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Clinical progression of naturally occurring canine distemper encephalomyelitis cases

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Abstract

Canine distemper is an endemic disease in India. The present study was undertaken to deduce the clinical progression of naturally occurring canine distemper encephalomyelitis cases. None of animal in our study was vaccinated against distemper. Out of the 47 serologically confirmed nervous form of distemper cases, 20 cases have clear history of progression. The incidence of neurologic form of distemper was recorded to be higher in the age group of 1-3 years. The possible reason for this is neurological form occur when the environment favours clinical infection through virulent virus in immunologically deprived animals. Clinical progression was noticed in natural cases every 9-12 days on distemper encephalomyeleitis cases with a maximum of 3 or 4 clinical phases. Primary way distemper encephalomyelitis cases progress was initially catarrhal signs then appearance of epilepsy followed by paraplegia and finally either death/euthanasia. The Second way was epilepsy as initial sign which may progress to status epilepticus/cluster seizures then to coma and finally death/euthanasia. Glucocorticoid usage in these cases didn't show any clinical advantage. Poor herd immunity and inadequate vaccination might be the reasons for existence of distemper encephalomyelitis cases in India.

Key words: Progression, Encephalomyelitis, Vaccination, Glucocorticoids.

Canine distemper (CD) is a common infectious disease and has a cosmopolitan distribution. The disease is enzootic in the Indian domestic dog population (Vanak *et al*., 2007) and has a wide prevalence in the country (Pawar *et al*., 2011). The evidence for current or past exposure to CDV was found in 90.7% of animals in a survey of free ranging dog population of Great Indian Bustard Sanctuary, Maharashtra, India (Vanak *et al*. 2007). Latha *et al*. (2007) screened 160 conjunctival samples collected from dogs with clinical symptoms suggestive of CD using dot-ELISA, and found that 112 (70 %) cases were positive for the virus.

Disease manifestation ranges from virtually no clinical signs to severe disease, with mortality rates of up to 50% (Moritz *et al*., 2000; Schwab *et al*., 2007). Clinical features of CD vary between a catarrhal or nervous form or a combination of both, a condition termed as acute systemic form, and a chronic nervous manifestation can be distinguished in distemper (Beineke et al., 2009). Nervous signs are diverse and progressive and vary according to the area of the CNS involved (Greene and Appel, 2006; Amude *et al*., 2006a). The duration of the neurological disease varies from a few days to more than a month. Systemic signs occur by 10 days after infection, and neurologic signs may be observed beginning from 20 days and up to 40 to 50 days post infection (Martella *et al*., 2008). Clinical signs typically wax and wane over a period of time followed by a more rapid progression (Coates, 2004).

Once neurologic signs become evident, the prognosis is commensurately poor and euthanasia is frequently justified (Ford, 2010). Seizures in CDV infection are an unfavourable prognostic sign as they are generally difficult to control with anticonvulsants (Tiopld *et al*., 1992). Up to half the cases with a definite clinical diagnosis die or are destroyed, usually because of uncontrolled seizures or paralysis (McCandlish, 1999). The treatment of CDV myelitis is often unsuccessful (Coates, 2004).

To our knowledge, the progression or time course between the two clinical stages of distemper encephalomyelitis has not been elucidated in natural cases. The present study aims to record the progression or time course between the two clinical stages, variability in the age of infected dogs and the effect of corticosteroids on neurologic distemper cases.

Materials and Methods

The study was conducted at the Referral Veterinary Polyclinic, Indian Veterinary Research Institute, northern India. The quality of the dog life is

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highly associated with owner's socio-economic status and all the cases considered in the study were not vaccinated against CDV. The cases were identified by their institutional case number.

The sick dogs brought to the outpatient unit with clinical signs suggestive of nervous form of distemper, were selected and subjected to serological diagnosis. The recombinant nucleocapsid distemper virus specific capture immunoenzymatic assay for IgM and indirect immunoenzymatic assay for IgG were carried out. Both the kits (batch nos. 250309 & 030909) used in the study were procured from Inmunologia Y genetic Aplicada (Ingenasa, Madrid, Spain) and tests performed as per manufacturer's guidelines. The cases were considered as distemper when they were positive for IgM assay alone or for both IgM and IgG assays.

Clinical progression

The distemper encephalomyelitis cases with clear clinical progression were chosen for this study and progression was recorded carefully. The data obtained on progression is depending on the clinical observations during therapy and partly on owner's history. Development of additional sign and/or switch between catarrhal to nervous signs was considered as one stage. Therapeutic attempt was made for distemper encephalomyelitis cases on humanitarian grounds with the following regimen used on individual animal basis:

i. Polyionic fluids like Ringer's lactate and dextrose saline as per the requirements of the individual case.

ii. Antimicrobial therapy
   a. Ceftazidime – Vizidime[1] – Biovista Life Sciences[2] –30 mg/kg b.wt.
   b. Cefotaxime sodium + sulbactum – Taximax[1] – Alkem[2] – 25-50 mg/kg b.wt., Bid

iii. Neuroprotectants
   a. Ascorbic acid – 50 – 100 mg/kg, IV, Bid
   b. Methyl cobalamin – (Neurokind G[1] -Mankind[2])
   c. Pyritinol – 100 mg/animal, Td, (Encephabol[1] – Merck[2])
   d. Piracetam – 20-80 mg/kg, IV, Od (V-Tum[1] – Biovista Life Sciences[2])

iv. Seizure management
   a. Diazepam in status epilepticus only –- 0.5-1 mg/kg b.wt, IV (Calmpose[1]-Ranbaxy[2])
   b. Phenobarbital sodium – 2-3 mg/kg b.wt, IV/ PO.
   c. Levetriacetum – Levorexa[1] – Ranbaxy (solus) [2] – 10-20 mg/kg b.wt, PO.

v. Neuropathic pain management
   a. Pregabalin – 4 mg/kg, Safyvit – PR[1] –Star Biomed[2].
   b. Gabapentin — 10-20 mg/kg b.wt, Tid, PO Gabentin[1] – (Sun Pharma[2])

Outcome of the distemper encephalomyelitis cases were recorded whenever possible, as some of the owners failed to turn-up. The observations with reference to the duration of clinical stages was recorded and subjected to statistical analysis using SPSS software version 21 (SPSS Inc., 233 South Wacker Drive, 11th Floor, Chicago, IL 60606-6412).

Results and Discussion

Out of a total of 59 neurologic distemper suspected cases based on clinical signs, 12 were negative for both antibodies and 47 cases were found positive either for IgM only or for both. Among the positive cases, outcome was known in only 20 cases.

The highest numbers of cases fell under the age group between 1 – 6 years (32 cases) which constituted 68.09% of the total. Among these, 26 cases (55.32%) were aged between 1-3 years and 6 (12.77%) were in the 3-6 year age group. Nine cases (19.15%) were between 6 months to 1 year of age and 6 cases (12.77%) were aged more than 6 years. None of the cases was less than 6 months of age in our study.

Over all catarrhal signs appear before neurologic signs. The most common catarrhal signs were respiratory problems followed by gastro-enteritis in neurologic distemper. Many cases presented with neurologic signs were progressed as neurologic form without catarrhal signs. The details of the clinical signs are as follows:

Based on the observations, two most common pathways the distemper encephalomyelitis animals progress in two pathways

1. Catarrhal signs →Epilepsy →Paraplegia →Death/ Euthanasia

Stage 1 (n=20)	Stage 2 (n=20)	Stage 3 (n=16)	Stage 4 (n=11)
Catarrhal signs (n=10) Epilepsy (n=7) Myoclonus (n=2) Posterior paresis (n=1)	Epilepsy (n=6) Status epilepticus/ Cluster seizures (n=6) Posterior paresis/ Teteraparesis (n=5) Catarrhal signs (n=3)	Paraplegia (n=7) Coma & Death (n=5) Myoclonus (n=2) Catarrhal signs (n=1) Recover (n=1)	Death (n=8) Status epilepticus/ Cluster seizures (n=1) Myoclonus (n=1) Recover (n=1)

2. Epilepsy →Status epilepticus/cluster seizures →Coma →Death/Euthanasia

Epilepsy in these cases means generalized seizure as per the classification by Chandler (2006).

Varying degrees of pyrexia and anorexia were the other systemic catarrhal signs in observed in affected animals. Clinical progression of distemper encephalomyeleitis cases were noticed in every 9-12 days with a maximum of 3 or 4 clinical phases

Among the confirmed cases, none of the animal was vaccinated even a single time. From these 7 (35%) had been treated with betamethasone (Betnesol) or other corticosteroids, either by local vets or veterinary quacks during the initial phase of therapy. It was observed in our study that the usage of corticosteroids didn't prevent the development of nervous form of disease whenever the systemic form of distemper is present or vice-versa. Thus the glucocorticoid usage in these cases didn't show any clinical advantage.

Great variations in duration, severity and clinical presentation of distemper have been found in experimentally infected dogs as well as in animals suffering from this spontaneously occurring disease (Beineke *et al*., 2009). Susceptible dogs of any age may succumb to CDV infection (Pachauri, 1999). Latha *et al*. (2007) found in an epidemiological survey that the incidence of distemper was higher in the age group of 1-5 years. Before modified live CDV vaccines became available in the late 1950s, there was a high incidence of CD in young dogs between approximately 2 months and 2 years of age (Pachauri, 1999). CD occurs commonly in young unvaccinated dogs, usually in their first year of life, but many cases are also seen in adults (Tipold *et al*., 1992). The higher incidence rate observed between 1-3 years in our study was supported by the earlier reports. Additionally, the high mortality rate in acutely infected young pups before being presented to the clinic and the high variability in the age at which the animals are procured to be reared as pets, may contribute to the higher incidence in the aforesaid age group.

Systemic involvement may be absent in almost 1/3rd of the cases (Tipold *et al*., 1992) while the neurologic signs may be the only presentation of CDV infection in many others (Amude *et al*., 2006b; Amude *et al*., 2007b). Dogs that are initially presented with neurological manifestation may show systemic signs within a week or two (Amude *et al*., 2007a). Seizures and myoclonus are considered as the most frequent neurologic findings in natural cases (Alex and Danapalan, 1994; Thamas, 1998; Koutinas *et al*., 2002; Saito *et al*., 2006). The neurologic signs precede systemic signs or vice-versa and the signs observed in our study were well correlated with earlier reports. Neurologic disease associated with CDV infection tends to have a progressive course (Munana, 2004). The duration of the neurological disease varied from few days to more than a month. The inflammation of CNS is often associated with worsening of the tissue damage and progression of the neurological signs (Tipold *et al*., 1992). Systemic signs occur by 10 days after infection and neurologic signs may be observed starting from 20 days or at 40 to 50 days post infection (Martella *et al*., 2008). Neurologic signs first develop after 12 days and progress rapidly to seizures or paralysis, leading to death within 2-3 weeks after infection (Rudd *et al*., 2010). Though the progression or change of clinical phase in our study was between 9 to 12 days, individual differences and great variability were observed between the cases.

Table 1. Mean ± S.D. values of duration of clinical progression in distemper encephalomyelitis cases

S.No.	Clinical stage	1 (n=20)	2 (n=20)	3 (n=18)	4 (n=11)
1.	Mean	12.85	21.06	30.80	38.86
2.	Std dev	11.84	19.99	33.13	46.28

This may be directly related to the strain of virus and the immunocompetence of the affected animal (Tipold *et al*., 1992). Even though, CDV has only one antigenic type, co-circulating CDV genotypes of different virulence and cell tropism have been found (Pratelli, 2011). Lack of phylogenetic analysis and immunopathological studies in India makes it difficult to correlate the observations in this study with others. The high number of unvaccinated animals among sero-positive cases in our study vindicates the above mentioned statement. The corticosteroid therapy in CD cases poses a complication in the sense that two outcomes are possible by way of its use. Neurologic signs will often improve, at least temporarily, or prolonged therapy may lead to a state of immunosuppression which is deleterious in the long term, as the inflammatory response does lead to clearance of the virus (Thomas, 1998). Glucocorticoid administration may be beneficial in some dogs with CNS disease from chronic CDV infection, but its use is contraindicated in acutely infected dogs (Lappin, 2009). In the present study, the use of glucocorticoids in CDV encephalomyelitis cases didn't show any clinical advantage.

It is concluded that the incidence of neurologic form of distemper was higher in 1-3 years of age group in India. Clinical progression was noticed in natural cases every 9-12 days on distemper encephalomyeleitis cases with a maximum of 3 or 4 clinical phases. Primary way distemper encephalomyelitis cases progress was initially catarrhal signs then appearance of epilepsy followed by paraplegia and finally either death/euthanasia. The Second way was epilepsy as initial sign which may progress to status epilepticus/cluster seizures then to coma and finally death/euthanasia. Glucocorticoid usage in these cases didn't show any clinical advantage. Poor herd immunity and inadequate vaccination might be the reasons for existence of distemper encephalomyelitis cases in India

1- Trade name, 2 – Manufacturing Company

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