EEG findings in tick-borne encephalitis

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SUMMARY EEG findings of epidemiologically and serologically confirmed tick-borne encephalitis patients were compared with findings of patients having acute encephalitis of viral or undetermined origins. Tick-borne encephalitis patients had more bilaterally synchronous bursts of slow waves and more focal abnormalities than did controls. Moreover, their EEGs remained mildly pathological, with increased slow and beta activity and intermittent focal abnormalities in some patients, whereas, EEGs in the controls became normal or borderline, usually within two months. EEG can thus reveal differences between individuals' responses to encephalitis and between different types of encephalitis, even though the clinical pictures are rather similar. Finally, the study shows that tick-borne encephalitis causes changes in the EEG that persist long after the clinical disease appears to have resolved.

Tick-borne encephalitis is a disease caused by any of a number of Group B arboviruses (family *Togaviridae*, genus *Flavivirus*). Tick-borne encephalitis viruses in Eastern Europe, Scandinavia and Finland are closely related antigenically to those responsible for the more serious forms of tick-borne encephalitis, such as Russian spring-summer encephalitis found in Soviet Asia.^{1,2} In Finland, tick-borne encephalitis virus is transmitted by *Ixodes ricinus* ticks which form endemic foci of disease in certain islands of the Turku and Åland archipelagos³ by mechanisms not yet understood.

In most clinical cases of tick-borne encephalitis virus infection in Finland onset of the disease begins in August. The illness may have a biphasic course but more often is characterised by an incubation period of 3 to 5 days, followed by an influenza-like illness lasting 1 to 6 days. However, after an illness-free interval of 3 to 30 days, a second phase of the illness may occur. This is characterised by high fever, meningeal irritation, severe headache and, in some patients, a variety of CNS signs; the fever may remain elevated for as long as 10 days. No serious sequelae have been reported in Finnish patients with documented tick-borne encephalitis. Whereas a useful diagnostic indicator of tick-borne encephalitis

virus as the aetiological agent of an illness is the recollection of being bitten by ticks in the endemic area, definitive diagnosis is made by serological means, that is, the detection of virus-specific IgM antibodies in serum or cerebrospinal fluid after the onset of CNS symptoms or a four-fold rise or fall in antibody levels between paired sera. Isolation of the aetiological agent from serum is possible, but not frequent, during the first phase of illness.

The EEG is almost always abnormal in human encephalitis,⁴ including those patients with tick-borne encephalitis.⁵⁻⁷ We have studied long-term changes in the EEG after acute infections with tick-borne encephalitis virus and, as well, characteristic EEG changes in the acute phase compared to those in clinically similar encephalitides in which the specific viral aetiology was unconfirmed. We found that patients with tick-borne encephalitis, but not with other viral encephalitides, have continuing, possibly permanent, EEG abnormalities.

Methods

Between 1972 and 1982 14 patients with laboratory-diagnosed tick-borne encephalitis were admitted to the Department of Infectious Diseases, Turku City Hospital; we included all 14 in our study. For our purposes it was required that laboratory diagnosis be established serologically, that is by showing the presence of high titre specific IgM antibodies to tick-borne encephalitis virus or the presence of neutralising or complement-fixing antibodies against the Finnish topotype tick-borne encephalitis virus. All patients, seven males and seven females, 12 to 57 years

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Fig 1 Geographic distribution of locations of presumed tick-bites (filled circles). Two patients were bitten on a sailing trip (boat). Note the concentration of cases.

old, reported being bitten by ticks during visits to or residence in tick-borne encephalitis-endemic areas of the Turku or Åland archipelagos (fig 1). All had high fever, headache, nausea and a variety of CNS signs, with disease onsets from August 5 to September 15. None of the patients had permanent neurological deficits after subsidence of the acute illness; however, some complained of headaches and lethargy for many months after the acute phase of illness.

The control group consisted of 14 encephalitis patients with presumed viral or non-viral infections known not to be caused by tick-borne encephalitis virus. The following criteria were chosen in selecting this group: (1) All fulfilled the clinical criteria of meningoencephalitis and had white cells in their cerebrospinal fluids. (2) All had EEGs consistent with pathologic processes upon initial clinical examination. (3) Patients with suspected or known EEG abnormalities previous to the current illness were excluded, that is, those who had experienced stroke and other cerebral insults, nonviral encephalitides, epilepsy etc. (4) Children under 10 years old were excluded because physiological maturation may mask changes correlated with slow recovery from encephalitis. (5) At least two successful EEG recordings were performed three months apart, except in cases where the EEG became normal or borderline sooner than this.

Electroencephalography All recordings were made with a 16 channel ink-jet Siemens-Elema EEG recorder. Electrodes were placed according to the international 10/20 system. We visually (and independently) assessed the EEG curves and an interpretation was agreed upon after considering the following variables: normality, general disturbance, generalised slowing, asymmetry/focus, partial or generalised irritation and pathological rhythms.

We were able to obtain two to six recordings from the onset of illness to a maximum of 30 months after onset of

illness. The first recordings were made 2 to 21 (mean 12) days after the onset of the second (major) phase of the disease and the CNS signs. Subsequent recordings were made, on average, 52, 175, 281, 480 and, in one patient, 900 days after the onset of primary illness. In the control group two recordings (mean of 8 and 62 days after onset of illness) were usually sufficient to determine normality.

Results

EEG FINDINGS IN TICK-BORNE ENCEPHALITIS CASES

The first EEG, taken an average of 12 days after onset of illness, was pathological in all patients. All 14 had diffuse slowing, 8/14 bilaterally synchronous bursts of slow waves (fig 2) and 6/14 had focal intermittent abnormalities in their EEGs; beta activity was increased in 5/14 cases. In the second recording (13 patients) diffuse slowing was milder than at first. By the final examination (2 to 30 months from the start of the disease) none of the patients had completely normal EEGs (fig 3). Six of 14 had borderline EEGs with mild general slowing, 8/14 had pathological EEGs with moderate diffuse slowing and 4/14 had intermittent focal abnormalities, although none of the 14 had constant cortical EEG focus. Five of the 14 complained of headache and fatigue many months after the major disease. Eleven patients had intermittent focal abnormalities in some phase of their disease (fig 4). One patient, with a history of optic neuritis, had a relapse of multiple sclerosis just after the encephalitic phase.

Fig 3 Typical EEG recording of tick-borne encephalitis in the acute phase of the disease (5 days after the onset of the symptoms). General disturbance and frontal intermittent rhythmic delta activity (FIRDA) are prominent.

Fig 4 Same patient as in figure 3 about four months later. The general disturbance has resolved but distinct intermittent focal abnormality can be seen on the left temporal area.

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EEG FINDINGS IN CONTROLS

The first EEG, taken on an average of 8 days after the onset of illness, was pathological in every case. All had moderate or pronounced diffused slowing, 2/14 had bilaterally synchronous bursts of slow waves and 7/14 had slight EEG asymmetries early in convalescence. The second recording, made an average of 62 days after the onset of illness, was normal or borderline in 9/14 patients (fig 3). Four other patients whose second EEG remained pathological had third or fourth recordings taken, but by this stage of the disease the EEG abnormalities had resolved in all but two, both of whom had been shown to have had encephalitis subsequent to clinically-presumed infections with varicella virus.

Discussion

The diagnosis of meningitis versus meningoencephalitis is not always clear-cut. In aseptic meningitis the EEG is usually normal or shows only mild diffuse slowing with theta activity dominating, whereas in encephalitis the EEG is always abnormal.⁴ Therefore we included in the control group only those patients whose first EEG was pathological, in order to be certain that all had had encephalitis. Patients with tick-borne encephalitis were most severely affected, as far as EEG changes were concerned. Normally the course of infection with tick-borne encephalitis virus is mild or even subclinical; our case selection, however, was skewed toward inclusion of severe cases only. Many individuals living on islands in the Finnish archipelago where tick-borne encephalitis virus occurs focally and endemically have high titres of virus-specific antibodies in their sera but deny having had clinical encephalitis or been hospitalised for the disease.

Since this was a retrospective study there was considerable variation in the interval between the onset of disease and electroencephalography. The control group was somewhat younger than the tick-borne encephalitis group (means 30.0 and 35.6 years, respectively) but we do not consider this to have had significant impact upon the findings.

The central finding of this study was that even though the clinical picture is similar in uncomplicated encephalitides of different aetiology, none of the patients had neurological deficits following resolution of the apparent clinical symptoms and all returned to work or school, yet there were clear differences in EEG findings. Patients with tick-borne encephalitis had more generalised bilaterally synchronous slow waves and more focal intermittent abnormalities during some phase of their illness. Intermittent focal abnormalities may be a sign of subcortical lesions, while bilaterally synchronous

slow waves and diffuse slowing suggest diffuse encephalopathy.⁸ The most striking difference between tick-borne encephalitis and control patients was, however, the persistence of changes in those infected with the tick-borne encephalitis virus. None of the tick-borne encephalitis patients had completely normal EEGs in the follow-up period, while only two controls had persistent abnormal EEGs; these two patients had been diagnosed clinically as having had varicella. This postinfectious encephalitis resembled tick-borne encephalitis in its EEG manifestations.

Although all 28 patients' neurological statuses were normal after recovery from their illnesses, some patients in the tick-borne encephalitis group complained of headache and fatigue. One patient with previous optic neuritis had a relapse of multiple sclerosis shortly after the acute phase of tick-borne encephalitis, suggesting that tick-borne encephalitis was a significant contributor to or cause of the relapse. Considering these observations together with the documented EEG changes, it is possible that the disease process in tick-borne encephalitis continues some time after the severe and, debilitating secondary phase and may have its correlate in some unknown subtle performance deficit or altered vigilance states not detectable by present-day methods of neurological evaluations.

As regards the general EEG interpretation, this study has shown that tick-borne encephalitis, possibly postinfectious varicella encephalitis and other encephalitides, particularly viral encephalitides, may result in changes persisting for years or even for the life of the patient. Conversely, if an abnormal EEG with no obvious aetiology is found, evidence for a history of encephalitis should be sought.

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