Cerebral Amyloidosis in Natural Scrapie of Icelandic Sheep Is of Rare Occurrence

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In addition to spongiform changes and astrocytosis, cerebral amyloidosis has been described as a feature of the host response in spongiform encephalopathies. It has been studied extensively in experimental scrapie of mice, where the incidence has been shown to depend on special agent strain and host strain combinations. The occurrence of cerebral amyloidosis has, however, only been explored to a very limited extent in natural infection of sheep and goats, the natural hosts of scrapie. We therefore decided to study the incidence and character of cerebral amyloidosis in natural scrapie of Icelandic sheep, a unique breed almost entirely confined to Iceland.

MATERIAL AND METHODS

Brains from 36 scrapie sheep from 2 to 7 years of age were studied. In 16 cases, 9 planes of sections were examined and in 20 cases, 3 planes in the medulla oblongata were studied. Healthy sheep of similar age distribution served as controls. To detect amyloid, Congo-red stained sections were examined in polarized light for green birefringence. Positive sections were immunostained with rabbit anti-PrP, either directly or after pretreatment with proteinase K or formic acid, using the Avidin-Biotin peroxidase method with diaminobenzidine as substrate. For electron microscopy a histological block was deparaffinized, post-fixed in osmium, reembedded in Epon and the sections stained with uranyl acetate and lead citrate. For immune electron microscopy the sections were stained with rabbit anti-PrP and goat anti-rabbit Auroprobe One.

RESULTS AND DISCUSSION

Amyloid was only detected in one scrapie case, which is a much lower incidence than reported in field cases of sheep scrapie in Scotland, where it was detected
FIGURE 1. Perivascular amyloid. Rabbit anti-PrP (mouse ME7) 1:500, ×450.

FIGURE 2. Electron micrograph of perivascular amyloid fibrils. V = vessel. Uranyl acetate and lead citrate. × 25,000.
in 55% of cases. The amyloid was of a vascular form, confined to a small area in the thalamus. It stained weakly with H&E, but a distinct green birefringence was seen in Congo-red stained sections in polarized light. In sections pretreated with formic acid the amyloid stained intensely with anti-PrP (FIG. 1), whereas untreated sections showed a very weak staining, indicating that the amyloid consists of the abnormal isoform, PrP\textsuperscript{Sc}. Electron microscopy revealed typical straight, unbranched fibrils (Fig. 2), which were decorated by immunogold staining. The amyloid was neither associated with the main pathological changes nor with the highest concentration of PrP, according to quantitative evaluation of PrP distribution in the brain (unpublished results). This indicates, that deposition of amyloid is not merely dependent on the concentration of PrP but some other local conditions play a part. On transmission brain material from this case was highly amyloidogenic in certain strains of mice.

**IN SHORT**

Cerebral amyloidosis is rare in natural scrapie of Icelandic sheep. It is vascular and apparently composed of PrP\textsuperscript{Sc}. It is neither associated with the main spongiiform changes nor the highest concentration of PrP\textsuperscript{Sc}, indicating that its deposition does not merely depend on one or both of these parameters. Our findings support the view, that both agent strain and host factors play a pathogenic role in cerebral amyloidosis in scrapie.

**REFERENCES**