Transolfactory spread of virus in herpes simplex encephalitis

Unlike most encephalitides, acute necrotising encephalitis caused by *Herpesvirus hominis* type I exhibits several unique features, including a tendency to affect the limbic system, often asymmetrically and resulting in maximal damage to one or other temporal lobe. In a recent case1 herpesvirus was especially prevalent throughout the limbic system and in the olfactory bulbs, suggesting that transolfactory spread of virus may be important in pathogenesis. The next three cases were therefore similarly investigated.

**Case reports**

**Case 1**—A 78-year-old man was admitted in coma after three days of rapidly progressive confusion and drowsiness. Examination showed neck stiffness, fever, and hypertension. The cerebrospinal fluid contained 25 × 10⁶ red cells/l (25 000/mm³) and 82 × 10⁶ white cells/l (82/mm³) (48% lymphocytes); normal glucose and protein concentrations; and negative Gram and Ziehl-Neelsen. He developed prolonged seizures, deteriorated, and died after five days.

**Case 2**—A 66-year-old woman was admitted in coma after three weeks of gradually progressive dementia, right-sided weakness, and convulsions.

**Case 3.** Electronmicrograph of intranuclear inclusion bodies in cell of left olfactory bulb. Characteristic virions of herpes simplex are present, some of which (arrowed) show unusual swelling, loss of nucleic acid core, and partial fragmentation of thin nucleocapsids, presumably resulting from adenine arabinoside. × 26 000 (original magnification).

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Neck stiffness, right hemiplegia, and fever were present. CT brain scan was normal, and bilateral carotid angiograms showed brain swelling. Cerebrospinal fluid contained 40 × 10⁶ white cells/l (80% lymphocytes) and 2.8 g protein/l; Gram and Ziehl-Neelsen stains, culture, and complement fixation tests for herpes, mumps, and measles viruses gave negative results. She died four days after admission.

**Case 3**—A 24-year-old girl was admitted after a "febrile convulsion." She presented with pharyngitis, otitis media, fever, and a 12-hour history of left-sided facial twitching. The electroencephalogram and CT brain scan suggested encephalitis. Cerebrospinal fluid was normal. Viral studies, which included complement fixation tests on serum and cerebrospinal fluid, and a culture of cerebrospinal fluid were negative. Adenine arabinoside was started on the third day but she continued to deteriorate and died on the seventh day.

In each of these cases the brain showed all the features characteristic of acute necrotising encephalitis, including unilateral swelling and necrosis of the temporal lobe, panencephalitis without inclusion bodies, and abundant herpes simplex virus on electron microscopy. Herpes simplex virus was especially prevalent in the left and right temporal lobes and throughout the limbic system in cases 1 and 2, but in case 3 the virus was more evenly distributed throughout both hemispheres. Interestingly herpes simplex virus was found in the necrotic olfactory bulbs (figure). Necrotic cells containing herpes simplex virus were found in both right and left bulbs in each case and were associated with pronounced degeneration of myelinated fibres and prominent astrocytosis and gliosis in the olfactory tracts.

**Comment**

The route by which herpes simplex virus enters the brain in acute necrotising encephalitis is unknown. Haematogenous spread is the usual explanation, though in most cases no primary focus is found outside the nervous system. After the isolation of latent herpesvirus in various sensory ganglia,1 a theory was formulated whereby virus supposedly reaches the floor of the cranial fossae via tentorial branches from the trigeminal ganglia.2 My findings, however, would implicate a more direct route. The presence of herpes simplex virus in the olfactory bulbs, the degenerative changes in the olfactory tracts, and the distribution of the virus within the rhinecephalic areas suggest that the olfactory apparatus is the principal pathway in the pathogenesis of acute necrotising encephalitis in man.


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Acute haemolysis and renal failure after nomifensine overdosage

Nomifensine is an antidepressant unrelated to the tricyclic or tetracyclic amines. No serious toxicity has been reported after overdosage,2 but we report a case of acute haemolysis and renal failure requiring haemodialysis in a patient with nomifensine poisoning.

**Case report**

The patient, a previously well 25-year-old man, was admitted two hours after taking nomifensine 2 g (80 capsules), nitrazepam 100 mg, and chloridiazepoxide 300 mg. She had been prescribed nomifensine six months before and had taken it regularly for three months and then intermittently. On admission she was unconscious although responding to stimulation, her blood pressure was 110/70 mm Hg, and her pulse was regular at 120/min. She regained consciousness after six hours but remained drowsy. Two days later she complained of bilateral joint pain and was noted to be pale and oliguric. Her plasma and urine were the colour of cressotide and there was evidence of acute intravascular haemolysis. Her plasma haemoglobin concentration...