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Leukocyte migration inhibition by a brain tissue antigen and electroencephalography in uncomplicated measles

By

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In 11 patients with uncomplicated measles and in 10 control patients with acute enteritis, electroencephalography and leukocyte migration inhibition test using basic myelin protein as antigen were carried out. There were no EEG abnormalities and no migration inhibition in the control group. Leukocyte migration inhibition was observed in 9 measles patients; among these 5 had slight or moderate EEG abnormalities. It is suggested that EEG abnormalities have the same pathological background in uncomplicated measles as in measles encephalitis.

In cases of uncomplicated measles EEG changes are often observed [1, 2, 3, 4, 5, 7, 9, 10, 11, 13], though the pathological processes eliciting these EEG-abnormalities are far from being understood. In a previous study [8] we have shown by the leukocyte migration inhibition (LMI) technique that a cellular reactivity to brain tissue antigens could be found in a high percentage of patients with measles encephalitis. This reactivity usually disappeared after clinical recovery, but persisted when EEG-changes were still present. These observations have made us to examine uncomplicated measles cases in order to study whether autoimmune processes were involved in the pathogenesis of this clinically inapparent cerebral disorder associated with measles.

MATERIALS AND METHODS

Patients. Two groups of hospitalized patients were tested. The first group comprising ten, 4 to 12 years old children with acute enteritis, served as control. The second group consisted of eleven, 4 to 12 years old patients with uncomplicated measles. Neither of the patients had had any neurological disease nor did they display any clinical sign of a nervous system disease during their stay at the hospital. EEG-tracings and LMI test were carried out on the same day. Patients of the control group were tested on one occasion each. Measles patients were examined twice, *viz.* on the 1st or 2nd and on the 7th or 8th day after the onset of rash.

Electroencephalography was carried out by an Alvar Reega-VIII type portable encephalograph. Fifteen electrodes were applied to the frontopolar, precentral, central, parietal, occipital and the three temporal areas. Bipolar conventional leads were used. The time constant was 0.3 sec,

paper speeds were 15 and 30 mm per sec. Under favourable conditions a three min hyperventilation was applied. The recordings were analyzed visually.

LMI tests were carried out by the method described by SØBORG and BENDIXEN [12]. Basic myelin protein (BMP) prepared from human brain by the method of KIES [6] was used as an antigen, at a concentration of 100 μg/ml in the test chambers. Migration indices (MI) were calculated as described previously [8]. MI-s less than 0.8 meant significant inhibition when evaluated with Student's *t*-test and were therefore considered "positive" throughout the study.

RESULTS

All the control patients had a normal EEG. Of the 11 measles patients, 5 had an abnormal EEG in the acute phase of the disease, showing slight or moderate background activity slow-down (Figs. 1, 2). There were no focal alterations, but in two patients unilateral slow-down predominated. In one case slightly sharp theta group could be seen in the left central area. In the convalescent period, 3 of these 5 patients still displayed slight EEG changes.

LMI values are presented in Fig. 3. Each patient of the control group had a normal MI value. Of the 11 measles patients 7 in the acute phase and 5 in the convalescent phase had a MI of less than 0.8. Only three patients were positive both in the acute and in the convalescent phase, so we found 9 patients altogether who had a positive LMI test at least once throughout the study. EEG changes and LMI

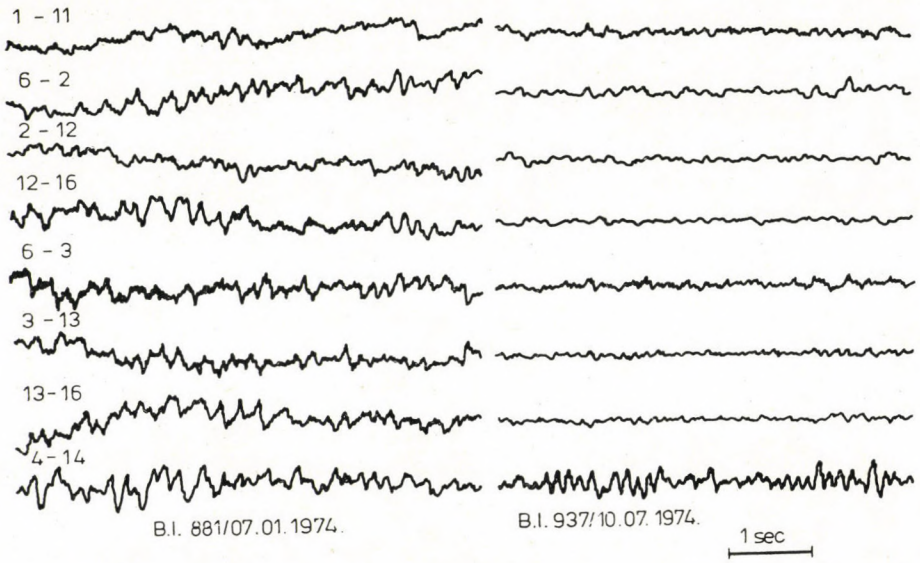

FIG. 1. EEG in uncomplicated measles. B. I. 5 year-old girl. I.: 1st day after onset of rash. Polyrhythmic theta waves with 7—8/sec alpha periods. Slight diffuse slow-down. II: 8th day after onset of rash. Background activity consisting of alpha waves. Normal EEG

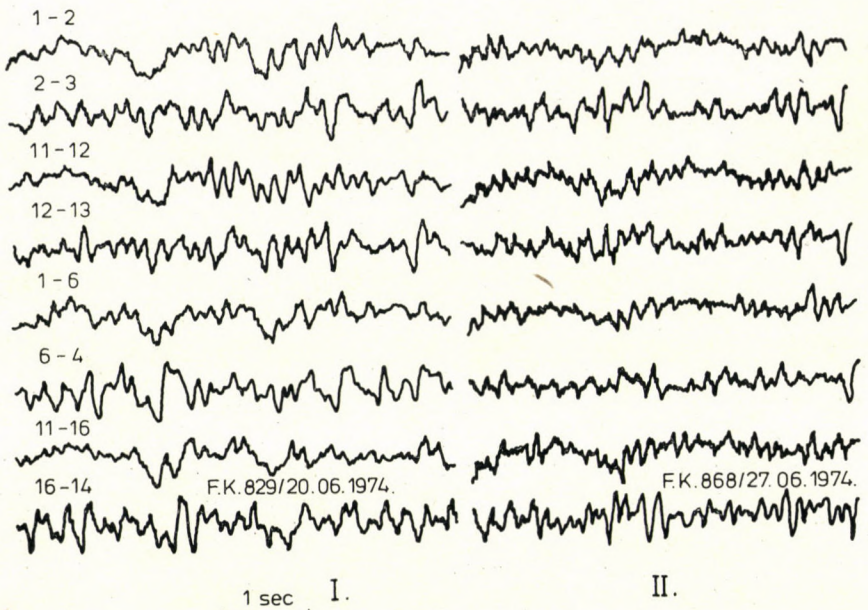

FIG. 2. EEG in uncomplicated measles F. K. 8 year-old boy. I: 1st day after onset of rash. Diffuse slow background activity with 2—3 cps delta periods. Moderate diffuse functional disturbance. II.: 7th day after onset of rash. Mixed alpha-theta background activity. Theta groups present all over the brain. Slight diffuse slow-down

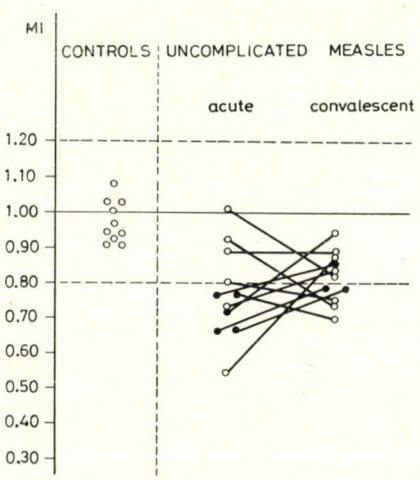

FIG. 3. *Leukocyte migration indices by basic myelin protein and EEG positivity in acute enteritis (controls) and in uncomplicated measles.* Symbols: Dots indicate MI-values with EEG abnormality; circles indicate MI-values with normal EEG at the time of testing

positivity showed a fairly good correlation; every patient with an EEG abnormality was LMI positive at least once during the disease. In 4 patients with LMI positivity no EEG changes could, however, be registered either in the acute phase or during convalescence.

Discussion

In accordance with other authors [2, 3, 4, 7, 13] we found EEG abnormalities in about one half of our patients with uncomplicated measles. It is of theoretical and practical interest to know whether the CNS disturbances thus detected developed on the same pathological basis as does a clinically apparent encephalitis. The EEG supplies scanty information in this respect since different pathological conditions can lead to the same EEG changes. It is more promising to approach the problem by considering the EEG together with the LMI test. A positive LMI test means that the patient's leukocytes are hypersensitive to myelin substances. For the sensitization to take place, myelin has to be released as a consequence to myelin sheath injury. Thus LMI positivity, i.e. inhibition of LM by BMP, can be regarded as evidence of a certain type of nervous tissue damage.

In a previous study we found that EEG abnormality and LMI positivity were closely related in patients with measles encephalitis [8] and the same relation was observed in the present study for measles without encephalitis. Thus, myelin destruction seems to have an important role in the alterations detected by EEG, and cerebral damage in uncomplicated measles is probably more frequent than can be detected by EEG with the usual leads, since we found four patients with a normal EEG but with a positive LMI test.

EEG abnormalities are less pronounced and less persistent in measles without than with encephalitis. LMI positivity was also less persistent in uncomplicated measles than in measles encephalitis [8]. Besides, some authors [9, 10, 11] found similar though less marked abnormalities of the CSF in uncomplicated measles than in measles encephalitis. On the bases of these observations it may be suggested that pathological processes in the nervous system differ quantitatively in measles encephalitis and uncomplicated measles though the development of clinically apparent encephalitis may well be due to some additional pathogenetic factors.

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