Integrative Management of Canine Seizure Disorder: A Case Report

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ABSTRACT

A 17-year-old neutered male Longhaired Dachshund with lung carcinoma developed cluster seizures. Anti-seizure drug therapy was initiated but caused unacceptable side effects including hemorrhagic diarrhea, vomiting and ataxia. A multimodal anti-seizure therapy was designed using Western herbal medicine, nutraceuticals, environmental modifications and acupuncture to target multiple mechanisms in the seizure pathway. The treatment achieved a successful seizure control, as defined by ≥75% reduction in seizure frequency and improved quality of life, without anti-seizure drugs.

HISTORY

Jack was a 17-year-old neutered male Longhaired Dachshund, who was enjoying a relatively healthy adult life apart from routine dental procedures he received every five years. He was taking traditional Chinese medicine (TCM) and Western herbal formulas in the past two years for age-related conditions including cognitive decline, hearing and vision loss, asymptomatic and stable chronic kidney disease (IRIS Stage 1/4 without proteinuria), asymptomatic mitral valve regurgitation (ACVIM Stage B1) and intermittently and mildly elevated alanine aminotransferase (ALT). In March 2024, lung carcinoma was found in the right middle lobe (4.3 × 2.0 × 2.1 cm) and right caudal lobe (1.9 × 1.6 × 2.6 cm) during investigation of leukocytosis. Metastatic lesions were not found on radiographs, computed tomography (CT) and ultrasound examinations. Since the tumor was not amenable to surgical resection, he was conservatively managed with anti-tumor herbs, autologous cancer vaccine, intravenous high-dose vitamin C infusion and hyperbaric oxygen therapy (HBOT). He was asymptomatic with clear lung sounds and no history of cough or dyspnea.

In May 2024, he experienced three generalized, tonic-clonic seizures within 12 hours, which required midazolam administration (0.1 mg/kg IV). Laboratory findings included markedly elevated ALT [405 U/L (reference range, 16-90 U/L)] and urea [33.1 mmol/L (2.5-9.6)]. All other values including glucose, ammonia and bile acid were within normal limits. On physical examination, he was weighing 4.4 kg (body condition score, 4/9) and mildly dehydrated. He did not have organomegaly or lymph node enlargement. Grade I/VI left apical systolic heart murmur was unchanged, and arrhythmia was not detected. Neurological examination was not possible, but he was ambulatory until the onset of the seizures. Differential diagnoses included cerebral vascular accident, metastatic brain tumor, paraneoplastic limbic encephalitis, age-related structural change, hepatopathy, azotemia, undetected electrolyte imbalance, hypoxia and late-onset idiopathic epilepsy. Magnetic resonance imaging was indicated but was not pursued; however, CT and radiographs taken three weeks earlier showed stable diseases. Following discharge, he was maintained on oral levetiracetam (20 mg/kg q8–12h), but he became ataxic and developed hemorrhagic diarrhea and vomiting. Dose and frequency reduction did not resolve adverse reactions, and levetiracetam was discontinued due to poor quality of life (QOL). Cannabidiol oil (CBD; 1–2.5 mg/kg) was tried twice but triggered seizures both times. Other anti-seizure drugs (ASDs) considered were bromide and imepitoin for their lack of hepatic metabolism (Podell et al. 2016), though the latter is not indicated for cluster seizures.

HOLISTIC ASSESSMENT

Jack was a typical “Fire” type dog when he was young (Beinfield & Korngold 1991). This type of dogs is joyful, affectionate but emotionally fragile and tends to develop disorders associated with sympathetic and neuroendocrine overactivity, e.g., heart disease and anxiety disorders. He had been on a complete and balanced home-cooked raw diet with organic and rotating ingredients and species-appropriate freeze-dried and air-dried commercial diets [<10% carbohydrate, 60-70% protein and 20-30% fat on dry matter basis]. Although his liver and adrenal gland sizes were near the lower end for the breed, his skin and gastrointestinal health were impeccable for his entire life with no history of food allergy or intolerance. Hair mineral and fecal microbiome analyses after cancer diagnosis ruled out mineral deficiency, heavy metal toxicity, pesticide toxicity and gut dysbiosis. Titer testing had been used instead of vaccination for the past 10 years, and heartworm preventives were discontinued after the cancer diagnosis.

His seizures typically occurred when he was sleeping and lasted for 1 to 5 minutes. He usually had a superficial wiry pulse and a purple-red, moist thin tongue. He had a radiating heat from his head during the ictal phase. Postictally, he was restless and anxious, and he had increased thirst and transient but complete vision loss.

In terms of stress and vitality, he had separation anxiety and thunder phobia when he was young, but not after he lost hearing. He had lost a sibling dog four months earlier. Although he was maintaining his daily activities, his physical and mental debilities due to aging and cancer were undeniable.

INTEGRATIVE THERAPEUTIC APPROACH

The goals of integrative management of canine seizure disorder are improved QOL, reduction of seizure frequency and severity, minimized use of ASDs, and management of post-ictal signs and side effects of ASDs when used.

Dietary therapy: Ketogenic medium-chain triglyceride (MCT) oil has shown efficacy in reducing seizure frequencies in epileptic dogs and humans (Berk et al. 2020; Han et al. 2021; Law et al. 2015, 2016). Unfortunately, Jack did not tolerate even a small amount of MCT oil, coconut oil or butter. They caused vomiting and/or diarrhea. However, he was able to eat raw poultry skin and animal fat. The dietary fat content was gradually increased for ketogenesis. He was also on krill oil and algae oil supplements (50 mg/kg as DHA/EPA BID).

Environmental modification: The epileptogenic potential of essential oils has been reported in human patients (Bahr et al. 2019). Although Jack was living in a low-chemical environment, essential oils were frequently used in household cleaners and detergents. Essential oils with reported pro-convulsive effects were removed (e.g., eucalyptus, sage, fennel and cedar), but anxiolytic and anti-convulsant chamomile, lavender and frankincense essential oils were allowed. Water and air filtration systems were already in use.

Western herbal medicine: Various herbal constituents have shown anti-seizure activities in *in vitro* and animal studies. Table 1 summarizes the reported and potential anti-seizure mechanisms of Western herbs. Herbs that have multiple disease-modifying effects were selected and included in his herbal formula. Because the patient had a history of idiosyncratic reactions to nervine herbs (e.g., aggression on withania, seizures on CBD oil), herbs were introduced one by one starting from the lowest dose.

Final herbal prescription and dosage:

Valerian root (1:2)	*Valerian officinalis*	Warm	Anxiolytic, anti-epileptic, nervine relaxant, hypnotic, spasmolytic	15%
Passionflower aerial parts (1:2)	*Passiflora incarnata*	Cool	Anxiolytic, anti-epileptic, nervine relaxant, hypnotic, analgesic	15%
Zizyphus seed (1:2)	*Zizyphus jujuba*	Sour, neutral, sweet	Digestive tonic, nutritive, anti-arrhythmic, anti-epileptic, nervine relaxant	30%
Skullcap aerial parts (1:2)	*Scutellaria lateriflora*	Cool	Anti-inflammatory, astringent, analgesic, anti-epileptic, nervine relaxant, nervine tonic, analgesic	10%
Bacopa whole herb (1:2)	*Bacopa monnieri*	Cold, slightly sweet	Cardiotonic, anti-epileptic, anxiolytic, cognitive enhancer, nervine tonic, nervine trophorestorative, adaptogen, thyroid stimulant	30%

Alcohol was removed by gently warming up the glass container in hot water. 1 mL BID plus 0.5 mL before bed. Overall cooling formula. All herbs were sourced from Mediherb (Integria, QLD, Australia).

Mediherb Boswellia Complex

Boswellia resin	*Boswellia serrata*	Cool, bitter	Anti-(brain)tumor, anti-inflammatory, analgesic, anti-diarrheal, anti-bacterial	90 mg extract/day
Turmeric rhizome	*Curcuma longa*	Warm, drying	Anti-tumor, anti-inflammatory, antioxidant, hepatoprotective, cholagogue	28 mg extract/day

Celery seed	*Apium graveolens*	Moist and cool, bitter, sweet	Alterative, diuretic, anti-inflammatory	333 mg dry herb/day
Ginger rhizome	*Zingiber officinale*	Dry, warm	Anti-inflammatory, antioxidant, circulatory stimulant, anti-emetic, cholagogue	100 mg dry herb/day

1/3 tablet once daily.

Acupuncture: Acupuncture was given twice weekly. Although different acupuncture points were selected at every session according to the patient's response, the most consistently used points were LU 5, LI 4, HT 7, BL 17, BL 18, BL 23, KI 2, KI 3, LV 3, CV 15 and GV 14.

Prodrome management: Many epileptic dogs show preictal sings that can be recognized by pet owners minutes to days before a seizure episode. Jack's seizures occurred during sleep, frequently preceded by head tremor, which resembled hypnic jerks in people. When this was recognized, a dose of a liquid TCM formula, Long Dan Xie Gan Tang (Kan Essentials, Santa Cruz, CA; later replaced by liquid Tian Ma Gou Teng Yin) (Appendix 1), was administered orally (1 mL/dose), and oxygen inhalation was started. Cold/warm compress was used when heat/coldness was felt.

Emergency ASDs: A single dose of midazolam (0.2 mg/kg IN) or diazepam (0.5 mg/kg rectally) was used when the prodrome management failed.

Other complementary therapies: Cancer vaccine was discontinued, because this was the latest addition to his anticancer regimen before the onset of seizures. Intravenous high-dose vitamin C infusion was also discontinued due to the development of intolerance (vomiting). Subcutaneous acetate Ringer's fluid therapy was used as necessary to correct dehydration with or without injectable vitamin B complex. HBOT was continued once or twice weekly. He also had mushroom extracts (agarics, chaga, maitake, reishi, cordyceps, lion's mane and turkey tail), and reishi and lion's mane were continued.

MONITORING AND OUTCOME

Treatment, seizure frequency (the number of seizures per month) and selected laboratory values are summarized in Table 2. His herbal therapy before the onset of seizure included Jia Wei Xue Fu Zhu Yu Tang (JWXFZYT; 1/4 teaspoon twice daily) (Appendix 1) and Western

herbal formulas containing rehmannia, hawthorn, bupleurum, nettle seed, milk thistle, dan shen, dandelion leaf, maritime pine and gingko. JWXFZYT and milk thistle (Mediherb Silymarin; 1/4 tablet SID) were continued for cancer, heart and liver care.

As shown in Table 2, introduction of valerian, passionflower, ziziphus and melatonin (1 mg/kg/day) resulted in 70% reduction in monthly seizure frequency (5 in May to 1.5 in June and July) without ASDs. Further introduction of boswellia, skullcap and L-theanine, however, did not affect the seizure frequency. It was the addition of bacopa that eliminated seizures eventually. The patient was seizure-free for the following two months until he passed away from progression of cancer.

The patient did not experience side effects from the anti-epileptic herbs. He slept well through the night, and appetite and his gastrointestinal health were maintained until his last day. Hypnic jerks were still observed about once or twice weekly but rarely progressed to seizures. He had vomiting and/or diarrhea after administration of midazolam, after retrial of MCT oil and during HBOT. These were all manageable by herbal remedies. Marshmallow glycetract, chamomile and goldenseal (a source of berberine) were used most frequently.

DISCUSSION

Cluster seizures are defined as >2 self-limiting seizures over a period of 24 hours (Berendt et al. 2015; Charalambous et al. 2024). Effective clinical management is paramount, as repeated seizures can lead to irreversible neuronal loss and alterations, systemic complications and progression to status epilepticus, which is associated with high mortality. At the same time, patients can quickly develop resistance and unacceptable adverse reactions to ASDs.

While long-term (>12 months) seizure freedom is considered a primary goal of anti-seizure therapy, it is rarely achieved with any ASD protocols. Therefore, achievement of a seizure-free interval that is three times longer than the pretreatment interictal interval or >50-75% reduction in seizure frequency is often defined as treatment success in clinical trials (Berendt et al. 2015; Gallucci et al. 2017). Because the pre-treatment interictal interval was very short in the present case, % reduction in monthly seizure frequency was used to monitor the treatment response. A seizure reduction of 70% was achieved in the first month of therapy, and the overall % reduction was 100%. It should be noted that these response rates were achieved by a strategic combination of multiple alternative therapies without prophylactic use of ASDs. In this approach, Western herbs played a primary role in modification of the multiple seizure pathways (Table 1). HBOT was used for deep tissue oxygenation and to facilitate the delivery of active constituents (Royce

& Goodworth 2024). TCM formulas were used as a rescue remedy, while acupuncture was aimed to balance the whole-body energetics and circulation. The role of diet was to deliver energy source, essential nutrients, antioxidants and anti-inflammatory compounds in their natural forms to normalize the intracranial environment, while preventing cachexia and sarcopenia. Dietary fat was increased gradually but did not reach the level to induce ketogenesis.

Nocturnal seizures in humans commonly occur during Stage 1 (light) non-REM phase, shortly after sleep and before awakening (Moore et al. 2021). Similarly, seizures in the present case predominantly occurred in early sleep and occasionally before awakening. This is when complex synchrony must occur between the sympathetic and parasympathetic nervous systems and among glutamatergic, serotonergic and GABAergic neurons in the brain. Ketogenic diet, pregabalin and levetiracetam have been shown to promote deeper non-REM sleep in human patients (Moore et al. 2021). Though not indicated for generalized seizures, pregabalin (or gabapentin) would have been a good option to try if herbal medicine had failed in the present case. Pregabalin inhibits gluamatergic signaling by blocking the presynaptic calcium influx; bacopa, reishi and DHA had a similar role in the present case, partly explaining the seizure-free status achieved after addition of bacopa.

Other possible causes of seizure in the present case were hepatopathy (elevated ALT with normal ammonia and bile acid) and azotemia (elevated urea), as serum ALT and urea decreased in parallel with seizure frequency (Table 2). Although the patient did not have clinical signs of hepatopathy or azotemia, but he had undergone multiple sedation and anesthesia for cancer diagnosis and monitoring before the onset of seizures. These procedures could have impacted his already aging kidneys and liver. Involvement of brain metastasis and paraneoplastic syndrome was empirically ruled out, as they are typically progressive and difficult to control even with ASDs.

CONCLUSION

Western herbs have multiple disease-modifying effects in seizure disorders. When used in combination with other complementary therapies, they have a potential to significantly decrease seizure activity in patients who are refractory or intolerant to conventional anti-seizure drugs.

Table 1. Seizure pathway and proposed disease modifying effects of Western herbs and nutraceuticals

General Brain Health		
Anxiolytic	Bacopa, chamomile, lavender, passionflower, verbena	α-Casozepine, L-theanine, L-tryptophan, magnesium, melatonin
Reduces neuronal inflammation and death	Bacopa, boswellia, gingko, gotu kola, mistletoe, skullcap, St. John's wort, turmeric, withania	Berberine, curcumin, melatonin, PEA, probiotics
Reduces oxidative stress	Bacopa, ginger, gingko, gotu kola, lavender, passionflower, St. John's wort, withania, ziziphus,	DHA, melatonin, quercetin
Protects blood-brain barrier	Astragalus, bilberry, gingko	Berberine, resveratrol, olive leaf
Neurosteroid homeostasis	Passionflower, St. John's wort	α-Casozepine, DHA, PEA
Neuroepigenetic modulation	Apigenin and genistein containing herbs	Curcumin, epigallocatechin, resveratrol
Support astrocytes/glial cells	Bacopa, ginger, skullcap, St. John's wort	PEA, DHA
Glutamatergic Neurons (Excitatory)		
Presynaptic		
Ca channels (inhibit Ca^{2+} influx)	Bacopa, kava, lavender oil, reishi	DHA
Na channels (inhibit Na^{+} influx)	Bacopa, kava	
Reduces glutamate concentration/release	Kava, lavender, zizyphus	Zinc
Postsynaptic		
AMPA receptor	St. John's wort, withania, zizyphus	
NMDA receptor	Bacopa, lavender, St. John's wort	
GABAergic Neurons (Inhibitory)		
Presynaptic		
Glutamine uptake and conversion to GABA (glutamic acid decarboxylase)	Bacopa	
GABA reuptake inhibition	Passionflower	
GABAergic	Mistletoe, St. John's wort, valerian	
GABA mimetic	Withania	GABA
Postsynaptic		

$GABA_A$ receptor partial agonist	California poppy, chamomile, passionflower, skullcap, St. John's wort, valerian	Certain flavonoids
Increases/enhances $GABA_A$ receptor	Bacopa, Devil's claw, gastrodia, lavender, lavender oil	Melatonin
Cl^- influx	Ginger	
Other Pathways		
Anti-adrenergic	St. John's wort	
Serotonergic	Ginkgo, passionflower, skullcap, St. John's wort,	5-HTP, DHA, L-tryptophan, magnesium, probiotics, SAMe
Dopaminergic	Passionflower, St. John's wort	L-theanine, DHA/EPA, SAMe, vitamin B,
mTOR inhibition	Ginkgo with L-carnitine, rhodiola	Curcumin, quercetin
Anti-cholinergic	Bacopa, gotu kola	
Unknown mechanism	Corydalis, verbena	

(From Bavarsad et al. 2023; Essawy et al. 2022; European Scientific Cooperative on Phytotherapy. 2023; Fougère 2024; Gupta, Srivastava & Lall 2019; Hu et al. 2024; Liu et al. 2017; Lokanathan et al. 2016; Walker & Pellegrini 2024; Wynn & Fougère 2007; Yonezawa et al. 2023; Zhang et al. 2009)

Herbs and nutraceuticals indicated in blue were used daily in the present case. Note: Herbs contain numerous active compounds, and their effects are not limited to those listed on this table and extend beyond the realm of current scientific understanding. **Abbreviations:** 5-HTP, 5-hydroxytryptophan; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GABA, gamma-aminobutyric acid; PEA, palmitoylethanolamide; SAMe, S-adenosyl-L-methionine.

Table 2. Treatment, seizure frequency and selected laboratory values.

	April	May	June	July	Aug	Sep	Oct
# of Seizures	0	5	1.5	1.5	1	0.5	0
Emergency & prodrome management		Midazolam Levetiracetam CBD oil Liq LDXGT	Midazolam Liq TMGTY	Diazepam Liq TMGTY	Midazolam Liq TMGTY	Liq TMGTY	Chamomile
Anti-seizure herbs		Valerian Passionflower Ziziphus	Valerian Passionflower Ziziphus Boswellia[1)]	Valerian Passionflower Ziziphus Boswellia[1)] Skullcap	Valerian Passionflower Ziziphus Boswellia[1)] Skullcap	Valerian Passionflower Ziziphus Boswellia[1)] Skullcap Bacopa	Valerian Passionflower Ziziphus Boswellia[1)] Skullcap Bacopa
Nutraceuticals	PEA Turmeric Magnesium Bilberry DHA/EPA	PEA Turmeric Magnesium Bilberry DHA/EPA Melatonin	PEA Magnesium Bilberry DHA/EPA Melatonin	PEA Magnesium Bilberry DHA/EPA Melatonin L-Theanine	PEA Magnesium Bilberry DHA/EPA Melatonin L-Theanine	PEA Magnesium Bilberry DHA/EPA Melatonin L-Theanine	PEA Magnesium Bilberry DHA/EPA Melatonin L-Theanine
# of HBOT	2	4	6	5	6	3	0
Anti-cancer & anti-aging support	JWXFZYT Adaptogen[2)] Silymarin	JWXFZYT Adaptogen[2)] Silymarin SC Fluid	JWXFZYT Adaptogen[2)] Silymarin SC Fluid	JWXFZYT Adaptogen[2)] Silymarin SC Fluid	SQDBT Silymarin SC Fluid Vitamin Bs	JWXFZYT Adaptogen[2)] Silymarin SC Fluid	SQDBT Silymarin SC Fluid Vitamin Bs

	WH formula[3] Cancer vaccine IV HDVC	Vitamin Bs IV HDVC	Vitamin Bs	Vitamin Bs		Vitamin Bs	
ALT [16-90] U/L	320	405		191		126	
SDMA [1-14] µg/dL	15			13		13	
Cre [50-130] µmol/L	100	129		98		90	
Urea [2.5-9.6] mmol/L	27.9	33.1		22.6		10.8	
BP	120/70	120/65	125/75	120/65	120/60	120/65	120/60
Lung mass size	Unchanged		Unchanged			Unchanged	

Seizure score: 0.5 indicates a partial seizure without loss of consciousness. **Abbreviations:** ALT, alanine aminotransferase; BP, blood pressure; CBD, cannabidiol; Cre, creatinine; JWZFZYT, Zia Wei Xue Fu Zhu Yu Tang; HBOT, hyperbaric oxygen therapy; IV HDVC, intravenous high-dose vitamin C infusion; Liq LDXGT, liquid Long Dan Xie Gan Tang; Liq TMGTY, liquid Tian Ma Gou Teng Yin; PEA, palmitoylethanolamide; SC fluid, subcutaneous acetate Ringer's fluid. SDMA, symmetric dimethylarginine; SQDBT, Shi Quan Da Bu Tang.

1) Given as Boswellia Complex (boswellia, turmeric, celery seed, ginger).
2) Astragalus, Siberian ginseng and echinacea.
3) Western herbal formula for cognitive, renal and cardiac support: Rehmannia, hawthorn, bupleurum, nettle seed, dan shen, dandelion leaf, maritime pine and gingko.

Appendix 1: Herbal ingredients in the traditional Chinese herbal formulas used in the present case.

Jia Wei Xue Fu Zhu Yu Tang (Indicated for intrathoracic tumor and mitral valve disease. Support circulation)

- Tao Ren (Peach kernel, Persica seed)
- Hong Hua (Safflower flower, Carthamus)
- Chan Xiong (Sichuan lovage root, Ligusticum)
- Chi Shao Yao (Red peony root)
- Chuan Niu Xi (Cyathula root)
- Chai Hu (Bupleurum root)
- Sheng Di Huang (dried Rehmannia)
- Jie Geng (Platycodon root)

- Zhi Ke (Bitter orange)
- Dan Gui (Angelica root)
- Gan Cao (Licorice root)
- San Leng (Sparganium rhizome)
- E Zhu (curcuma)

Long Dan Xie Gan Tang (Indicated for epileptic seizures with Liver Fire. Aggressively cooling)

- Sheng Di Huan (dried Rehmannia)
- Dan Gui (Angelica root)
- Long Dan Cao (Gentian root)
- Ze Xie (Alisma tuber)
- Mu Tong (Akebia)
- Chai Hu (Bupleurum root)
- Che Qian Zi (Plantain seed)
- Gan Cao (licorice root)
- Huang Qin (Scutellaria root)
- Zhi Zi (Gardenia fruit)

Tian Ma Gou Teng Yin (Indicated for epileptic seizures with Empty Heat. Heat draining but also a tonic)

- Shi Jue Ming (Haliotis shell)
- Du Zhong (Eucommia bark)
- Fu Shen (Poria)
- Gou Teng (Uncaria stem)
- Sang Ji Sheng (Loranthus)
- Tian Ma (Gastrodia tuber)
- Y Jiao Teng (Fleeceflower stem)
- Chuan Niu Xi (Cyathula root)
- Yi Mu Cao (Leonurus)
- Huan Qin (Scutellaria root)
- Zhi Zi (Gardenia fruit)

Shi Quan Da Bu Tang (Indicated for significant debility and intrathoracic tumor in chilly patients. Warming and adaptogenic)

- Ren Shen (Korean ginseng)
- Shu Di Huang (cooked Rehmannia)
- Huang Qi (Astragalus)
- Rou Gui (Cinnamon)
- Dang Gui (Angelica root)
- Bai Zhu (Atractylodes)
- Fu Ling (Poria)
- Bai Shao (White peony)
- Chuan Xiong (Ligusticum)
- Gan Cao (Licorice root)

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