Letters

Herpes simplex virus: a role in the aetiology of Alzheimer's disease?

Sir: A Herpes simplex virus aetiology for Alzheimer’s disease1 offers an explanation for adult onset and the selectivity for temporal lobe.2 However, serological studies3–4 have not shown a consistent increase in antibody titres to Herpes simplex virus. Although sparse Herpes simplex virus immunoreactivity has been reported in normal and in Alzheimer brain tissue,6 and there is report of Herpes simplex virus DNA in three out of four brain smears,7 the Herpes simplex virus hypothesis has not been confirmed in other larger DNA hybridisation studies.8–10 Even if Herpes simplex virus infection were present it is not clear that it could account for the selective pattern of neurochemical defect (decrease in choline acetyl transferase,11 reduction in SHT2 receptor12 and somatostatin immunoreactivity13–14) seen in cases of Alzheimer’s disease. We have investigated an Herpes simplex virus aetiology for Alzheimer’s disease using two approaches:—(1) a survey to look for the presence of Herpes simplex virus antigenicity (an active infection) in 25 cases of histologically diagnosed Alzheimer’s disease and 32 non-neurological controls. (2) an investigation to determine if known cases of herpes encephalitis (human and a mouse model) produced a similar destruction of somatostatin-containing neurones in the temporal lobe to that seen in Alzheimer’s disease.

For the first study brains were obtained post mortem and fixed in 10% formalin. Blocks of tissue containing temporal lobe structures were dissected out and embedded in paraffin. Sections 15 μm thick were cut and processed for immunocytochemistry using the PAP method and an anti-Herpes simplex virus antibody (DAKO, dilution 1:500). Additional sections were processed for absorption controls and a confirmed case of human Herpes simplex virus encephalitis was used as a positive control.

Abundant immunoreactivity was present in temporal lobe areas in the encephalitis case with large numbers of neurons and glia showing evidence of active infection. No Herpes simplex virus antigenicity was seen in any temporal lobe area in the Alzheimer’s disease cases or the controls.

For the second study material from the Herpes simplex virus encephalitis case and from mice infected intracranially 3 days previously with Herpes simplex virus were processed in the same fashion as above (formalin fixation, paraffin embedding, immunocytochemistry) and stained with a number of antisera to different peptides: somatostatin, CCK, VIP etc. These studies showed that the damage caused by Herpes simplex virus infection was extensive, and loss of immunoreactivity was found for each of the peptides studied. This contrasts with the selective depletion, previously reported, of somatostatin immunoreactivity in Alzheimer’s disease.15

The absence of significant Herpes simplex virus-immunoreactivity in Alzheimer’s disease and our failure to detect Herpes simplex virus DNA4 (subsequently replicated10) taken together with the general depletions in peptide immunoreactivity and recent reports that the depletion in CAT activity11 and SHT2 receptor number12 found in Alzheimer’s disease are not found in Herpes simplex virus infected mice12 make it unlikely that Herpes simplex virus has any role in a aetiology of Alzheimer’s disease.

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References

Legionella brainstem encephalopathy and peripheral neuropathy without preceding pneumonia

Sir: Neurological manifestations of legionellosis are diverse, commonly involving encephalopathy1 and less frequently brainstem encephalopathy,2 cerebellar dysfunction,3 cranial nerve involvement,4 myelopathy,5 and peripheral neuropathy.6 Diagnosis of the cause of the neurological deficit usually depends upon the recognition of a preceding atypical pneumonia, with subsequent serological confirmation. However, legionellosis is a multisystem disease with variable abdominal, renal and haematological manifestations; pulmonary involvement may be slight or absent.8–10 We describe a patient with severe brainstem encephalopathy in whom diarrhoea was the only prodromal feature of legionella infection.

A 49-year-old woman experienced diarrhoea for a week, followed by a rapidly progressive neurological deficit. She had familial pes cavus without significant disability and had been able to run and dance. She had been otherwise fit. She was admitted two days after developing progressive drowsiness, diplopia, dysarthria, dysphagia, unsteadiness and peripheral parasthesia.