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Appearance of the canine meninges in subtraction magnetic resonance images

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Running head: Canine meningeal anatomy

Abstract

The canine meninges are not visible as discrete structures in non-contrast magnetic resonance (MR) images, and are incompletely visualized in T1-weighted, post-gadolinium images, reportedly appearing as short, thin curvilinear segments with minimal enhancement. Subtraction imaging facilitates detection of enhancement of tissues, hence may increase the conspicuity of meninges. The aim of the present study was to describe qualitatively the appearance of canine meninges in subtraction MR images obtained using a dynamic technique. Images were reviewed of 10 consecutive dogs that had dynamic pre- and post-gadolinium T1W imaging of the brain that was interpreted as normal, and had normal cerebrospinal fluid. Image-anatomic correlation was facilitated by dissection and histologic examination of two canine cadavers. Meningeal enhancement was relatively inconspicuous in post-gadolinium T1-weighted images, but was clearly visible in subtraction images of all dogs. Enhancement was visible as faint, small rounded foci compatible with vessels seen end-on within the sulci, a series of larger rounded foci compatible with vessels of variable caliber on the dorsal aspect of the cerebral cortex, and a continuous thin zone of moderate enhancement around the brain. Superimposition of color-encoded subtraction images on pre-gadolinium T1- and T2-weighted images facilitated localization of the origin of enhancement, which appeared to be predominantly dural, with relatively few leptomeningeal structures visible. Dynamic subtraction MR imaging should be considered for inclusion in clinical brain MR protocols because of the possibility that its use may increase sensitivity for lesions affecting the meninges.

Introduction

The meninges (dura mater, arachnoid, and pia mater) are affected by a variety of inflammatory and neoplastic conditions in dogs and, therefore, are tissues of importance for radiologists interpreting magnetic resonance (MR) images of the canine head. The lack of a blood-brain barrier in the meninges[1,2] facilitates accumulation of gadolinium chelates, hence use of post-gadolinium MR images has been emphasized for clinical examination of the meninges.[3-8] Numerous clinical reports include descriptions of meningeal lesions in post-gadolinium T1-weighted MR images of dogs.[9-14]

In contrast, descriptions of the appearance of normal canine meninges in MR images are relatively sparse. Based primarily on descriptions of humans, the meninges are not considered to be visible as discrete structures in non-contrast MR images, but appear as short, thin curvilinear segments with minimal enhancement in T1-weighted post-gadolinium images.[3,7,15] Meningeal enhancement may be divided into pachymeningeal (affecting the dura and the periosteum on the inner aspect of the skull) and leptomeningeal (affecting the pia and arachnoid).[3] The pachymeninges appear continuous with the falx and/or tentorium and have no sulcal indentations, whereas the leptomeninges occupy the spaces between sulci, cerebellar folia and cisterns.[3] A slight degree of enhancement of both the pachymeninges and the leptomeninges is considered normal in dogs.[7] Because the meninges are well-vascularized and lack a blood-brain barrier, they may be expected to enhance much more than the brain; however, the normal dura mater is said to have insufficient water content to allow the T1 shortening necessary for significant enhancement.[3,15]

The conspicuity of enhancement in MR images may be increased by subtracting the T1-weighted pre-gadolinium images from the post-gadolinium images.[16-19] Subtraction imaging facilitates detection of mild enhancement, particularly at tissue boundaries, areas of complicated anatomy, or in tissues with high signal intensity pre-gadolinium administration.[16,18] In humans, subtraction MR images have been found to be useful in the diagnosis and follow-up of patients with a variety of intra-cranial conditions.[16-19] Sensitivity of observers for detecting enhancement in MR images is higher when using subtraction images than when making a comparison of a parallel (side by side) image pair.[20]

Subtraction MR imaging has received little attention in veterinary medicine. We recently compared the accuracy of T1-weighted pre- and post-gadolinium images, subtraction images, T2-weighted images, and fluid-attenuated inversion-recovery (FLAIR) images for diagnosis of meningeal conditions in a series of dogs.[21] In that study, subtraction images had similar accuracy to T1-weighted post-gadolinium images, but an advantage of subtraction images may have been masked because of technical limitations, including misregistration in some cases.[21] Since then we have introduced a dynamic method for obtaining subtraction images, based on a single T1W sequence that is paused halfway for injection of gadolinium. This method minimizes misregistration due to patient movement and optimizes the image intensity scale for subtraction.[18] The aim of the present study was to describe qualitatively the normal appearance of canine meninges in subtraction MR images obtained using this dynamic technique.

Methods

Medical records were searched for 10 consecutive dogs that had dynamic pre- and post-gadolinium T1-weighted imaging of the brain that was interpreted as normal, and had normal cerebrospinal fluid. All MR studies were done with dogs under general anesthesia in dorsal recumbency using flexible surface coils in a 1.5T magnet.[*] Spin-echo T1-weighted (TR 570ms, TE 15ms) pre- and post-gadolinium transverse images and T2-weighted (TR 4000ms,

[*] Intera Pulsar System, Philips Medical Systems, Reigate, UK

TE 110ms) transverse images were acquired with image slice thickness 3.5mm and inter-slice gap 1mm. Field of view was adjusted individually; typical values for a medium-sized dog were 120 x 120mm with a 224 x 224 image matrix, hence pixel size was approximately 0.5 x 0.5mm. Subtraction of pre- from post-gadolinium T1-weighted images was performed using a dynamic study sequence comprising two T1-weighted image series separated by an interval during which the sequence was paused, an intravenous bolus of 0.1mmol/kg gadobuterol[†] was administered, and the sequence restarted within 1 minute.

Subtraction images were color-encoded using commercially available DICOM image viewing software[‡], and superimposed on pre-gadolinium T1-weighted and T2-weighted images. Evidence of misregistration of color-encoded subtraction images superimposed on T1- and T2-weighted native images was judged subjectively by reference to anatomic landmarks other than the meninges, including the interface between the calvaria and the temporal muscles, nasopharyngeal mucosa, and large blood vessels. Misregistration was characterized by malalignment of the color-encoded signal and corresponding anatomic boundaries by the same distance and in the same direction across the entire image. When necessary, misregistration was corrected manually.

Distribution of gadolinium in each dog was assessed by CRL on the basis of sequential side by side viewing of T1-weighted pre- and post-gadolinium images, post-gadolinium and gray-scale subtraction images, and pre-gadolinium T1-weighted and T2-weighted images with well registered, superimposed color-encoded subtraction images. In post-contrast and subtraction images, a curvilinear signal continuous with the falx and/or tentorium without sulcal indentations was considered compatible with pachymeninges, whereas a curvilinear

[†] Gadovist 1.0mmol/ml, Bayer plc, Newbury, UK

[‡] OsiriX 64-bit, version 5.2.2, Pixmeo, Switzerland

signal superimposed on the sulci was considered compatible with leptomeninges. Emphasis was on the cerebral cortex in the parietal and temporal regions, where the image plane was approximately perpendicular to the calvaria. At least five consecutive images were assessed for each dog.

To complement the imaging studies, dissection of two grossly normal 28kg and 30kg mesaticephalic dogs (not subject to MR imaging) was performed by SF. A median section of the head of one animal was made and the half brain removed from the cranium to visualize the blood vessels on the surface of the cerebral cortex, leaving the dura mater in situ. The dura mater was then reflected away from the cranial calvaria to examine the large dural vessels. Sections of meningeal tissue of both dogs were prepared for histologic examination. Serial sections of 6µm thickness were cut on a microtome, mounted on glass slides and stained using Hematoxylin and Eosin.

Results

Median (range) age of dogs having MR imaging was 2.9 (1-11) years; there were 8 males (5 neutered) and 2 neutered females. Median (range) body weight was 17.3 (6.9-31.0) kg. Eight different breeds were represented, including 6 mesaticephalic dogs (Beagle, German shepherd dog, Labrador retriever, two Labradoodles, one mixed breed) and 4 brachycephalic dogs (Boxer, Bichon frisé, two Staffordshire bull terriers). Clinical diagnoses were idiopathic epilepsy in 7 dogs, vestibular syndrome in 2 dogs, and compulsive behavioral disorder in one dog.

No signs of misregistration of color-encoded subtraction images on T1-weighted images were evident in any dog. Slight misregistration (< 2 pixels) of color-encoded subtraction images on

T2-weighted images was identified in two dogs, probably reflecting patient movement between image acquisitions.

On the basis of sequential side by side viewing of T1-weighted pre- and post-gadolinium images, enhancement of tissues close to the surface of the brain was visible as faint, small rounded foci compatible with vessels seen end-on within the sulci, a series of larger rounded foci compatible with vessels of variable caliber on the dorsal aspect of the cerebral cortex, and a continuous, but indistinct, thin zone of moderate enhancement on the dorsal aspect of the cerebral cortex (figure 1). Linear foci of variable caliber compatible with vessels were also visible within the diploë, in some places perforating the inner table of the calvaria and communicating with the dorsal sagittal sinus. On the lateral aspects of the cerebral cortex, where there was no diploë, the calvaria appeared relatively thicker and foci of enhancement appeared smaller and less numerous.

On the basis of side by side viewing of T1-weighted post-gadolinium images and corresponding gray-scale subtraction images, foci of enhancement were more conspicuous in subtraction images in all dogs (figure 1). The continuous zone of enhancement around the brain appeared thicker in subtraction images. Enhancement superimposed over the diploë was also more conspicuous because of increased contrast with the bone marrow, which had similar hyperintensity to gadolinium in native images.

When color-encoded subtraction images were superimposed on T1-weighted images, the continuous zone of enhancement on the dorsal aspect of the cerebral cortex was superimposed over the inner aspect of the broad zone of signal void around the brain (figure 2). When color-encoded subtraction images were superimposed on T2-weighted images, the continuous zone of enhancement was dorsal to the hyperintense zone representing cerebrospinal fluid in each dog, hence this zone of enhancement was interpreted as representing the dura. Therefore, the broad zone of signal void normally observed around the dorsal aspect of the brain in T1- and T2-weighted MR images appears to be formed by the dura on its inner aspect and cortical bone on its outer aspect.

Based on dissection of two canine cadavers, the enhancement seen on the dorsal aspect of the brain in MR images was thought to primarily represent gadolinium in meningeal veins within the dura (figure 3) and in cerebral veins within the leptomeninges (figure 4).

Discussion

Meningeal enhancement following gadolinium administration was observed consistently in this series of dogs likely to be free of meningeal disease. The degree of meningeal enhancement observed in subtraction images was greater than expected based on previous studies.[7-10] Furthermore, the finding that the continuous zone of enhancement on the dorsal aspect of the brain was consistently dorsal to the cerebrospinal fluid space when color-encoded subtraction images were superimposed on T2-weighted MR images provides evidence that meningeal enhancement in dogs is predominantly dural, with relatively few leptomeningeal vessels visible. This observation could help explain why pachymeningeal enhancement is observed more often than leptomeningeal enhancement in clinical patients with meningeal disease.[21]

Dural enhancement is likely to predominantly represent gadolinium in meningeal veins, which have larger caliber and slower flow rates than the corresponding arteries. Anatomic studies of the intracranial vasculature of dogs have concentrated on the cerebral vessels and venous sinuses[22] with little emphasis on the blood supply to the dura. Although the meningeal arteries and veins are described briefly in standard veterinary anatomy texts[23], they are frequently omitted from diagrams illustrating meningeal anatomy.[24,25] In humans, the degree of dural enhancement in normal individuals is limited by vascularity and the amount of extracellular fluid[3,15], but marked enhancement may occur when there is vascular congestion and expansion of the extracellular fluid space, which occurs after craniotomy[3] and in association with various conditions affecting the meninges, including meningioma[26,27] and meningitis.[28]

Small leptomeningeal vessels were mainly seen end-on within sulci, where they are orientated perpendicular to the image plane. This distribution may reflect partial volume averaging associated with use of 3.5mm image slices, which will tend to minimize visibility of small contrast-containing vessels parallel to the image plane. In addition to limitations associated with partial volume averaging, the relatively low in-slice spatial resolution of the images in the present study, which is typical of clinical MR images, limited the precision of image-anatomic correlations. Attempts to make measurements of meningeal vessels, the dura and the calvaria in the present study were unsatisfactory because of low image resolution. In MR images displayed at true size, curved interfaces appeared stepped because of the relatively large size of pixels. In images displayed at greater than true size (and interpolated), the interfaces between anatomic boundaries and enhancing structures were too blurred for confident placement of calipers. Even if higher resolution MR images could be obtained, attempted correlations between measurements of small anatomic structures in MR images and in fixed specimens will tend to be undermined by post mortem changes in blood volume of organs, which alter the diameter of vessels, and the effects of fixation, which causes contraction of soft tissues.

Meningeal enhancement was relatively inconspicuous in native post-gadolinium T1-weighted images, but was more clearly visible in subtraction images in all dogs. This finding is in agreement with a previous study, which mentioned briefly the appearance of canine meninges in subtraction MR images.[7] Dynamic subtraction is a low-tech method for obtaining consistently well-registered and optimally scaled MR images that clearly depict the distribution of gadolinium-chelates.[18] Improved registration reflects the minimal elapsed time between pre- and post-gadolinium sequences when using a dynamic technique, which helps avoid patient movement. Optimal gray-scale is possible when using a dynamic subtraction technique because the pre- and post-gadolinium images are within the same series. In most MR scanners, image scaling is automatically set by the workstation, and the software sets the highest signal intensity in a series of images at white and the lowest at black, scaling all other signal intensities relative to these levels. Fat normally corresponds to the highest signal in pre-gadolinium T1-weighted images and is assigned white, but in post-gadolinium images gadolinium is the highest signal so it is assigned white, and fat has a lower signal so is assigned light gray. Thus the signal intensity gray scale of all tissues varies between the two sequences. This difference may not be perceived by observers when examining pre- and post-gadolinium images side by side; however, if these images are then subtracted, the resulting images will include variations due to differences in image gray-scale as well as presence of gadolinium. Dynamic acquisition of pre and post contrast T1W images ensures that the image scale factors remain constant, thus enabling more accurate subtraction.[18] Use of the term 'dynamic' for this subtraction technique reflects a change in the state of the subject during the acquisition. Another example of a dynamic technique is MR imaging performed throughout a period of contrast infusion in order to estimate the kinetics of contrast uptake and wash-out from tissues.[29]

Alternatively, the conspicuity of meningeal enhancement may be increased by suppressing the MR signals from fat. Similar to subtraction MR imaging, elimination of high intensity signals from fat allows reassignment of high intensity signals from gadolinium to the highest point in the greyscale spectrum.[30] Fat suppression is a useful additional MR sequence when enhancing lesions are adjacent to fat[30], but it may not be necessary after post-gadolinium subtraction imaging, which reduces the signal from all minimally-enhancing tissues, including fat.

Color-encoding subtraction images helps observers distinguish the difference information from the underlying anatomic information.[20] Although subtraction images do not capture primarily anatomic information, the use of color-encoded subtraction images superimposed on the native pre-gadolinium images in the present study, with corroborating evidence from dissections, facilitated determination of the location of vascular structures, including the meninges, relative to anatomic boundaries displayed in native images.

In summary, normal canine meningeal enhancement appears to be predominantly dural, with relatively few leptomeningeal structures visible. Meningeal enhancement is more conspicuous in dynamic subtraction than in native post-gadolinium T1-weighted images. Dynamic subtraction MR imaging should be considered for inclusion in clinical brain MR protocols because of the possibility that its use may increase sensitivity for lesions affecting the meninges.

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Legends

Figure 1. Examples of native T1-weighted MR images of two dogs before (A, D) and after (B, E) intravenous administration of gadolinium, and (C, F) corresponding gray-scale subtraction image. Dog in A, B and C is a 7 year old male Labrador retriever with idiopathic epilepsy; dog in D, E and F is a 1 year old male Boxer with idiopathic epilepsy. In each instance, following gadolinium administration there is faint enhancement within the sulci compatible with small leptomeningeal vessels (L), a series of rounded foci of variable caliber compatible with vessels close to the gyri (arrows), a broad, indistinctly marginated zone of moderate enhancement superimposed on the broad zone of signal void around the brain (between arrowheads), and curvilinear foci compatible with vessels within the diploë (D). The dorsal sagittal sinus (S) is clearly visible in F.

Figure 2. Same dogs as in Figure 1. Examples of native T1-weighted (A and C) and T2-weighted (B and D) MR images with superimposed color-encoded subtraction images. In each instance, it is evident in both T1- and T2-weighted images that the majority of signal from gadolinium is superimposed on the broad hypointense line around the dorsal aspect of the brain, and that in T2-weighted images the gadolinium is predominantly dorsal to the subarachnoid space. This distribution is compatible with dural enhancement. Multiple foci of gadolinium are also visible superimposed on the diploë, compatible with diploic veins.

Figure 3. Dural vessels. A) Dissection of a canine head showing reflected from inner aspect of the calvaria. Veins that bulge from outer aspect of dura (white arrow) normally lie in superficial grooves in the bone (black arrow). B) Low magnification section through dura showing a large meningeal vein (V) on its dorsal aspect. In this specimen, the diameter of the vein is 1.4mm. The periosteum (small arrows) has become partly detached from the dura

during processing. C) High magnification section of dura showing blood vessels (large arrows). The periosteum is visible as a thin layer of cells (small arrows) on the dorsal aspect of the dura. Bar = 100µ.

Figure 4. Leptomeningeal vessels. A) Left-dorsal aspect of the brain removed from the skull. The largest vessels on the surface of the brain are the veins that lie along the gyral-sulcal boundaries. Vessels over the surface of gyri are relatively fine. B) Low magnification section through the leptomeninges showing veins (V) at the gyral-sulcal boundary. In this specimen, the diameter of the larger vein is 1.2mm.