Case Report

SUCCESSFUL MANAGEMENT OF CENTRAL VESTIBULAR DISEASE WITH PROGESTERONE IN A KANNI DOG – A CASE REPORT

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ABSTRACT

A 2-year-old male Kanni dog was presented to the Veterinary College and Research Institute, Orathanadu with a history of head tilt, unable to balance while walking and with suspicion of traumatic brain injury. On clinical examination, neurological signs like compulsive walking, head tilt, circling, nystagmus, staggering gait, decreased proprioception and tactile reflexes were observed. The blood samples were analyzed for hematological and biochemical profile analysis and all parameters were in normal range except mild leukocytosis. The cerebro-spinal fluid was collected and neuron specific enolase (NSE), a neural biomarker was estimated. The CSF was red-tinged and had elevated NSE value (41.42 ng/ml). Based on history, clinical signs and NSE values, the case was diagnosed as central vestibular disease. The animal was treated with polyionic fluids – inj. ringers lactate @ 10ml/kg I/V, inj. hydroxyprogesterone caproate @ 2mg/kg, I/M, inj. cefotaxime @ 25 mg/kg I/V and Inj. B Complex vitamins, I/V. The animal was prescribed with oral micronized progesterone @ 5 mg/kg. On day 7, only mild head tilt and nystagmus were noticed. On day 14 post therapy, the clinical signs were resolved and NSE value became normal.

Keywords: Kanni dog, central vestibular disease, neuron specific enolase, progesterone.

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INTRODUCTION

The vestibular system, also known 'special proprioception' is classified into two components namely central vestibular system and peripheral vestibular system [Rossmeisl, 2010; Lahunta and Glass, 2009]. The peripheral components consist of the inner ear and its receptor along with

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peripheral axon of vestibulocochlear nerve whereas the central vestibular system includes medullar nuclei and neurons of cerebellum [Lowrie and Vetmb, 2012]. The most common clinical sign of vestibular disease is vomiting followed by head tilt, ataxia, pathological nystagmus and strabismus [Radulescu *et al.*, 2020]. Some of the common etiologies for central vestibular disease include infectious causes like canine distemper encephalitis, rickettsial encephalitis, fungal encephalitis, granulomatous meningoencephalitis and non-infectious causes like traumatic brain injury, metronidazole toxicity and neoplasia related to middle and inner ear [Thomas, 2000]. Even though findings of neurological examination are essential for the diagnosis of vestibular syndrome, its reliability to differentiate between central and peripheral vestibular syndrome is uncertain. Therefore, using advanced diagnostic aids like magnetic resonance imaging (MRI), computed tomography (CT) and cerebrospinal fluid (CSF) analysis are more reliable [Boudreau *et al*., 2018]. Some human study findings claim that vestibular signs are more commonly seen in acute traumatic brain injury with ataxia being the most common sign [Marcus *et al*., 2019].

Progesterone has been observed to promote the repair of the blood-brain barrier, reduce edema and dampen the inflammatory response. Furthermore, progesterone's protective effects may involve safeguarding or reconstructing the blood-brain barrier, decreasing the development of cerebral edema, suppressing the inflammatory cascade and limiting cellular necrosis and apoptosis [Stein *et al.*, 2008]. These mechanisms are all plausible explanations for its neuroprotective properties. In studies involving animal models of traumatic brain injury, progesterone has demonstrated neuroprotective effects, including the reduction of edema and infarct/lesion volume, the regulation of the inflammatory response and the promotion of neurological recovery [Stein, 2008; Jiang *et al*., 2011].

This article reports the successful management of central vestibular disease with traumatic brain injury in a Kanni dog with progesterone.

CASE PRESENTATION

A 2-year-old male Kanni dog weighing around 20 kg was referred to Veterinary College and Research Institute, Orathanadu with the history of vomiting, head tilt, unable to balance while walking and the owner suspecting traumatic injury. On physical examination, the dog had dull and depressed mentation while other clinical parameters like rectal temperature, conjunctival mucous membrane and lymph nodes were unremarkable. On the day of presentation (Day 0), a complete neurological examination including postural reflexes, cranial nerve reflexes and spinal reflexes was performed and the results were recorded (Tables 1, 2 and 3). The observation included the presence of ataxic gait, head tilt towards right side, spontaneous vertical nystagmus of both eyes and medial strabismus of the right eye (Figure1). All other reflexes were unremarkable.

The degree of encephalitis was graded using Meyer's criteria and the signs showed that the dog was in grade 3 while presented. Other diagnostic tests included hematological and serum biochemical estimation, otoscopic examination, radiography and cerebro-spinal fluid examination. The results of hematological and biochemical profile were normal except mild leukocytosis. No abnormalities were detected in lateral radiographic view of skull and no signs of internal injuries were seen in otoscopic examination. Under general anesthesia, cerebro spinal fluid was collected from cerebellomedullary cistern according to the standard procedure and the CSF was red tinged in color. Estimation of Neuron specific enolase (NSE) enzyme was done on the collected fluid. NSE was measured by solid phase enzyme immuno assay using commercial ELISA kit of XEMA Medica Co. Ltd., Russia. The concentration of NSE in the sera sample was calculated based on the ELISA test absorbance at 450 nm and the standard concentrations in BioTek Gen 5 by Standard curve analysis. The result revealed an elevated NSE value of 41.42 ng/ml (Normal range – 5-20 ng/ml) in the CSF collected on the day of presentation. Based on this value the dog can be diagnosed to have traumatic brain injury with central vestibular disease.

TREATMENT

A treatment plan with progesterone was made for the dog. The animal was treated with polyionic fluids – inj. ringers lactate @ 10ml/kg I/V, inj. hydroxyprogesterone caproate @ 2mg/kg, I/M, inj. cefotaxime @ 25 mg/kg I/V and inj. B complex vitamins, I/V. Oral progesterone administration was initiated on Day 1 and the animal was prescribed with oral micronized progesterone - (Tab. Sustan 200mg) at a dose rate of 5 mg/kg PO along with supportives. On day 7 - mild head tilt and nystagmus were noticed and on day 14 clinical signs were resolved (Figure 2). The NSE examination was performed on day 14 and the value was within the normal range of 15.68 ng/ml.

RESULT AND DISCUSSION

Progesterone commonly known as pregnancy hormone, is a steroid hormone synthesized from corpus luteum, placenta and adrenal glands. In recent years, it has been discovered that progesterone has various functions apart from its role in reproduction. Progesterone and its analogues have neuroprotective, anti-inflammatory, immune-modulatory and to a certain extent anti-neoplastic effects [Nagy *et al.*, 2021]. Progesterone is considered a neurosteroid as it is also synthesized locally in the nervous system [Guennoun *et al*., 2015]. Extensive and pre-clinical studies have been conducted in human medicine to determine the neuroprotective effects of progesterone in multiple sclerosis, alzheimer's, parkinson's disease, stroke, traumatic brain injury, spinal cord trauma, central and peripheral neuropathies [González, 2020]. The exact mechanism of action of progesterone in neurological cases is unclear. However, studies conducted on laboratory animal models claim that there are numerous progesterone receptors (PR) in the neurons

which exhibit various signaling pathways during neuronal damage [Kraus *et al.*, 1993]. Progesterone also showed good response in mitigating the demyelinationin experimental studies with cuprizone-induced mice [Ye *et al*., 2013].

Enolase is a glycolytic enzyme that is exhibited in the form of three isomers namely enolase α, enolase β and enolase γ. Of these three isomers, enolase γ is more specific to neurons and neuroendocrine cells and hence termed as neuron-specific enolase (NSE). Any damage to the neurons will lead to release of NSE into the blood circulation and hence it acts as a potential biomarker for neurological cases especially for traumatic brain injury cases. The amount of NSE in serum or CSF corresponds to the extent of the damage.

CONCLUSION

Unlike human medicine, the research studies on effects of progesterone in neurological cases in veterinary medicine is limited. Based on the literature review, this is the first case report showing successful management of a neurological disorder with progesterone therapy in a dog in India.

CONFLICT OF INTEREST

None of the authors have any conflict of interest to report.

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Table 1. Neurological observations done on the day of presentation

Mentation	Inappropriate
Gait	Vestibular ataxia
Posture	Head tilt towards right

Table 2. Results of cranial nerve examinations

Test	Right	Left
Menace response	Normal	Normal
Direct Pupillary light reflex	Normal	Normal
Palpebral reflex	Normal	Normal
Spontaneous nystagmus	Present (vertical)	Present (vertical)
Positional strabismus	Present (medial)	Absent
Jaw tone	Normal	Normal
Gag reflex	Normal	Normal

Table 3. Results of Spinal reflexes examination.

Spinal reflexes	Right	LEFT
Flexor withdrawal (thoracic limbs)	Delayed	Normal
Crossed extensor (thoracic and pelvic limb)	Normal	Normal
Flexor withdrawal (pelvic limbs)	Normal	Normal

Fig.1. Before treatment

Fig.2. After treatment

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