Herpes simplex type II encephalitis in a non-immunocompromised adult

Sir: At least five of the double stranded DNA herpes family of viruses are known to infect the human nervous system, (HSV I, HSV II, EBV, CMV, VZV).\(^1\)\(^\text{-}^3\) The clinical and pathological involvement is relatively specific for each individual virus species, but is also significantly influenced by age and immune status of the host.

A 19 year old, previously normal, male presented with a 4 day history of generalised headache, fever, anorexia and vomiting. His parents reported that he had appeared slightly disorientated the day prior to admission. Further questioning revealed no history of head trauma, epilepsy, travel, drug intake or recent sexual contact.

On initial examination he was fully conscious but appeared agitated with slowed mentation. He was pyrexial (rectal temperature 39°C). There was no meningism nor signs of increased intracranial pressure. Further systemic examination revealed nil of note. Initial laboratory investigations including full blood count, erythrocyte sedimentation rate, serum urea and electrolytes, serum glucose and urine microscopy were normal. Cerebrospinal fluid obtained on admission revealed an opening pressure of 20 cm H\(_2\)O, raised protein (131 mg/100 ml) and normal glucose level. There were 42 neutrophils and 244 lymphocytes per mm\(^3\). Gram stain and bacteriological culture were negative.

Over the next 12 hours he deteriorated markedly, becoming stuporose with neck stiffness and myoclonic jerking of his left arm as well as twitching of the right side of his face. At this stage computed tomography of the brain showed an area of low density in the right temporal lobe. An electroencephalogram showed diffuse background slowing with high amplitude sharp waves in the left fronto-temporal area. A tentative diagnosis of herpes encephalitis was made and therapy with intravenous acyclovir commenced. There was further deterioration in the following 24 hours and a right temporal lobe biopsy was performed.

Histological examination and electron microscopy revealed inclusion bodies typical of Herpes simplex encephalitis. However, no virus could be isolated in tissue culture or demonstrated by immunofluorescence. Thereafter followed a prolonged course of gradual recovery, complicated by episodes of hypotension, bradycardia, hypothermia, manic psychosis and an episode of malignant neuroleptic syndrome (produced by haloperidol).

He has subsequently made a remarkable recovery. He is presently on anti-epileptic therapy and has had no further convulsions. Except for an apparent long-term memory deficit there is no clinical neurological deficit. Relevant serological investigations included those for Herpes simplex virus. Antibodies (Ab) for Herpes simplex virus were determined in blood and cerebrospinal fluid (CSF) by the indirect immunofluorescence (IFA) method.\(^4\) On admission the HSV II IgM (IFA) titre was 1:20 and 2 weeks later 1:640, that for HSV II IgG 1:40 on admission and 1:160 2 weeks later. The HSV I IgM (IFA) titre remained negative. Complement fixation revealed a 1:16 titre for HSV I on admission as well as 2 weeks later.

The use of serological virus identification and antigenic typing techniques has enabled the delineation of specific illness profiles associated with each herpes virus type.\(^4\)\(^\text{-}\)\(^6\) Several methods are available for detecting Ab to HSV in body fluids. The complement fixation test (CFT), formerly in wide use, has largely been supplanted by more sensitive and convenient techniques. Disadvantages of the CFT are that it cannot differentiate Ab to HSV-I from HSV-II, rises in Ab titre may be obtained in recurrent as well as acute infections, and IgM cannot be determined. More sensitive and specific techniques include the indirect haemagglutination test,\(^7\) immunoassay,\(^8\) neutralisation test\(^9\) and IFA test.\(^6\) In this patient the clear seroconversion around the 14th day of illness, the presence of the rising titre of specific IgM and the temporal relationship of these with the patient’s illness are highly suggestive of an acute HSVII encephalitis.

Of the group of herpes viridae, the Herpes simplex viruses are probably the commonest cause of severe nervous system infection. However, the two types produce fairly distinct clinico-pathological disease entities. According to Adams,\(^10\) three central nervous system pathological entities can be distinguished. These are acute necrotising encephalitis, encephalitis associated with widespread virus dissemination, and aseptic meningitis. Acute necrotising encephalitis occurs at any age except the neonatal period and very early childhood. The cause is HSVI,\(^1\) which is believed to gain access to the brain either by the olfactory nerve or from a reactivated latent viral focus in sensory ganglia.\(^11\)\(^\text{-}\)\(^12\) Characteristically the infection produces a widespread but asymmetrical necrotising encephalitis mainly involving the temporal lobes.\(^11\)\(^\text{-}\)\(^13\) Clinical features include herpes labialis, fever, headache, photophobia, meningism, obtundation, seizure, focal neurological deficit, coma and death.\(^12\)\(^\text{-}\)\(^13\)

Without early recognition and treatment the prognosis is grave. Diagnostic modalities include serological investigation, cerebrospinal fluid analysis, electroencephalography and computed tomography of the brain.\(^5\)\(^\text{-}\)\(^14\)\(^\text{-}\)\(^15\) Brain biopsy remains the most reliable investigation for early diagnosis.\(^16\) High degrees of sensitivity and specificity have been reported,\(^16\) especially when involved brain sites can be located by EEG and or computed tomography.\(^16\)\(^\text{-}\)\(^17\) The current drug of choice is acyclovir, which has been reported to lower dramatically both morbidity and mortality rates.\(^18\)\(^\text{-}\)\(^19\)

Encephalitis associated with widespread viral dissemination is seen typically in neonates and is usually caused by HSVII.\(^1\) The commonest presumed source of infection is from an infected genital tract, the virus being transmitted to the neonate at birth.\(^1\) Post natal transmission from another infected infant or personnel may occur. Typically multiple organ systems are involved, including the central nervous system, eye, skin, reticuloendothelial and respiratory systems.\(^1\) Both diffuse and focal brain involvement have been described. The prognosis of this form of infection is also extremely poor.

Aseptic meningitis due to HSV usually occurs in young adults and is due to venereally acquired HSV Type II. The prognosis is excellent, almost all cases recovering spontaneously.
Our case presented with the clinicopathological picture of acute necrotising herpetic encephalitis. Serological evidence indicated the virus type involved to be HSV II.

This report probably represents a previously unrecognised entity, namely acute necrotising encephalitis due to HSV Type II in a non-immunocompromised adult.

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References


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Adult coeliac disease and brainstem encephalitis

SIR: Various neurological disorders have been reported in association with adult coeliac disease. 1–4 Vitamin E deficiency, gluten toxicity and the HLA-A8-antigen are frequently related to coeliac disease. Their possible influence on the development of neurological disorders has often been stated but has never been clarified in detail. 3–5 The neuropathological findings most commonly included degenerative changes whereas inflammatory lesions were rare. 1 7 8 In our case the diagnosis of brainstem encephalitis was established by clinical and CSF investigations. Neuropathological analysis revealed an atypical subacute panencephalitis, an uncommon finding in adult coeliac disease.

The 45 year old male patient in whom coeliac disease had been diagnosed from a jejunal surgical specimen in summer 1985, noticed a marked decrease in vitality in November 1985, 2 weeks after he had returned from a trip to Georgia (USSR). Subfebrile temperature was measured there and in early December 1985 rhythmic jerking of the left arm, the left half of the mouth, the tongue and the soft palate occurred and led to his admission to the neurological clinic on 17 December. Arhythmic myoclonic movements of the left arm, the tongue and the soft palate as well as slight dysarthria and mild unsteadiness in Romberg's test were found on examination. CSF investigation revealed 20 cells/ml, mostly lymphocytes, and an increase of total protein to 82 mg/dl. Thus, the diagnosis of a brainstem encephalitis was established. However, neither serum nor further CSF investigation could determine viral, bacterial or fungal microorganisms as causative agents. In addition, antibodies against glia- 

Fig 1 Section of brain stem. (Luxol fast blue for myelin counterstained with nuclear fast red.) Note the partially necrotic irregular periventricular lesions on the right side (arrows) also involving the hilus of the right dentate nucleus.