Familial Scrapie Cases with Shortened Incubation Periods

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ABSTRACT. Two familial scrapie cases successively occurred in 29-month-old and 30-month-old Corrieadle dams and in three of their offspring as early as 10–19 months of age in a small flock. They showed ataxy but no pruritus. Histopathological and immunocytochemical examinations of those sheep revealed vacuolation of nerve cells in brain tissue and presence of PrPSc, a component of scrapie-associated fibris, in brain, spleen and lymph node tissues. We discuss about shortened incubation periods and lacking pruritus in the present scrapie cases.—KEY WORDS: familial scrapie, shortened incubation period.

Scrapie, a transmissible spongiform encephalopathy in sheep and goats, is a fatal, progressive degenerative disease of the central nervous system. The disease is characterized by neuronal vacuolation in the central nervous system [3] and presence of PrPSc [7] which is a major component of scrapie-associated fibrils and is an abnormal isoform of a membrane glycoprotein, PrP [10].

It is thought in general that most natural scrapie sheep are infected at birth or shortly thereafter directly from their dams. However, precisely how and when transmission occurs has not yet been fully determined. Majority of scrapie cases are between two and four years old, and cases occurring before 18 months of age are rare [2]. Only a few cases of natural scrapie have been reported in sheep as early as 7 and 10–12 months of age [1]. Host genetic factors, doses and strains of the infectious agent are influential in the length of the incubation period [2, 8]. It has been noticed that the age of the scrapie onset tends to decrease to 18–24 months over the time in scrapie contaminated flocks due to the increase in exposure to the agent [4].

We report here 2 familial scrapie cases which successively occurred in about 2.5-year-old dams and their progenies as early as 10–19 months of age in a small flock.

When the diseased sheep showed difficulties in standing they were euthanized and necropsied. For the histopathological examination, tissues collected from almost all organs were fixed in 10% buffered formalin. Sections were stained with hematoxylin and eosin. Remaining tissues of brain, spleen and lymph nodes were kept at −80°C for the detection of PrPSc [10], a marker of scrapie infection [7, 9]. Detection of PrPSc in the tissues was carried out by Western blotting using a rabbit antiserum to sheep PrP as described previously [7].

When the first scrapie case occurred, the flock kept in K farm consisted of one 3-year-old Suffolk ram, nine 4-year-old ewes of mixed breed of Suffolk and Finnish Landrace, two 29-month-old Corrieadle dams, and two each of 4-month-old male and female lambs which were the offspring of the Corrieadle dams. The Suffolk and the mixed breed sheep were introduced from a private ranch and the Corrieadle sheep came from a national breeding stock farm when they were 5 months old.

Owner of the flock noticed that one Corrieadle dam separated herself from the other sheep and appeared to be demented when the dam was 29 months old which was 4 months after the parturition of 2 offspring. The dam had ataxy progressing to recumbency and died. The duration of the symptoms was about one and a half month. The cause of the disease was not determined. Just after the death of the dam, another 30 months old Corrieadle dam showed almost the same symptoms as those of the first dam, and fell into recumbency. This diseased sheep was euthanized and necropsied to determine the cause of the disease. Four offspring of both dams were kept under observation at the University farm.

One male lamb showed ataxy at 10 months of age and 2 months later fell into recumbency. The remaining 2 (male and female) of 3 lambs also showed almost the same symptoms at 14 months and 19 months of age, respectively. Duration of illness of those lambs also was about 2 months. One female being apparently healthy was euthanized for other experimental purposes at 20 months of age.

The necropsied dam lacked significant lesions in all organs examined macroscopically. Histopathologically, however, vacuolated nerve cells (Fig. 1), that are characteristic for scrapie [3], were observed in the mid brain, pons, medulla oblongata and spinal cord. No other significant changes were found in other organs and tissues. The vacuolated nerve cells were also observed in the

Fig. 1. Vacuolated nerve cells in medulla oblongata of the dam showing progressive ataxy. HE × 198.
medulla oblongata, which was the only tissue of all diseased lambs examined histopathologically (data not shown).

Figure 2 shows three bands of PrPSc detected in the samples of brain, spleen and lymph node of the lamb showing ataxy at 14 months of age, though lane S of the spleen sample soiled due to long exposure. The bands were also detected in tissues from 2 other lambs and in the brain tissue from the one dam, but not in tissues from one apparently healthy female used for other purposes (data not shown).

We diagnosed those sheep, one dam and 3 lambs, with ataxy as scrapie from the histopathological findings and the presence of PrPSc. The symptoms and clinical course of the dam that died from an unknown cause was very similar to the present series of scrapie cases. Therefore, we concluded that this dam also died from scrapie.

While scrapie was observed in a national breeding stock farm where the Corriedale ewes had been produced [5], no scrapie had occurred in the K farm until the present cases and the private ranch supplying the remaining sheep to the K farm had been free from scrapie. Therefore, the Corriedale ewes probably received the pathogenic agent in the national breeding stock farm.

In Japan, from the beginning of the eighties scrapie occurred in Suffolk sheep which had derived from breeding sheep introduced from Canada in 1974 into the national breeding stock farm. All diagnosed cases were Suffolk and showed pruritus, and their ages were between 3 to 6 years old [5, 6]. In the present cases, both dams were Corriedale, and developed scrapie without pruritus when about 2 and a half years old. These facts indicate that horizontal transmission had occurred in the national breeding stock farm and scrapie contamination in the farm might progress, because it has been noticed that the age of the scrapie onset tends to decrease over time in scrapie-contaminated flocks [4]. Recent scrapie cases including the present cases tend to lack pruritus and the age of occurrence seems to decline [11, unpublished observations]. Spread of scrapie across the sheep breeds by horizontal transmission and increasing scrapie contamination in flocks may contribute to diversity of the clinical features and shortening of the incubation period.

The reason why 3 of 4 lambs developed scrapie as early as 10 to 19 months of age is that both dams delivered in a individually partitioned pen and were kept there together with their offspring for about 2 months. The lambs contacting intimately with their scrapie-infected dams might have been exposed to high doses of the agent during the time. If the lamb, which was euthanized as being healthy and used for other purposes was also negative for either neuronal vacuolation or PrPSc at 19 months of age, were kept longer, this also might have developed scrapie later on.

It is probable that some scrapie cases have been misdiagnosed like the first case of dam which was diagnosed as of unknown cause because of lacking pruritus. Therefore, it is necessary to examine brain tissue histopathologically and immunochemically for scrapie in cases showing ataxy or any other clinical signs due to damage of the central nervous system even if the age of the patients is below one year. Since PrPSc is detected only in scrapie animals [7, 9] and is stable in tissues which are not suitable for histological examination due to autolysis (unpublished observation), it is recommendable to keep frozen tissue of brain, spinal cord, spleen and lymph node for an accurate diagnosis of scrapie by the immunological method.

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