Magnetic Resonance Imaging Findings of Hepatic Encephalopathy in a Dog with a Portosystemic Shunt

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ABSTRACT. A 6-year-old ShihTzu presented with tonic-clonic cluster seizure. T2-weighted magnetic resonance (MR) images showed bilateral diffuse hyperintense lesions at the cerebral cortex with enlarged sulci. Computed tomography revealed a portosystemic shunt (PSS) and azygos continuation. Based on the clinical signs, blood examinations and diagnostic images, the dog was diagnosed with hepatic encephalopathy secondary to PSS. The neurologic signs were gradually improved after medical therapy for hyperammonemia. This is the first report of hyperintensity of the cerebral cortex on T2-weighted MR images associated with acute hepatic encephalopathy in a dog.

KEY WORDS: canine, hepatic encephalopathy, MRI, portosystemic shunt.


Hepatic encephalopathy (HE) is a neurologic syndrome caused by hepatic dysfunction. The most common cause of HE in dogs and cats is portosystemic shunt (PSS), which is abnormal blood flow between the portal veins and systemic circulation [21]. Shunting blood flow in PSS contains numerous gut-derived toxins including ammonia and circulates through systemic venous systems [21]. Moreover, shunt-induced hyperammonemia can feasibly induce astrocyte swelling and interference with the actions of neurotransmitters in the central nervous system. Ultimately, it may cause cerebral edema and increased intracranial pressure, which are associated with manifestation of various neurologic signs [5, 10, 15]. The clinical signs of HE include significant mental changes, seizure activities and proprioceptive deficits [21]. According to the reports previously described, histologic intracranial lesions in dogs with HE showed diffuse cortical necrosis, spongiform changes and astrogliosis [8, 14]. Magnetic resonance imaging (MRI) may be useful for the diagnosis of HE through identification of these neurologic sequelae. However, MRI features are not well known in dogs and cats with HE [19, 20]. In this case report, we described the clinical and characteristic MRI findings of acute HE associated with PSS in a dog.

A 6-year-old, 2.94 kg, spayed female ShihTzu was presented due to acute onset of tonic-clonic cluster seizure. The dog had severe anorexia and diarrhea for three days prior to the onset of neurologic signs. On the day of presentation, the patient showed severe generalized involuntary muscle contraction and intermittent seizure activities with obscured consciousness. Neurologic examination revealed absent postural reactions and cranial nerve deficit including miosis with delayed pupillary light reflex and faint menace reflex. Complete blood count showed mild leukocytosis with a stress leukogram and microcytic normochromic non-regenerative anemia. Serum biochemical profiles showed mildly elevated hepatobiliary and bile acid levels, mild hypoaalbuminemia and hyperammonemia (Table 1). Routine abdominal radiographs (Fig. 1) and ultrasonographs demonstrated microhepatica and bilateral renal calculi. Based on these findings, a tentative diagnosis of HE was made.

Because HE associated with PSS was suspected, MRI of the brain was combined with computed tomography (CT) scanning of the abdomen on the same day. T1-, T2- and postcontrast T1-weighted images (WIs) were obtained using a 0.2 tesla MR system (E-scan®; ESAOTE, Genova, Italy).

Table 1. Complete blood count (CBC) and serum biochemical profile in this case

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Reference</th>
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<tbody>
<tr>
<td>PCV (%)</td>
<td>33.24</td>
<td>37–55</td>
</tr>
<tr>
<td>WBC (× 10³/μl)</td>
<td>23.58</td>
<td>6.0–17.0</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>99</td>
<td>19–70</td>
</tr>
<tr>
<td>AST (U/l)</td>
<td>92</td>
<td>15–43</td>
</tr>
<tr>
<td>ALP (U/l)</td>
<td>145</td>
<td>15–127</td>
</tr>
<tr>
<td>ALB (g/dl)</td>
<td>2.7</td>
<td>2.9–4.2</td>
</tr>
<tr>
<td>NH₃ (μmol/l)</td>
<td>123</td>
<td>0–92</td>
</tr>
<tr>
<td>Glu (mg/dl)</td>
<td>102</td>
<td>70–118</td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>9.8</td>
<td>8.8–11</td>
</tr>
<tr>
<td>Postprandial BA (μmol/l)</td>
<td>59.8</td>
<td>&lt; 25.0</td>
</tr>
<tr>
<td>Na (mmol/l)</td>
<td>145</td>
<td>141–152</td>
</tr>
<tr>
<td>K (mmol/l)</td>
<td>3.9</td>
<td>3.8–5.0</td>
</tr>
<tr>
<td>Cl (mmol/l)</td>
<td>115</td>
<td>102–117</td>
</tr>
</tbody>
</table>

On T2WIs, symmetrical hyperintense lesions were observed in the cerebral cortex from the parietal lobes to the occipital lobes (Figs. 2 and 4). No signal changes were found in the T1WIs and postcontrast images. In addition, bilateral lesions in the cerebral cortex were more apparent on the transverse images, as were generalized widened sulci, which is consistent with brain atrophy (Fig. 2). According to these findings, significant cerebral edema and cytotoxic damage were strongly suspected. Abdominal CT revealed a PSS between the left gastric vein and azygos vein near the esophageal hiatus (Fig. 5A). Additionally, continuation of the azygos vein to renal veins with segmental caudal vena cava aplasia was also noted (Fig. 5B).

Cerebrospinal fluid (CSF) analysis revealed no remarkable findings. Canine distemper virus was not detected in the serum and CSF by reverse transcription polymerase chain reaction. Based on the clinical manifestations, blood work and diagnostic imaging, the dog was definitively diagnosed with HE secondary to PSS.

Treatment was initiated with retention enema and fluid therapy. To decrease cerebral edema, mannitol (Mannitol; Dai Han Pharm., Seoul, Korea) was administered at 1 g/kg by constant rate infusion for 30 min twice daily. Additionally, metronidazole (Flasinyl; CJ Pharma, Seoul, Korea) (15 mg/kg, PO, twice daily), silymarin (Silymarin; Sinil, Seoul, Korea) (35 mg/dog, PO, once daily), biphenyl dimethyl dicarboxylate (Lefotil; Skynew, Gyeonggi, Korea) (25 mg/dog, PO, once daily) and lactulose (Duphalac; Choongwae, Seoul, Korea) (1 ml/kg, PO, twice daily) were also prescribed to correct hyperammonemia. For seizure control, potassium bromide (KBr; Sigma-Aldrich Korea, Gyeonggi, Korea) was added at an induction dose of 100 mg/kg 4 times for 6 hr each and then at 40 mg/kg once daily. Small amounts of low protein diet (l/d®; SungBo Science Tech., Seoul, Korea) were also prescribed.

After 1 week of supportive therapy, the neurological abnormalities of the dog resolved significantly, and the seizures disappeared. However, as the client refused to surgical ligation, the dog was maintained with only supportive medication, and the symptoms were well controlled.

At 1 month after the initial MR examination, a 2nd scan was performed to monitor the brain lesions. Most of the cortex lesions were retained, and their signal intensities were significantly increased compared with those of the 1st T2WI. On the other hand, the T1WI had become diffusely hypointense in the cortical grey matter, and this was suspected as being polioencephalomalacia. Development of an increasingly widened subarachnoid space and ventromegaly compared with the initial images also supported for the deterioration of brain atrophy (Figs. 3 and 4). The results of CSF analysis were normal as in the initial analysis.

Even though severe seizure activity appeared in this case, the ammonia blood level was mildly elevated compared with the normal range. There are several studies and case reports showing that blood ammonia levels not always correlate with the degree of neurological symptoms [1, 11, 12]. Additionally, clinically important discrepancies in serum ammonia levels with mild elevation were reported in a
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In the present case, the diagnosis of HE was based on the distinctive history, routine blood examination and diagnostic imaging including an MRI and CT scan. Diagnosis based on neuroimaging techniques in human and animals with metabolic encephalopathy is uncommon [10, 15, 19, 20]. In one report, no abnormalities were found in the brain of a dog with PSS by CT scan [21]. In other reports, the intracranial lesions of the dogs and cats with HE were commonly characterized as selective vulnerabilities of the brain that occur through localized specific locations such as the lentiform nuclei, showing hyperintensity on T1WI, with

Fig. 2. Transverse T2-weighted (3800 ms for TR, 90 ms for TE; A, B, C, D) and T1-weighted (540 ms for TR, 26 ms for TE; E, F, G, H) images of a dog with hepatic encephalopathy. Left images show the same level as right images. (A, B, C, D) Diffuse bilateral symmetrical hyperintense signals are demonstrated in the cerebral cortex from the parietal lobe to the temporal lobe (arrows) on the T2-weighted images. (E, F, G, H) No signal changes are visible on the T1-weighted images. Note the generally widened cerebral sulci.

Fig. 3. Transverse T2-weighted (3800 ms for TR, 90 ms for TE; A, B, C, D) and T1-weighted (540 ms for TR, 26 ms for TE; E, F, G, H) images of same dog with HE after 1 month. Left images show the same level as right images. (A, B, C, D) Bilateral symmetrical hyperintense signals of T2-weighted images have become severely intense (arrows). Well-defined lesions of increased signal intensity are clearly limited in the grey matter. (E, F, G, H) Hypointense signal changes in the T1-weighted images of lesions are visible. Note the development of a widened subarachnoid space, which is consistent with cerebral atrophy, and developed ventromegaly compared with the initial MR images.
generalized enlarged sulci [19, 20]. However, in the present case, hyperintense lesions are predominantly and diffusely involved in the cerebral cortex from the parietal lobe to the occipital lobe on T2WIs. Additionally after one month, these lesions were revealed as more intense T2WI hyperintensities with T1WI hypointensities suggesting polioencephalomalacia, compared with the initial images.

In human medicine, HE is classified as acute and chronic forms according to underlying liver disease and development of neurologic signs. In the acute form of HE, development of neurologic symptoms is precipitated by a clinical state that causes acute hyperammonemia in previously asymptomatic patients [15]. Cerebral edema following cortical laminar necrosis is suspected to be the main pathologic event associated with demonstration of diffuse cortical lesions in acute HE [2, 3]. On the other hand, the chronic form of HE presents neurologic symptoms persistently or relapsing episodes continually with underlying chronic liver disease. In chronic HE, hyperintense T1WIs predominantly involved in lentiform nuclei are characteristic [10, 15].

In most cases of HE secondary to PSS in humans, MRI features mainly corresponds to the chronic form of HE [13,
In previous descriptions in the veterinary literature, HE secondary to PSS also exhibited similar lesions on MRI to those predominantly found with chronic HE [19, 20]. On the other hand, the present case showed diffuse cortical lesions, which are characteristic findings of acute HE in humans, as well as features of chronic HE, such as widened sulci and a widened subarachnoid space [2, 3]. It appears that acute hyperammonemia caused by PSS in present case could cause cerebral edema that leads to neurologic crisis and ultimately results in poineoencephalomalacia. Accumulation of glutamine induced by hyperammonemia in astrocytes produces osmotic stress and causes cell swelling, which consequently results in astrocyte swelling, cerebral hypoperfusion, necrosis and ischemic damage [2, 3, 18]. One report in veterinary medicine also noted a mild hyperintense signal on T2WIs in the cerebral cortex with other severe chronic HE lesions in a dog with PSS [20].

Therefore, cerebral cortical necrosis in the present case may have been initially induced by acute hyperammonemia and then progressed to chronic lesions, such as edema, widened sulci and a widened subarachnoid space. As the patient was 6 years old, it is natural that MRI findings include chronic findings. As acute HE can occur episodically at acute decompensation in chronic liver disease patients, it is possible to find both characteristics of MRI lesions.

Additionally, the lesion involved predominantly at the grey matter in the present case was also characteristic. A previous report described histopathological changes in dogs with HE in which lesions were also associated with the grey matter [8]. Although the involvement of lesions including the midbrain and pons area was not found in our case, no predilection for the white matter and involved grey matter of brain lesions in two dogs with HE is a remarkable finding when compared with the present case.

In present case, the dog showed normal CSF. Previously, pathological study of acute hyperammonemia revealed severe edema with neuronal damage without inflammatory infiltration (2). Similarly, most of the cerebrospinal fluid findings in dogs with PSS are normal (21).

In the present case, the dog showed PSS with another vascular anomaly, azygos continuation. Azygos continuation, which is also known as segmental caudal vena cava aplasia, is a condition in which the caudal part of the vena cava is absent and the azygos vein is connected with other systemic veins [6, 7, 16]. However, there are various forms of this condition; for example, the patient described in the present case had no caudal vena cava between the kidney and liver. As a result, blood flow from the renal veins was anastomosed with the azygos vein directly into the nearby esophageal hiatus area. Although numerous cases of azygos continuation accompanied with PSS have been reported, it is not clear if it has any direct clinical significance [6, 7, 16].

We described here atypical MRI features of both of acute and chronic HE secondary to PSS in a dog. Symmetrical diffuse cerebral cortical lesions, which are consistent with acute HE in humans, and cerebral atrophy, which is chronic findings, were found in this case. To the best of our knowl-


