Description of Feline Nonsuppurative Meningoencephalomyelitis ("Staggering Disease") and Studies of Its Etiology

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A spontaneous neurological disease in domestic cats is described. The clinical signs included staggering gait, hind limb ataxia, and paresis. Histologically, a nonsuppurative meningoencephalomyelitis with a characteristic distribution pattern was found, indicating a viral etiology. In serum samples from diseased cats, antibodies to Borna disease virus were demonstrated.

An identical disease of the central nervous system (CNS) of the domestic cat has been observed in Sweden (9) and Austria (16); the dominating clinical sign is an unsteady (staggering) gait. The cats become more and more depressed and subsequently lose their ability to jump and to climb stairs. Ataxia of the hind limbs frequently occurs; this is followed in some cases by hind limb paresis. Histologically, a nonsuppurative meningoencephalomyelitis, predominantly in the gray matter, is present in all animals. The distribution of the lesions is unique and differs significantly from that in known feline diseases. Severe inflammation, characterized mainly by thick perivascular cuffs of histiocytes and lymphocytes, is observed in the cortex, brain stem, and spinal cord. Additionally, some glial nodules as well as neuronal degeneration and neuronophagy (Fig. 1) are seen. The cerebellum is far less affected. Meningitis, however, is most prominent over the cerebellum (Fig. 3). Diseases resembling "staggering disease," but with differences in their clinical or pathomorphological aspects, have been noticed worldwide (Morocco [11], Australia [2], the United States [15], and Switzerland [7]).

The present report is based on 12 cases of the disease in cats that we received for postmortem examination from January 1990 to December 1994. The case histories were very similar. All cats originated from an area of about 850 km² northeast of Vienna. Most of the affected cats were neutered males and were between 1.5 and 2 years old, and all cats had been allowed to roam outdoors. Owing to the poor prognosis, the cats were euthanized 1 to 8 weeks after the onset of clinical signs. The histological lesions imply a viral etiology. However, no cytopathic effect could be observed after inoculation of brain suspension onto different feline cell cultures (CRFK, primary feline kidney and feline brain cells). Hemagglutination tests (with human, guinea pig, rabbit, sheep, and chicken erythrocytes and different buffer systems) also proved negative. Following intracerebral (i.c.) inoculation with a suspension of brain from the affected cats, newborn and adult mice remained clinically normal and showed no microscopic lesions. By means of immunofluorescence and immunoperoxidase techniques, rabies, Aujeszky’s disease, tick-borne encephalitis, and canine distemper were all eliminated. Serologically, there was no evidence for infection with feline immunodeficiency virus, encephalomyocarditis virus, or tick-borne encephalitis virus. The presence of a few seroreactors to feline leukemia virus (one cat), feline infectious peritonitis virus (two cats), and feline herpesvirus type 1 (two cats) corresponds well with the average prevalence of the respective infections. Finally, a spongiform encephalopathy could be excluded histologically. On the other hand, in accordance with the investigators of the cats in Sweden (10), an indirect immunofluorescence antibody assay showed the presence of antibodies to Borna disease virus (BDV) in the sera of the diseased cats. The titers ranged from 1:20 to 1:640.

Borna disease, a progressive encephalopathy of horses and sheep, occurs sporadically in certain areas of Central Europe (6, 8, 12); recently, the infection has also been reported in cattle (1, 4). In recent months the causal agent has been identified as a negative-, single-stranded RNA virus (3, 5). Despite the striking serological evidence for a BDV infection in cats with "staggering disease," all attempts to demonstrate BDV, viral antigen, or viral sequences in the feline brains have failed: infectivity assays in rabbit fetal brain cells, immunofluorescence and immunohistology (with monoclonal antibodies as well as polyclonal antisera), a Western blot (immunoblot) for antigen detection, and BDV PCR showed negative results.

Experimentally, rabbits are highly susceptible to infection with BDV. We therefore inoculated laboratory rabbits i.c. with homogenates of brain from the affected cats. During an observation period of 4 months, the rabbits remained clinically healthy; rectal temperature, blood cell counts, and differential blood cell counts were normal. In particular (in sharp contrast to the picture after the inoculation with BDV isolates from...
horses and sheep), the rabbits showed no signs of central nervous system disorders and no histological lesions. Nevertheless, the rabbits developed BDV-specific antibodies (titers, 1:20 to 1:80).

Intriguingly, antibodies to BDV have been reported in humans with psychiatric disorders (14). In attempts to isolate BDV, cerebrospinal fluid from seropositive patients was inoculated i.c. into rabbits. As with our “staggering disease” rabbits, these rabbits also remained clinically normal and showed no histological alterations, but they developed BDV-specific antibodies (13). It is therefore possible that the causal agents of Born disease, “staggering disease,” and perhaps certain mental disorders in humans are related viruses with different properties. Nevertheless, identification of the virus that is the etiologic agent will be necessary to verify this hypothesis.

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REFERENCES