LOCAL IgG SYNTHESIS IN THREE PEDIATRIC PATIENTS WITH CUBAN EPIDEMIC NEUROPATHY

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ABSTRACT- Three pediatric patients with Cuban epidemic neuropathy were studied. Cerebrospinal fluid and sera were simultaneously obtained. Albumin and IgG were quantified by immunodifusion. Albumin quotient and local synthesis of IgG were calculated by Reiber/Felgenhauer formula. A patient with optic neuritis had a dysfunction of the blood-cerebrospinal fluid barrier. All the group had local synthesis of IgG.

KEY WORDS: Cuban epidemic neuropathy, optic neuritis, peripheral neuropathy, cerebrospinal fluid, intrathecal synthesis.

PATIENTS

Sera and cerebrospinal fluid (CSF) from three pediatric patients suffering from symptoms of CEN were taken. The diagnosis of CEN was made by clinical criteria according to PAHO's Expert Committee.

CEN has two main presentations: the first one, an optic neuritis and a second form as peripheral neuropathy. Optic neuritis is retrobulbar, the optic nerve head appears normal. The visual acuity is decreased, and there is abnormal color perception, an afferent pupillary defect, and always a central scotoma.

Peripheral neuropathy produces a motor neuropathy with mild sensory impairment. The distribution of symmetrical distal weakness, with foot drop or wrist drop, paresthesias in the feet and legs. Sensation is decreased and the tendon reflexes are depressed. Cranial nerve involvement is unusual and the CSF protein content is normal, helping to differentiate from Guillain-Barre's syndrome.
A) Patient 1. Age: 12 years old. $Q_{Alb}$ and $Q_{IgG}$ of the Patient 1 with optic neuritis. $Q_{Alb}<6.5$, age dependent limit, i.e. no blood/CSF barrier dysfunction and an additional intrathecal synthesis of IgG.

B) Patient 2. Age: 6 years old. $Q_{Alb}$ and $Q_{IgG}$ of Patient 2 with optic neuritis. $Q_{Alb}>5$, age dependent limit. This patient has a blood/CSF barrier dysfunction and an additional intrathecal synthesis of IgG.

C) Patient 3. Age: 10 years old. $Q_{Alb}$ and $Q_{IgG}$ of Patient 3 with peripheral neuropathy. In contrast to Patient 2, this patient has normal $Q_{Alb}$ ($Q_{Alb}<5$, age dependent limit) and an additional local synthesis of IgG.

Fig 1. Reiber/Felgenhauer quotient diagram.

In the diagram, $Q_{IgG}$ (IgGCSF/IgGSERUM) is shown as a function of $Q_{Alb}$ (AlbuminCSF/AlbuminSERUM) representing the blood/CSF barrier function. Below the discrimination line (fitted by a hyperbolic curve) the fraction in CSF is primary blood-derived. Above the discrimination line, an increasing contribution of the locally CNS synthesized IgG can be demonstrated (given as a percent of locally synthesized IgG of the corresponding total CSF concentration). The dashed lines represent the percentile curves of local IgG synthesized in the central nervous system.
Patient 1. Female. She had 12 years old. Had optic neuritis. CSF analysis: colorless, transparent, non-cells, normal CSF protein content, normal glucose concentration. Bacteria and virus were not found by conventional microbiology and virology tests. No oligoclonal bands was performed.

Patient 2. Female. She had 6 years old. Had optic neuritis. CSF analysis: colorless, transparent, non-cells, normal CSF protein content, normal glucose concentration. Bacterial and virus analysis were negative. No oligoclonal bands was performed.

Patient 3. Male. He had 10 years old. Had peripheral neuropathy. CSF analysis: colorless, transparent, 4x10⁶ cells/L; both normal protein and glucose concentration. No bacteria or virus were found. No oligoclonal bands was performed.

METHODS

IgG and albumin were measured in serum and CSF by NOR and LC Partigen immunodiffusion plates, respectively (Behringwerke AG, Marburg).

The calculations were performed by the Neuroimmunolab⁷. IgG intrathecal synthesis was calculated by the improved⁸ Reiber/Felgenhauer formula⁸.

Albumin quotient (Qalb = AlbCSF / AlbSERUM) was calculated.

RESULTS

Fig 1 shows the Reiber/Felgenhauer quotient graph. The black points indicate each studied patient. All the three patients were placed over the reference curve. It means a local synthesis of IgG.

The Patient 2 (Fig 1b) has a blood/CSF barrier dysfunction and an additional intrathecal synthesis of IgG.

DISCUSSION

The diagnosis of CEN was made by PAHO's Expert Committee. The diagnosis was performed during the outbreak of CEN. No other neurological disease were involved in the patients.

Albumin quotient (Qalb) is a measure of the blood-CSF barrier function. Albumin serve as a marker of the protein diffusion through this barrier because of its exclusive hepatic synthesis. Albumin also has not great variations between pathological and normal conditions and it does not change in CSF.

A patient with optic neuritis has blood-CSF dysfunction because its Qalb is greater than the Qalb age dependent limit. This phenomenon has been described in several adult patients with the optic neuritis form of CEN².

The patients had local IgG synthesis according to Reiber/Felgenhauer formula and diagram. In principle, one must differentiate between two cases of IgG local synthesis: a first case, in which a biological agent would be the etiologic agent of the disease; and a second case, where secondary polyspecific immune reaction took place without a persistent antigen or corresponding clinical signs of a virus infection.

No infectious agent was isolated from CSF culture in our patients. The disease appears suddenly without clinical signs of a previous viral or bacterial infection.

On the other hand one must keep on mind that local synthesis in the brain is a long process, often occurring over many years⁶ and it does not indicate precisely the acuity of the process.

It is not possible to establish that local IgG synthesis is a common characteristics of CEN because this paper shows the results of only three patients. Also a local IgG synthesis is a common mechanism in many neurological diseases but it do not indicate a common etiologi.

The increased amounts of intrathecal IgG play a prominent role in inflammation and demyelination. This view is supported by the demyelination activity of aggregated IgG in form of immune complex in the peripheral nervous system³.
REFERENCES


