Surgery

Electrocorticographic and Histological Findings in a Shetland Sheepdog with Intractable Epilepsy

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ABSTRACT. A Shetland sheepdog with epilepsy refractory to antiepileptic drugs was brought to the division of Veterinary Radiology at Nippon Veterinary and Animal Science University. Scalp electroencephalography and computed tomography was performed, but no abnormality was detected in either examination. To obtain detailed information, electrodes were implanted on the dura mater, and the electrocorticogram (ECoG) was recorded. In the ECoG, sporadic spikes were detected in the left parietal region, suggesting the presence of the epileptic focus in this region. After the dog’s death, abnormalities of gyri were found in the region where spikes were detected in the ECoG. On histopathological examination, laminar malacia of the cingulate gyrus was observed. Furthermore, in the hippocampus, neuronal loss of pyramidal cells was observed.

KEY WORDS: electrocorticogram, epilepsy, Shetland sheepdog.

Epilepsy is the most common cause of seizure in dogs. Scalp electroencephalographies (sEEG) obtained by various leads have been reported in the small animal clinical field [1–4], but the use of invasive EEG performed in the human medical field \([13]\) such as electrocorticograms (ECoG) and depth EEG with chronic electrodes, and intraoperative EEG has not been reported in veterinary literatures.

In this study, we performed ECoG by using the chronic epidural electrode method in a Shetland sheepdog with epilepsy refractory to antiepileptic drug (AED) therapy, and localized the seizure focus to some extent. We also noted histopathological abnormalities in the region, which may have been the focus.

The animal was a male Shetland sheepdog weighing 12 kg. Because this animal was captured for protection, the exact age, the age at the initial seizure, and the history until captured were unknown, but this animal was in adulthood, estimated by us to be about 4 to 5 years old. Since the animal had epilepsy refractory to various AED (phenobarbital, potassium bromide, zonisamide) prescribed at a local veterinary hospital and had seizures about once a month, it was transferred to the division of Veterinary Radiology at Nippon Veterinary and Animal Science University.

The dog was in a postictal state when it was admitted, and was conscious but its behavior seemed abnormal, occasionally showing star gazing-like behavior. After several days, the dog completely recovered to normal (became in an intraictal state), and no physical, neurological, or hematological (complete blood cell count, chemistry) abnormalities were detected. We then concluded that this dog has idiopathic epilepsy.

To obtain the epileptic focus of this dog, 20 \(\mu g/kg\) of medetomidine (Domitol; Farmos, Turku, Finland) was intramuscularly administered to the dog to perform general sEEG. In the sEEG, the referential derivation with eight electrodes was performed. Although it was difficult to read the sEEG due to mixing with the electromyogram, mainly low amplitude fast waves were observed. Sharp waves and high amplitude fast wave were occasionally observed, but the focus could not be determined because the waves were synchronized in several derivations and artifacts.

To exclude the possibility of structural lesions in the brain, the dog was examined by computed tomography (CT), and no structural abnormality was found. The dog had seizures about 20 days after transfer to our laboratory. Seizures occurred every several hr, 20 times in four days. Clinical seizure symptoms, although they differed slightly every time, in the most frequent pattern, the animal sat after salivation, and tetanic convulsion of the forelimbs occurred for 20–30 sec, then extended to the whole body and generalized tonic-clonic convulsion started. The ictal period persisted between 1 min 30 sec and 2 min, and the postictal period continued for 1–7 min. Based on these seizure symptoms, the seizure type was diagnosed as complex partial seizure (CPS) and subsequent secondary generalized tonic-clonic seizure. After the end of the cluster seizure, a state similar to that observed when the animal was brought in was observed.

Considering surgical therapy for the therapeutic policy, we decided to perform ECoG by placing chronic epidural (EP) electrodes. The EP electrodes were a conducting wire connected to a silver ball with solder and connected to a nine-pinned socket. Under general anesthetic condition, boreholes for the placement of EP electrodes were made at the sites on the cranial bones, and the electrodes were implanted in each holes. The socket was fixed with stainless steel screws at the midline of the parietal bone, and covered...
with dental cement. The stainless steel screws fixing the socket were used for the ground electrode. The referential electrode was subcutaneously implanted in the cervical skin. For one week after surgery, enrofloxacin (Baytrill; Bayer, Leverkusen, Germany) was administered orally. The socket region was disinfected 1–2 times daily with an iodine agent.

After the surgery, an ECoG was recorded weekly in the conscious state and under medetomidine-induced sedation during the interictal state. In the ECoG while conscious, low amplitude fast waves were mainly observed, but high amplitude slow waves were observed while under sedation. Nevertheless, while both conscious and under sedation, a higher amplitude was detected in the parietal region, particularly on the left side: 80–100 µV and 100–140 µV waves while conscious and under sedation, respectively, and specific 300–400 µV spikes with a duration of about 60 msec were sporadically observed (Fig. 1). Based on these paroxysmal discharges, we tentatively diagnosed that the focus was localized in the parietal lobe.

Unfortunately, the dog died unexpectedly during the cluster seizure period, but death was not attributed to the surgery or EEG recording.

Immediately after death, the brain was excised for histopathological examination.

On macroscopic observation, some morphological abnormalities were observed in the gyrus. Two precuneate gyri and two postcruciate gyri were present in bilateral hemispheres, showing X shapes, and calcification was found in the center (Fig. 2A). In the left cerebral hemisphere, the endomarginal sulcus was lost, and the marginal gyrus and the ectomarginal gyrus were adhered to each other.

On histopathological examination, a marked loss of pyramidal cells was observed in both hippocampi, especially in the left hippocampus. Some mild ischemic changes were also observed in the parahippocampal gyrus, frontal lobe cortex, and cerebellar cortex. The most marked pathological change was found in the midline medial surface of the hemispheres (cingulate gyrus and a part of the geniculate gyrus), under the abnormal cruciate sulcus. The cortex of this region showed laminar malacia, and marked gliosis was observed in this lesion (Fig. 2B).

In this study, we performed sEEG and epidural ECoG, which is directly derived from the brain, by using referential derivation. The amplitude of the sEEG is low because such tissues as cerebrospinal fluid, meninx, cranial bones, muscles and scalp are present between the cerebral cortex and the electrode. In dogs, except for brachycranial breeds, marked artifacts are mixed into the sEEG due to the thick temporal muscle. In contrast, artifacts of these tissues are small in ECoGs, and more detailed readings can be made, as shown in this study.

The spikes detected in the left parietal region were synchronously observed in the right parietal region, although the amplitude was low. Such symmetrical spikes with small amplitude are often considered to be a mirror focus. In this case, the abnormality in the cruciate sulcus and the histological lesion in the cingulate gyrus were almost symmetrical.

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**Fig. 1.** Electroctogram (ECoG) under medetomidine-induced sedation. The ECoG consisted mainly of high amplitude slow waves. Specific 300–400 µV spikes with a duration of about 60 msec which were suggestive of the epileptic focus were observed in LP (arrows). L, left; R, right; F, frontal; P, parietal; T, temporal; O, occipital.

**Fig. 2.** Pathology of the brain. (A) The abnormal cruciate sulcus, which had an X shape was observed (arrow). This abnormal cruciate sulcus was in accordance with the electroencephalographic abnormalities. In the left cerebral hemisphere, the endomarginal sulcus was lost, and the marginal gyrus and the ectomarginal gyrus were adhered together (arrow heads), but there were no histological changes in these gyri. (B) Laminar malacia of the cingulate gyrus, which was under the abnormal cruciate sulcus. Nerve cell bodies and neuropils were lost, and marked gliosis was observed. HE stain. (× 10)
and these were consistent with the electroencephalographic findings, although it was not mirror focus in the strict meaning. If the abnormal cruciate sulcus or the histological lesion in the cingulate gyrus were the source of the abnormal waves, both sides may have been the primary focus, but the left side was clearly dominant and preceded the right side on the EEG.

Major histological changes were located deep in the abnormal gyrate region (geniculate gyrus, cingulate gyrus), and the abnormal discharges detected in the ECoG may have reflected the abnormality in this region. Yamasaki et al. [14] reported histopathological evaluation of a similar case of intractable epilepsy in a Shetland sheepdog. Their evaluation was very similar to our histological evaluation, and the most severely disordered region was found in the cingulate gyrus and the medial surface of the frontal lobe. Morita et al. [7] who evaluated familial epilepsy of Shetland sheepdogs also reported that the electroencephalographic and pathological abnormalities were localized in the same regions as those in this study. Considering these reports together, a genetic factor might participate in intractable epilepsy in Shetland sheepdogs. Indeed, the loss of hippocampal pyramidal cells observed in this dog was also observed in most epileptic patients, and is called hippocampal sclerosis (HS) and/or mesial temporal sclerosis (MTS) in humans [6, 9–11]. HS may be the primary epileptic focus, but when the focus was located in a region other than the hippocampus, HS is important as an epileptic encephalopathy (secondary encephalopathy), which called “dual pathology”. Therefore, the attention should be paid to HS and MTS as an examination item for epilepsy in the clinical field of small animals. Although it is difficult to decide whether the region was a primary or secondary lesion, we thought that the epileptic focus was present in the abnormal cruciate sulcus and/or the laminar malacia of the cingulate gyrus, and HS as the secondary encephalopathy in this case, and was produced by recurrent seizures.

REFERENCES