aggregation of microtubules derived from cytoskeletal components and 3) formation by lamellar phospholipid structures. In the present study, the AB were positive for Alcian Blue pH 2.5 and 1. This result suggests the presence of phospholipids in AB. AB were negative for collagen because they were not stained by Masson's trichrome and were negative for vimentin. These findings agree with the results of Papadimitrio and Drachenberg (9). Inside the inflammatory macrophages, dense osmiophilic concentric lamellar structures positive for Luxol were observed. These results confirm the myelin nature of the intracytoplasmic compound (3). This myelin most likely occurred within the cytoplasm of the macrophages due to phagocytosis of the damaged white matter.

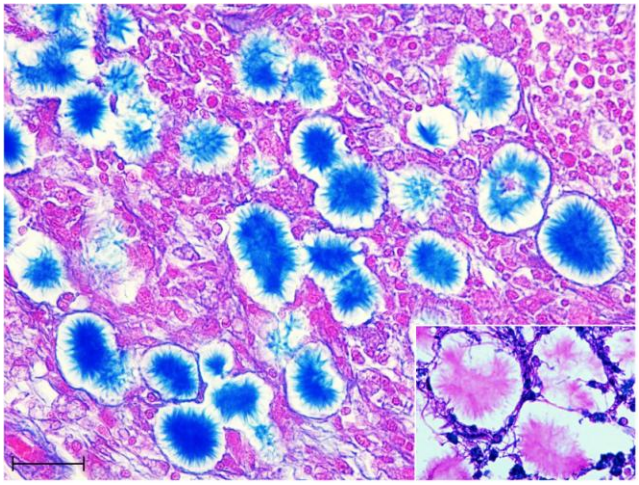

Figure 3. Asteroid bodies stained blue. Alcian Blue pH 2.5. Bar, 42 µm. Detail: Asteroid bodies negative for Luxol.

The main differential diagnoses for AB include cytoplasmic inclusions, such as hematoidin crystals, calcium oxalate crystals, cholesterol crystals and Schaumann bodies (8). Hematoidin crystals and asteroid bodies have a characteristic stellate microscopy; however, in contrast to asteroid bodies, hematoidin crystals are a bright golden color (2). Calcium oxalate crystals, unlike asteroid bodies, are colorless refractile crystals that are not stellate in shape. Schaumann bodies are formed from oxalate crystals and contain calcium and iron (7). The asteroid bodies were negative for Von kossa staining, indicating the absence of calcium. Cholesterol crystals are cracks in negative image within giant cells, which were not observed in this case.

In human medicine, AB are observed in association with granulomatous inflammation (14). In veterinary medicine, although granulomatous processes are common, the presence of asteroid bodies is extremely rare. In this report, the animal had granulomatous meningoencephalitis. Infectious causes for this condition were investigated and discarded because no infectious agent was observed in the Goodpasture, Warthin–Starry, Giemsa, and Ziehl–Neelsen stains or in the electron microscopy evaluation. Thus, the meningoencephalitis was likely idiopathic or autoimmune in nature, similar to cases reported in the literature (1,13).

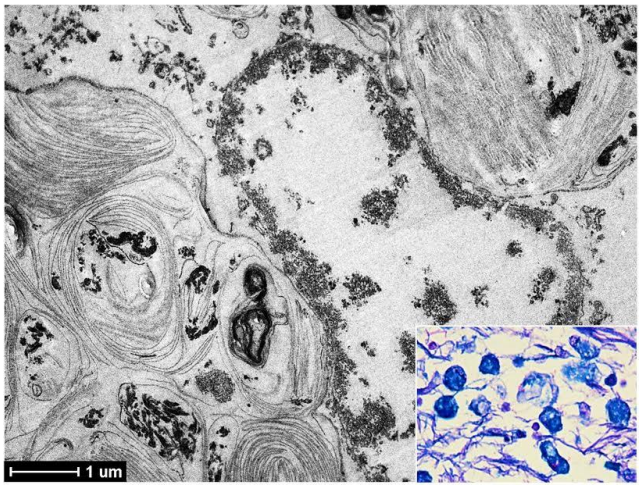

Figure 4. Within the cytoplasm of macrophages were dense osmiophilic lamellar concentric structures typical of phagocytized myelin. Transmission electron microscopy. Detail: Macrophages positive for Luxol.

Based on the gross and histopathological findings, the diagnosis of asteroid bodies associated with granulomatous meningoencephalitis was confirmed.

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