LETTER TO THE EDITOR

UNUSUAL OCCURRENCE OF TEMPORO-SPATIAL CLUSTER OF HUMAN PRION DISEASE IN NORTHERN PART OF CENTRAL SLOVAKIA

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SUMMARY

Objectives: Clusters of human prion diseases have been reported in several endemic regions, notably in Slovakia, Italy, Chile, and Israel, predominantly linked to genetic forms (E200K mutation). Isolated temporo-spatial clusters that include sporadic forms are rarely documented and remain poorly understood. This report describes a unique cluster of prionopathies observed in northern central Slovakia.

Methods: Between July 2021 and March 2022, three definitive cases of prion disease were identified in two neighbouring rural villages, Pribovce and Rakovo, in the Martin District of Slovakia. The villages, located within a radius of approximately three kilometres, have a combined population of 1,468. Clinical records, epidemiological data, and neuropathological findings were reviewed in all cases.

Results: The cluster included one genetic Creutzfeldt-Jakob disease (gCJD) with the *PRNP* E200K mutation and M/M genotype at codon 129; one sporadic CJD (sCJD); and one sporadic fatal familial insomnia (sFFI), the first such case reported in Slovakia. The cases occurred sequentially within a ten-month interval. No familial, environmental, or iatrogenic links were identified.

Conclusions: The coexistence of distinct prionopathies in such a confined population and period is exceptional. Despite comprehensive investigation, no explanatory factor was found, and this cluster likely represents a chance occurrence of epidemiological interest. The finding underscores the importance of systematic neuropathological confirmation, molecular testing, and regional surveillance in prion disease monitoring.

Key words: Creutzfeldt-Jakob disease, fatal familial insomnia, temporo-spatial cluster, epidemiological surveillance

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Clustering of prion diseases has been well documented worldwide, with notable endemic foci in Slovakia, Israel, Italy, and Chile, predominantly associated with genetic forms of prion disease involving the E200K mutation (1). In contrast to these well-established genetic clusters, reports of isolated, localised temporo-spatial clusters are scarce, and their spatial and temporal characteristics remain poorly understood (2–4).

We report a rare temporo-spatial cluster of three histopathologically confirmed prion diseases that occurred within a ten-month period and within an area of approximately three kilometres in the Martin District of northern central Slovakia. Between July 2021 and March 2022, three cases were identified in two neighbouring rural villages, Pribovce and Rakovo, with a combined population of 1,468, according to 2023 census data (Fig. 1) (5).

The definitive diagnoses comprised a sporadic form of CJD (sCJD), a genetic form of Creutzfeldt-Jakob disease (gCJD) with a *PRNP* E200K mutation and a sporadic form of fatal familial insomnia (sFFI), representing the first documented case of sFFI in Slovakia.

The co-occurrence of these distinct prionopathies within such a small population and short time frame is particularly striking. Epidemiological history revealed no common environmental, familial, or iatrogenic links among the cases. One relevant consideration is the proximity of the Martin District to the Orava Region, which has a high incidence of genetic CJD associated with the *PRNP* E200K mutation. Dissemination of this mutation has been documented into neighbouring regions, and the incidence of prion disease in the Martin District is estimated at approximately 6 per million inhabitants, compared with up to 17 per million in the Orava Region. Although no epidemiological connection with the Orava Region was identified, an underlying genetic association cannot be excluded (6, 7).

The occurrence of this cluster underscores the need to consider multiple potential influences on prion disease distribution, including genetic predisposition, environmental factors, and diagnostic awareness. Enhanced neuropathological confirmation, molecular testing, and regional surveillance remain crucial for the early detection and understanding of such rare events. Despite thorough investigation, no explanatory factor could be identified, and this cluster may therefore represent a chance occurrence of epidemiological interest.

Fig. 1. *Left: Geographical location of prion disease cases in the Martin District, Slovakia. Right: All three cases occurred within a radius of less than 3 km over a 10-month period.*

1–3 – individual cases of prion disease; gender: M – male, F – female; age – years; date of onset – day/month/year.

Adherence to Ethical Standards

All procedures performed in this study involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. As all patients were deceased and data were anonymised, formal informed consent was not required under institutional policy.

Authors' Contributions

All authors have read and approved the final manuscript.

Conflicts of Interest

None declared

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