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Effect of epileptic seizures on the cerebrospinal fluid — A systematic retrospective analysis

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Summary
Objective: Analyses of the cerebrospinal fluid (CSF) are obligatory when epileptic seizures manifest for the first time in order to exclude life-threatening causes or treatable diseases such as acute infections or autoimmune encephalitis. However, there are only few systematic investigations on the effect of seizures themselves on CSF parameters and the significance of these parameters in differential diagnosis.
Methods: CSF samples of 309 patients with epileptic and 10 with psychogenic seizures were retrospectively analyzed. CSF samples were collected between 1999 and 2008. Cell counts, the albumin quotient, lactate and Tau-protein levels were determined. Findings were correlated with seizure types, seizure etiology (symptomatic, cryptogenic, occasional seizure), and seizure duration.
Results: Pathological findings were only observed in patients with epileptic but not with psychogenic seizures. The lactate concentration was elevated in 14%, the albumin quotient in 34%, and the Tau protein level in 36% of CSF samples. Cell counts were only slightly elevated in 6% of patients. Different seizure types influenced all parameters except for the cell count: In status

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epilepticus highest, in simple partial seizures lowest values were seen. Symptomatic partial and generalized epileptic seizures had significantly higher Tau-protein levels than cryptogenic partial seizures. In patients with repetitive and occasional epileptic seizures, higher Tau-protein levels were seen than in those with psychogenic seizures. Duration of epileptic seizures was positively correlated with the albumin quotient, lactate and Tau-protein levels. High variability of investigated CSF parameters within each subgroup rendered a clear separation between epileptic and psychogenic seizures impossible.

Significance: Elevated cell counts are infrequently observed in patients with epileptic seizures and should therefore not uncritically be interpreted as a postictal phenomenon. However, blood–CSF barrier disruption, increased glucose metabolism and elevation of neuronal damage markers are observed in considerable percentages of patients and depend on many factors such as etiology, seizure type and duration.

Introduction

Epilepsy is one of the most common neurological diseases. Approximately 1% of the world's population suffers from epilepsy (recurrent seizures) and about 5% of all people have at least one epileptic seizure during life time. Epileptic seizures can be promoted by a genetic predisposition, be related to alcohol and other intoxications or metabolic aberrations, or be caused by acute or chronic cerebral structural alterations/injuries (most commonly inflammation, cerebrovascular disease, tumor, CNS malformation or neurodegeneration) (Amatniek et al., 2006; Cloyd et al., 2006; Guerrini and Dobyns, 2014; Hauser et al., 1993; Ong et al., 2014; Pallud et al., 2014; Ramantani et al., 2014; Scheffer and Mefford, 2014; Sisodiya et al., 2009; Wood, 2014). They manifest with a variety of symptoms and several classification systems have been proposed and revised so far (Berg et al., 2010; Engel, 2006; Fisher et al., 2005, 2014). Commonly they are divided into seizures with partial onset such as simple partial seizures, complex partial seizures and secondarily generalized tonic–clonic seizures and in primarily generalized seizures such as absences, myoclonic seizures and primarily generalized tonic–clonic seizures. Epilepsy patients may present with only subjective perceptions (auras) or with objective motor or autonomic phenomenona. The duration of epileptic seizures varies between few seconds (e.g. absences), few minutes (simple and complex partial seizures, generalized tonic–clonic seizures), >5 min (status epilepticus), and can even last for years (epilepsia partialis continua). They can become manifest at any age, the highest incidence for epilepsy onset is seen during the first year of life and in older people (>60 years). Moreover, psychogenic (non-epileptic seizures) can mimic the semiology of epileptic seizures and sometimes it is difficult to differentiate between both entities (Cuthill and Espie, 2005). A clear differentiation, however, has important implications on treatment (Reuber et al., 2002).

The diagnostic procedure following a first epileptic seizure includes cerebral imaging, blood examinations, electroencephalography and an investigation of the cerebrospinal fluid (CSF) in order to exclude dangerous causes which require immediate treatment. The basic CSF investigation programm comprises the determination of cell counts, glucose and lactate levels in serum and CSF as well as of albumin, IgG, IgM, IgA and their quotients. The Tau-protein level is a parameter for neurodegeneration and axonal damage and is usually investigated under special questions. These parameters give already a broad overview over possible inflammation, blood–CSF barrier function, glucose metabolism, and neuronal damage (Brettschneider et al., 2005; Chow et al., 2005; Deisenhammer et al., 2009; Stangel et al., 2013; Steinhoff et al., 1999).

In the present systematic study, we asked if CSF parameters like cell count, albumin quotient, lactate and Tau-protein level are altered in patients with epileptic seizures. Moreover, we analyzed whether seizure types (simple partial, complex partial, primarily generalized or secondarily generalized seizures), seizure etiology (cryptogenic, symptomatic, occasional) and duration of the seizure had an influence on these parameters. Finally, we investigated if it is possible to differentiate between epileptic and psychogenic, non-epileptic seizures with the help of CSF analyses.

Patients and methods

Patient selection

Patients were retrospectively collected between 1999 und 2008. All patients were treated at the University of Ulm, Department of Neurology, Germany. A total of 319 patients were included. Three hundred and nine patients suffered from epileptic seizures, 10 patients had psychogenic seizures. Information on the patients' history such as age at lumbar puncture, epileptic syndrome (idiopathic/cryptogenic versus symptomatic epilepsy), MRI data, seizure semiology, duration of seizures, and time interval between seizure and lumbar puncture were extraced from the medical charts. Table 1 gives a summary of the clinical characteristics of included patients. The diagnosis of an epileptic seizure was based on clinical history, electroencephalography and magnetic resonance imaging (MRI) or cerebral computed tomography (CCT) data. Patients with a clinical, laboratory diagnostics and or neuroimaging signs of CNS inflammation as cause of the epileptic seizure were excluded. The mean time interval between seizure and lumbar puncture was 1.74 days (standard deviation 2.631 days), median 1 day. The maximal time interval was 14 days.