Results of cerebrospinal fluid analysis, neurologic examination findings, and age at the onset of seizures as predictors for results of magnetic resonance imaging of the brain in dogs examined because of seizures: 115 cases (1992–2000)

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Objective—To determine whether neurologic examination findings, results of CSF analysis, or age at the onset of seizures could be used to predict whether results of magnetic resonance imaging (MRI) would be normal or abnormal in dogs with seizures.

Design—Retrospective study.

Animals—115 dogs.

Procedure—Information on results of neurologic examination, results of CSF analysis, age at the onset of seizures, and results of MRI was obtained from the medical records.

Results—Results of MRI were abnormal in 61 dogs and normal in 54. Sensitivity and specificity of neurologic examination alone were 77 (47/61) and 91% (49/54), respectively. Sensitivity and specificity of CSF analysis alone were 79 (48/61) and 69% (37/54), respectively. Results of MRI were abnormal for 12 of 28 (43%) dogs with abnormal CSF analysis results and normal neurologic examination results but for only 2 of 35 (6%) dogs with normal CSF analysis and normal neurologic examination results. Similarly, results of MRI were abnormal for 36 of 37 (97%) dogs with abnormal CSF analysis and abnormal neurologic examination results but for only 11 of 15 (73%) dogs with normal CSF analysis results and abnormal neurologic examination results. Age at the onset of seizures (< 6 vs ≥ 6 years old) was not significantly associated with results of MRI.

Conclusions and Clinical Relevance—Results suggest that neurologic examination findings and results of CSF analysis are useful in predicting whether results of MRI will be abnormal in dogs examined because of seizures, but age at the onset of seizures is not. (J Am Vet Med Assoc 2002;220:781–784)

Seizures are a common neurologic abnormality in dogs. They are categorized as focal or generalized and further classified as primary, secondary, or reactive epileptic seizures. Reactive epileptic seizures (RES) arise from extracranial diseases such as metabolic disturbances and toxicoses, whereas secondary epileptic seizures (SES) arise from intracranial diseases such as encephalitis, neoplasia, degeneration, malformation, and trauma, and primary epileptic seizures (PES) arise from idiopathic epilepsy.

In dogs examined because of seizures, routine biochemical analyses must be performed to rule out diseases associated with RES and to assess hepatic and renal function before initiating treatment with anti-seizure medications. However, routine serum biochemical analyses, urinalysis, serologic testing, radiography, and ultrasonography are seldom useful in identifying the specific cause of the seizures in affected dogs. Analysis of CSF is recommended if multifocal CNS or meningeal disease is suspected on the basis of results of a neurologic examination. A decision to pursue more advanced diagnostic testing such as computed tomography (CT) and magnetic resonance imaging (MRI) is generally made on the basis of the patient's history, signalment, and neurologic examination findings. Because SES are more common in dogs < 1 or > 6 years old, age of the dog also plays a role in determining whether these advanced diagnostic tests are indicated.

Magnetic resonance imaging is the most sensitive imaging modality for identifying intracranial lesions. However, it can be cost-prohibitive and is not always readily accessible to veterinary patients. Therefore, it should be reserved for dogs with a high likelihood of having MRI abnormalities. The purpose of the study reported here was to determine whether results of a neurologic examination, alone or in combination with CSF analysis, could be used to predict whether dogs with seizures would have abnormal MRI results. In addition, because the incidence of idiopathic epilepsy is thought to decline sharply in dogs after 5 years of age, we also wanted to compare the frequency of MRI abnormalities in dogs that began to seizure before 6 years of age with frequency in dogs that began to seize at 6 years of age and older.

Criteria for Selection of Cases

The computerized record system at the Veterinary Hospital of the University of Pennsylvania was searched for dogs with a history of seizures that had undergone MRI of the brain between 1992 and 2000. Dogs were included in the study if results of serum biochemical analyses, urinalysis, serologic testing, radiography, and ultrasonography were normal or abnormal in dogs with seizures.

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analyses, a CBC, a complete neurologic examination, and analysis of a sample of CSF free from excessive blood contamination were available for review. Dogs were excluded from the study if results of the CBC or serum biochemical analyses were suggestive of an extracranial disease that could be causing the seizures.

**Procedures**

Dogs were classified as having normal or abnormal neurologic examination results, as having normal or abnormal CSF analysis results, as being < 6 or ≥ 6 years old at the time seizures began, and as having normal or abnormal MRI results. Results of the neurologic examination were considered abnormal if there was a menace deficit, compulsive circling, normal gait with a postural deficit, or vestibular signs. Altered mental status and signs of neck pain were not considered evidence of abnormal neurologic examination results. Results of CSF analysis were considered abnormal if the protein concentration was > 25 mg/dl or the nucleated cell count was > 5 cells/µl. Magnetic resonance images had all been examined by at least 1 board-certified neurologist; results of MRI were considered abnormal if abnormal anatomy or signal intensity or contrast enhancement was identified. For the present study, magnetic resonance images were reevaluated if results of the neurologic examination, CSF analysis, or MRI were classified as abnormal.

**Statistical analyses**—Sensitivity and specificity of using results of the neurologic examination alone (normal vs abnormal) and of using CSF analysis alone (normal vs abnormal) to predict results of MRI (normal vs abnormal) were calculated. Sensitivity was calculated as the percentage of dogs with abnormal MRI results that had abnormal neurologic examination or CSF analysis results. Specificity was calculated as the percentage of dogs with normal MRI results that had normal neurologic examination or CSF analysis results.

A Fisher exact test was used to determine whether results of CSF analysis were associated with results of MRI among dogs with normal neurologic examination findings and among dogs with abnormal neurologic examination findings. A receiver operating characteristic (ROC) curve was generated to determine the optimal CSF protein concentration for predicting whether results of MRI would be normal or abnormal. For all analyses, values of P < 0.05 were considered significant. All analyses were performed with standard software.

**Results**

One hundred fifteen dogs met the criteria for inclusion in the study. Of these, 97 were purebreds, and 18 were of mixed breeding. Fifty-seven were male, of which 38 were castrated, and 58 were female, of which 46 had undergone ovariohysterectomy. Dogs ranged from 6 months to 15 years old (mean, 6.7 years). Results of MRI were normal in 54 dogs and abnormal in 61.

**Results of neurologic examination and CSF analysis**—Results of the neurologic examination were classified as abnormal in 52 dogs and normal in 63. Of the 52 dogs with abnormal neurologic examination results, 47 (90%) had MRI abnormalities. In contrast, of the 63 dogs with normal neurologic examination results, only 14 (22%) had MRI abnormalities. Sensitivity and specificity of neurologic examination alone were 77 (47/61) and 91% (49/54), respectively (Table 1).

Results of CSF analysis were classified as abnormal in 65 dogs and normal in 50. Of the 65 dogs with abnormal CSF analysis results, 48 (74%) had MRI abnormalities. In contrast, of the 50 dogs with normal CSF analysis results, only 13 (26%) had MRI abnormalities. Sensitivity and specificity of CSF analysis alone were 81% (46/50) and 69% (37/54), respectively (Table 1).

Among dogs with normal neurologic examination results, results of CSF analysis were significantly (P < 0.001) associated with results of MRI. Results of MRI were abnormal for 12 of 28 (43%) dogs with normal CSF analysis results and normal neurologic examination results but for only 2 of 35 (6%) dogs with normal CSF analysis and normal neurologic examination results (Table 1). Similarly, among dogs with abnormal neurologic examination results, results of CSF analysis were significantly (P < 0.002) associated with results of MRI. Results of MRI were abnormal for 36 of 37 (97%) dogs with abnormal CSF analysis and abnormal neurologic examination results but for only 11 of 15 (73%) dogs with normal CSF analysis results and normal neurologic examination results.

Analysis of the ROC curve indicated that a CSF protein concentration of 35 mg/dl was associated with a sensitivity of 52% and specificity of 96% (Fig 1). A CSF protein concentration of 25 mg/dl had the closest paired sensitivity and specificity (76 and 70%, respectively).
Cerebrospinal fluid protein concentrations greater than or less than 25 mg/dl had a greater discrepancy between sensitivity and specificity.

**Association between age and results of MRI**—Fifty-seven dogs were < 6 years old at the time seizures began, and 58 were ≥ 6 years old (Table 2). Age of the dog at the onset of seizures (< 6 vs ≥ 6 years old) was not significantly associated with results of MRI (normal vs abnormal) for any group when dogs were grouped on the basis of neurologic examination and CSF analysis results.

### Table 2—Cross-correlation of age at the onset of seizures, results of a neurologic examination, results of CSF analysis, and results of MRI in 115 dogs examined because of seizures

<table>
<thead>
<tr>
<th>Age at the onset of seizures</th>
<th>Neurologic examination results</th>
<th>CSF analysis results</th>
<th>Abnormal MRI results</th>
<th>Normal MRI results</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 y</td>
<td>Abnormal</td>
<td>Abnormal</td>
<td>16 (94)</td>
<td>1 (6)</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>Normal</td>
<td>7 (78)</td>
<td>2 (22)</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Abnormal</td>
<td>7 (44)</td>
<td>9 (56)</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Normal</td>
<td>0 (0)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>≥ 6 y</td>
<td>Abnormal</td>
<td>Abnormal</td>
<td>20 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>Normal</td>
<td>4 (67)</td>
<td>2 (33)</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Normal</td>
<td>5 (42)</td>
<td>7 (58)</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>Normal</td>
<td>2 (10)</td>
<td>18 (90)</td>
</tr>
</tbody>
</table>

Results of the present study suggest that neurologic examination findings and results of CSF analysis are useful in predicting whether results of MRI will be abnormal in dogs examined because of seizures. Presumably, dogs with SES would be more likely to have brain lesions grossly identifiable with MRI than dogs with PES, and dogs < 1 year old or ≥ 6 years old are more likely to have SES than dogs between 1 and 6 years old. Therefore, we had expected to find that age at the time seizures began could also be used to predict whether results of MRI would be abnormal. In the present study, however, age at the time seizures began was not significantly associated with results of MRI.

Results of the present study may be useful when deciding whether to perform MRI in dogs examined because of seizures. Dogs examined because of seizures in which results of a neurologic examination are normal are often assumed to have idiopathic epilepsy and are, therefore, less likely to undergo MRI. Conversely, MRI is often recommended for older dogs examined because of seizures regardless of the results of the neurologic examination. Our findings suggest that a CSF analysis should be performed regardless of results of the neurologic examination in dogs examined because of seizures. In the present study, for instance, dogs with normal neurologic examination results were 7 times as likely to have MRI abnormalities if they had abnormal CSF analysis results than if they had normal results. Similarly, dogs in the present study with abnormal neurologic examination results were 1.3 times as likely to have MRI abnormalities if they had abnormal CSF analysis results than if they had normal results.

We also examined, by constructing an ROC curve, how establishing various CSF protein concentrations as the cutoff between normal and abnormal CSF analysis results affected sensitivity and specificity of using CSF analysis to predict whether dogs had MRI abnormalities. In the population of dogs studied, a CSF protein concentration ≥ 35 mg/dl reliably identified dogs with abnormal MRI results (≥ 96% specificity). Therefore, only 4% of the dogs with CSF protein concentrations exceeding 35 mg/dl had normal MRI results. The ROC curve analysis demonstrated that a CSF protein concentration of 25 mg/dl had the closest pairing of sensitivity and specificity. This is the value commonly cited in textbooks as the upper limit of the reference range for total protein concentration in CSF.

Human patients with a recent history of seizures have been reported to have postictal CSF pleocytosis. Pleocytosis is most common in patients with nonidiopathic seizures and is more likely to occur following repeated or prolonged seizures. In addition, elevations in CSF protein concentration are common following electroconvulsive therapy. Therefore, it is possible that CSF abnormalities in dogs in the present study were seizure induced. If CSF abnormalities were dependent on the time since the last seizure, rather than on the nature or severity of the underlying disease, then results of CSF analysis could have been falsely classified as abnormal in dogs that had recently had seizures, resulting in a decision to pursue MRI in dogs unlikely to have any intracranial abnormalities. Whether the amount of time that elapses between the last recorded seizure and collection of CSF collection has an effect on CSF protein concentrations in dogs is currently unknown.

The incidence of idiopathic epilepsy in dogs is thought to decline sharply after 6 years of age; therefore, age is often considered to be an important criterion in determining whether MRI should be performed in dogs examined because of seizures. At our hospital, for instance, MRI is routinely recommended for dogs that begin to seizure at or after 6 years of age and is less likely to be recommended for dogs that begin to seizure at a younger age. However, results of the present study suggest that age at the onset of seizures was not associated with whether results of MRI would be normal or abnormal. Seven of the 31 (23%) dogs < 6 years old at the onset of seizures that had normal neurologic examination findings and 7 of the 32 (22%) dogs ≥ 6 years old at the onset of seizures that had normal neurologic examination findings had abnormal MRI results. In fact, frequency of MRI abnormalities was not significantly different between dogs < 6 years old at the onset of seizures and dogs ≥ 6 years old at the onset of seizures for any combination of neurologic examination and CSF analysis results. None of the dogs in the present study that were < 1 year old at the onset of seizures had MRI abnormalities.

References

**Notes**
1. SAS statistical software, version 8.0, SAS Institute Inc, Cary, NC.