Neuropathology and Applied Neurobiology

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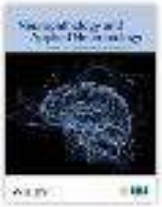

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ORIGINAL ARTICLE

Neuronal infection is a major pathogenetic mechanism and cause of fatalities in human acute Nipah virus encephalitis

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Abstract

Objectives

Acute Nipah (NiV) encephalitis is characterised by a dual pathogenetic mechanism of neuroglial infection and ischaemia–microinfarction associated with vasculitis-induced thrombotic occlusion. We investigated the contributions of these two mechanisms in fatal cases.

Materials and methods

We analysed brain tissues (cerebrum, brainstem and cerebellum) from 15 autopsies using light microscopy, immunohistochemistry (IHC), in situ hybridisation and quantitative methods.

Results

Three types of discrete plaque-like parenchymal lesions were identified: Type 1 with neuroglial IHC positivity for viral antigens and minimal or no necrosis; Type 2 with neuroglial immunopositivity and necrosis; and Type 3 with necrosis but no viral antigens. Most viral antigen/RNA-positive cells were neurons. Cerebral glial immunopositivity was rare, suggesting that microinfarction played a more important role in white matter injury. Type 1 lesions were also detected in the brainstem and cerebellum, but the differences between cerebral cortex and these two regions were not statistically significant.

In the cerebral cortex, Type 1 lesions overwhelmingly predominated, and only 14% Type 1 vs 69% Type 2 lesions were associated with thrombosis. This suggests that neuronal infection as a mechanism of pathogenesis was more important than microinfarction, both in general and in Type 1 lesions in particular. Between the 'early' group (<8-day fever) and the 'late' group (≥8-day fever), there was a decrease of Type 1 and Type 2 lesions with a concomitant increase of Type 3 lesions, suggesting the latter possibly represented late-stage microinfarction and/or neuronal infection.

Conclusion

Neuronal infection appears to play a more important role than vasculopathy-induced microinfarction in acute NiV encephalitis.