NECROTIZING ENCEPHALITIS IN A YORKSHIRE TERRIER: CLINICAL, IMAGING, AND PATHOLOGIC FINDINGS

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A 5-year-old, male Yorkshire Terrier had chronic and progressive neurologic signs compatible with lesions in the right brain stem and right forebrain. In magnetic resonance images of the brain there were multifocal lesions at different stages of evolution, consistent with an inflammatory disease. The lesions were located in the white matter of the cerebrum, in the diencephalon and mesencephalon. These lesions were hypointense in T1-weighted images and hyperintense in T2-weighted images with no mass effect and minimal enhancement with gadolinium. Necrotizing encephalitis was confirmed post mortem. *Veterinary Radiology & Ultrasound*, Vol. 40, No. 6, 1999, pp 622–626.

Key words: encephalitis, MRI.

Introduction

Necrotizing encephalitis is a rare non-suppurative inflammatory disease of unknown etiology. It has been described in the Yorkshire terrier,¹⁻³ Pug,⁴⁻⁵ and Maltese terrier⁶⁻⁸ as a cause of brain stem and forebrain signs. The course of the illness is variable, but usually chronic, progressive and invariably fatal. Mildly to markedly elevated protein content and pleocytosis of monocytes and lymphocytes may be found in the cerebrospinal fluid (CSF),¹ the diagnosis must be confirmed by histologic examination.

Case History

A 5-year-old, male Yorkshire Terrier was referred for evaluation of chronic progressive neurologic signs. The dog was vaccinated against canine distemper virus, parvovirus, canine hepatitis virus, and leptospirosis, and had no prior medical history. Six months previously the dog had developed head tilt to the right, which resolved after treatment by the referring veterinarian with corticosteroids; however, clinical signs recurred two months later, at which time the dog also began to circle to the right and was uncomfortable when touched. Further treatment using meloxicam* induced no changes in neurologic signs, though the dog had fewer signs of pain.

When referred, the dog was markedly depressed and was recumbent because of pleurothotonos to the right. When helped to walk, he circles to the right and had compulsive movements including head pressing. Physical examination was otherwise unremarkable. Abnormal findings on neurologic examination were lack of menace response on the left, positional strabismus on the right, delayed physiological nystagmus, lack of proprioceptive positioning responses affecting the left thoracic and pelvic limbs and the right pelvic limb, and delayed response on the right thoracic limb. The hopping response was absent in all four limbs, and at the wheelbarrowing test the dog circled to the right. Spinal reflexes were normal. Complete blood cell count, serum biochemistry, and thoracic radiographs were normal.

The neurological findings were considered compatible with right brain stem and right forebrain lesions. Differential diagnosis included inflammatory diseases such as canine distemper encephalitis, necrotizing encephalitis of Yorkshire terriers, granulomatous meningoencephalitis (GME), and a right brain stem space-occupying lesion inducing secondary hydrocephalus.

T1 and T2-weighted and T1-weighted contrast-enhanced, 4 mm thick magnetic resonance images of the brain with an interslice gap of 0.4 mm, were obtained using a 0.5 Tesla superconducting magnet.† Contrast-enhanced images were made immediately after an IV bolus of gadolinium-calcium calteridolum, trometamime-hydrochloric acid‡ at 0.15 mmol/kg.

On MRI images it was possible to identify three distinct lesions. One was visible in the left frontal subcortical white matter; it was hypointense in T1 and hyperintense in T2 images. There was no mass effect identified. Ventricular

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*Metacam, Boeringer Ingelheim
†Phylilps Gyroscan 5T
‡ProHance, Bracco S.p.A, Milano, Italy, for Bristol-Meyers Squibb, New Brunswick, NJ
FIG. 1. (A) Dorsal T1 weighted contrast enhanced (TR 550 msec., TE 25 msec.) and (B) T2 weighted (TR 3000 msec., TE 120 msec.) magnetic resonance images of the brain of a five year-old male Yorkshire Terrier. Two lesions characterized by a signal similar to CSF are evident (arrow and arrowheads) in the deep white matter of the right frontal lobe and in the subcortical white matter of the left frontal lobe. On the T2 image it is possible to see the extension of the lesion toward the diencephalus and also the perilesional oedema (arrowheads).

dilatation was present without signs of ventricular hypertension such as transependymal reabsorption. The lesion's signal similar to CSF and the ipsilateral ventricular ex vacuo dilatation was consistent with an old lesion such as an area of colliquative necrosis. A similar lesion was located in the deep white matter of the right frontal lobe and it was not characterized by enhancement after contrast medium administration (Fig. 1). It was congruent with a different lesion occupying the right diencephalon and mesencephalon characterized by slight hypointensity in T1, slight hyperintensity in proton density and greater hyperintensity in T2 (Fig. 2-3). In this lesion it was difficult to distinguish the lesion from the perilesional edema (Fig. 1) because in the post contrast images there was only slight enhancement (Fig. 3).

These multifocal axial lesions were thought to be compatible with a single disease at different stages of evolution. The signal, pattern of contrast enhancement, and site suggested an inflammatory etiology.8,9

The owner declined CSF examination because of the poor prognosis given for distemper, necrotizing encephalitis and GME. The dog was treated with dexamethasone (0.2 mg/kg twice a day) to reduce brain inflammation or edema. Because all the inflammatory diseases considered in the differential diagnosis can cause seizures, phenobarbital (2.5 mg/kg every twelve hours) was given.10 There was no change in the clinical signs for five weeks, at which point the dog began rolling and was euthanized at the owner’s request.

Pathological Findings

Grossly, there was a moderate dilatation of the lateral ventricles and focal grey brown areas were observed in the diencephalon. Sections of the brain were stained with haematoxylin and eosin and luxol cresyl violet. Immunohistochemistry for canine distemper virus (CDV) was done using monoclonal antibody D110 specific for the nucleoprotein of the virus11 in a commercial kit.§ Immunohistochemistry for CDV antigens was negative. Histologically, there was

§Vectastain ABC Vector Laboratories Inc., Burlingame, CA 94010
granulomatous inflammation in the brain stem, diencephalon and cerebral white matter (Fig. 4). There were monocellular perivascular cuffs of lymphocytes, histiocytes, and macrophages surrounded by reactive astrocytes and microglial cells (Fig. 5). The brain stem lesions extended cranially from the pons, and there was a more severe involvement in the mesencephalon. The lesions were located around the mesencephalic aqueduct (Fig. 6) and the third ventricle, mainly unilateral and extending peripherally. In many areas a characteristic structure was observed with a dark inflammatory ring around a clear, sclerotic centre (Fig. 7) with microcavitations or necrosis. Moderate edema was associated with the granulomatous lesions. Especially in the mesencephalon and in the thalamus, the lesions were separated by sclerotic areas with necrosis and infiltration of numerous

Fig. 2. (A) Transverse proton density (TR 1715 msec., TE 20 msec.) and (B) T2 weighted (TR 1715 msec., TE 80 msec.) magnetic resonance images. A lesion slightly hyperintense in the proton density image and more hyperintense in the T2 weighted is evident in the right mesencephalon (little and bigger head of arrows).

Fig. 3. (A) Dorsal T1 weighted contrast enhanced (TR 550 msec., TE 25 msec.) magnetic resonance image. It is possible to see an alteration of the signal in the right mesencephalic area with a slight enhancement (black and white arrowheads). (B) Transverse T1 weighted contrast enhanced (TR 461 msec., TE 15 msec.) magnetic resonance image. A right mesencephalon lesion (arrows) characterized by slight hypointensity without enhancement except for a slight impregnated stripe (arrowhead).
reactive astrocytes and histiocytes. Neurones within the grey matter were often unaffected. In the cerebral white matter, especially near the lateral ventricles, areas of intense glial reaction around the small perivascular cuffs were present. The lesions detected were consistent with the diagnosis of necrotizing encephalitis.

**Discussion**

Antemortem diagnosis of necrotizing encephalitis is not possible because of the lack of specific clinical signs or clinicopathologic features. The differential diagnosis must include canine distemper encephalitis (leukoencephalomyelopathy) and GME. Each of these diseases occur in adult dogs, mostly involve the brain stem, and have a sub-acute onset with a chronic progressive course.

The cerebrospinal fluid in necrotizing encephalitis may be characterized by moderate pleocytosis with prevalence of mononuclear cells (lymphocytes, monocytes, plasma cells, and macrophages) and a mildly to moderate elevation of the protein concentration. CSF examination in dogs with distemper encephalitis may occasionally be normal but there is usually moderate pleocytosis with lymphocytes and a slightly increased protein content. The indirect fluorescent antibody testing for distemper virus in CSF mononuclear cells is positive in 82% dogs with the inflammatory form of distemper encephalitis. In GME, the CSF usually has moderate pleocytosis with prevalence of mononuclear and polymorphs and moderately increased protein. Rarely, CSF is normal in dogs with GME. Hence, the overlap in findings prevents reliable differentiation of necrotizing encephalitis, distemper encephalitis and GME by CSF analysis.

The MRI findings in this dog were suggestive of an inflammatory disease. MRI findings similar to those in this report have been described. In contrast similar MRI findings have been attributed to a cerebral infarction rather
than an inflammatory lesion. However, on MRI sequences, any lesions resulting from infarction (occlusion of a cerebral vessel by embolism or thrombus) tend to be localised to specific areas that correspond to the specific territory of the affected vessels. Also, in these instances the cerebral cortex is involved as well as the grey matter.

Histologically, in this report some observed lesions were similar to those seen in chronic CDV, especially the involvement of the white matter, although the typical demyelinating lesions were absent and immunocytochemistry for CDV-antigen resulted negative. As regards GME, histological lesions are characterized by dense aggregations of inflammatory cells, around blood vessels, especially lymphocytes, reticuloendothelial cells, and macrophages. Additionally the occurrence of epithelioid granulomas in GME is frequent, whereas the microcavitations, the necrosis and the extensive sclerosis, observed in the necrotizing encephalitis, are features lacking in GME.16,17

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