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Epilepsy in an elderly patient caused by Hashimoto's encephalopathy

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ABSTRACT – Late-onset seizures are frequently caused by cerebrovascular disease, head trauma, degenerative disorders or CNS tumors. In one-third of cases, the etiology remains obscure. In only 60-70% of adult-onset epilepsy is antiepileptic drug treatment successful. Although seizures are a well-known symptom of Hashimoto's encephalopathy, it is rarely taken into consideration as differential diagnosis in epilepsy. We describe a 74-year-old patient with seizures and slowly progressive cognitive deterioration. Previous therapeutic attempts with carbamazepine, lamotrigine and topiramate had not been effective. We suspected Hashimoto's encephalopathy, which was treated with prednisolone 100 mg/d over 6 months. This regimen led to a cessation of the complex partial seizures and cognitive improvement. We conclude that Hashimoto's encephalopathy is a possible differential diagnosis in epilepsy in the elderly. Glucocorticoid treatment should be considered if there are no important contraindications.

Key words: Hashimoto's encephalopathy, epilepsy in the elderly, glucocorticoid treatment, cognitive impairment

Elderly people have the highest incidence of seizures, epilepsy and status epilepticus among all age groups, with 1% of individuals over the age of 60 being affected (Cloyd *et al.* 2006). The most common causes of epilepsy in the elderly are cerebrovascular disease, head trauma, neurodegenerative disorders and CNS tumors, but in approximately one-third of cases the etiology remains obscure (Ramsay *et al.* 2004). In the elderly, the most frequent clinical symptoms are complex partial seizures, followed by generalized tonic-clonic seizures and simple partial seizures (Krämer 2001). Currently, antiepileptic medication is effective in only 60-70% of adult individuals (Duncan *et al.* 2006).

We present a case of an elderly patient suffering from epilepsy and mild cognitive impairment whose complex partial seizures did not respond to conventional antiepileptic treatment. Following a diagnosis of Hashimoto's encephalopathy (HE) we initiated treatment with prednisolone, which led to cessation of seizures and cognitive improvement. HE should be considered as a cause of epilepsy, especially when the condition is unresponsive to common antiepileptic treatment.

Case report

A 74-year-old retired farmer was referred to the Memory Clinic of the

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University Hospital, Tübingen in January 2005 because of memory impairment that had been progressing slowly over two years. He reported difficulty in finding words and impaired spatial orientation. Moreover, his wife described episodes of oral automatisms accompanied by unintelligible sounds, subsequent loss of consciousness and a post-ictal state of confusion lasting 15 to 30 minutes, which had all started in November 2002. After enduring these episodes twice a week, he was admitted to the University Hospital of Tübingen in December 2002. Magnetic resonance imaging of the brain revealed mild global atrophy. Extra- and transcranial Doppler sonography was unremarkable. The electroencephalogram (EEG) showed intermittently occurring spikes and sharp waves bifrontotemporal and complex partial seizures were diagnosed. An extensive cardiological workup revealed hypertrophic cardiomyopathy without obstruction, and asymptomatic ventricular salves. Metoprolole and carbamazepine were prescribed. After titrating carbamazepine up to a dose of 800 mg per day, the patient developed slight ataxia without any decrease in seizure frequency. Antiepileptic treatment was switched to lamotrigine up to a dose of 200 mg per day. After the patient developed a rash, he was put on topiramate at 100 mg per day. Seizure frequency dropped to once a week.

When we first saw him in January 2005, psychopathological findings were unremarkable. Neuropsychological testing showed impaired executive functions, reduced word fluency and deficits in verbal and figural memory. There were no pathological findings on medical and neurological examination.

The EEG still showed bifrontotemporal sharp waves *(figure 1A)*. Anti-thyroid peroxidase antibodies (TPO-Ab: 2.9 kU/L, normal value < 2.0) and anti-thyroglobulin antibodies (Tg-Ab: 23.1 kU/L, normal value < 1.0) were increased. Thyroid-stimulating hormone, free thyroxine and tri-iodthyronine were within the normal range. Thyroid ultrasound did not show a typical pattern of Hashimoto thyroiditis. A needle biopsy of the thyroid gland to demonstrate lymphocytic infiltration was not performed. Further, extensive workup of blood samples and clinical chemistry, including metabolic, infectious, paraneoplastic and immunological parameters, were unremarkable.

Cerebrospinal fluid analysis, including cell count, immunoglobulin G index, oligoclonal bands, tau-protein, beta-amyloid 1-42, protein 14-3-3, neuron-specific enolase (NSE), as well as bacteriological and virological examinations revealed no pathological findings.

We suspected HE and started treatment with prednisolone, 100 mg orally per day. Gradually, the frequency of seizures diminished and the EEG normalized showing finally an 8-9 Hertz alpha rhythm without epileptic discharges *(figure 1B)*. After six months of treatment with prednisolone, no further seizures occurred, and three months later topiramate was tapered with no clinical and electroencephalographic changes. Five months later we also started to taper prednisolone. No epileptic discharges were observed on the EEG, and the patient and his wife did not report any new seizures. TPO-Ab normalized and Tg-Ab concentrations remained stable (32.4 kU/L). Neuropsychological testing showed improvement in word fluency as well as verbal and figural memory. Executive functions were unremarkabel at this time.

Six months later, physical, neuropsychological and labarotory examination of the patient, as well as EEG findings, remained stable. No seizures were reported, despite the fact that the patient was receiving no antiepileptic medication or glucocorticoid therapy.

Discussion

The first patient with "Hashimoto's disease and encephalopathy" was described in 1966 (Brain *et al.* 1966). Since then, about 200 cases of this poorly understood disease have been reported. Diagnostic criteria include the presence of a neuropsychiatric syndrome associated with anti-thyroid antibodies (anti-thyroid peroxidase antibodies, TPO-Ab, anti-thyroglobulin antibodies, Tg-Ab), when other etiologies have been excluded. In most cases, the electroencephalogram shows abnormalities and frequently, a high concentration of cerebrospinal fluid protein is found. However, recent studies have shown that clinical, laboratory, and radiological findings associated with HE are more variable than previously reported (Castillo *et al.* 2006). Two subtypes of the disorder have been described: a vasculitis-like type, characterized by multiple, stroke-like episodes, and a diffuse progressive type, characterized by cognitive impairment and psychopathological symptoms. Antibody titres do not distinguish between these disease types and do not correlate with the severity of the clinical presentation (Kothbauer-Margreiter *et al.* 1996). Successful treatment with steroids and other immunosuppressants, and with plasma exchange has been reported (Hussain *et al.* 2005).

Seizures are a well-known clinical feature of HE. Recently, a case of recurrent generalized convulsive status epilepticus (GCSE) as the main feature of HE was reported, which responded well to intravenous methylprednisolone (Ferlazzo *et al.* 2006). Other cases of GCSE due to HE had unfavorable outcomes despite steroid treatment (Striano *et al.* 2006).

Anti-thyroid antibodies are not routinely measured in patients with late-onset seizures of unknown etiology. We would like to emphasize the importance of this procedure, especially in cases resistant to treatment. Regardless of a history of thyroiditis or abnormal thyroid function, even if only slightly increased titres of anti-thyroid antibodies are detectable, steroid treatment should be initiated. We initiated treatment with approximately 1.5 mg/kg prednisolone per day, adapting a recommended scheme for middle-aged patients (Kothbauer-Margreiter *et al.* 1996)

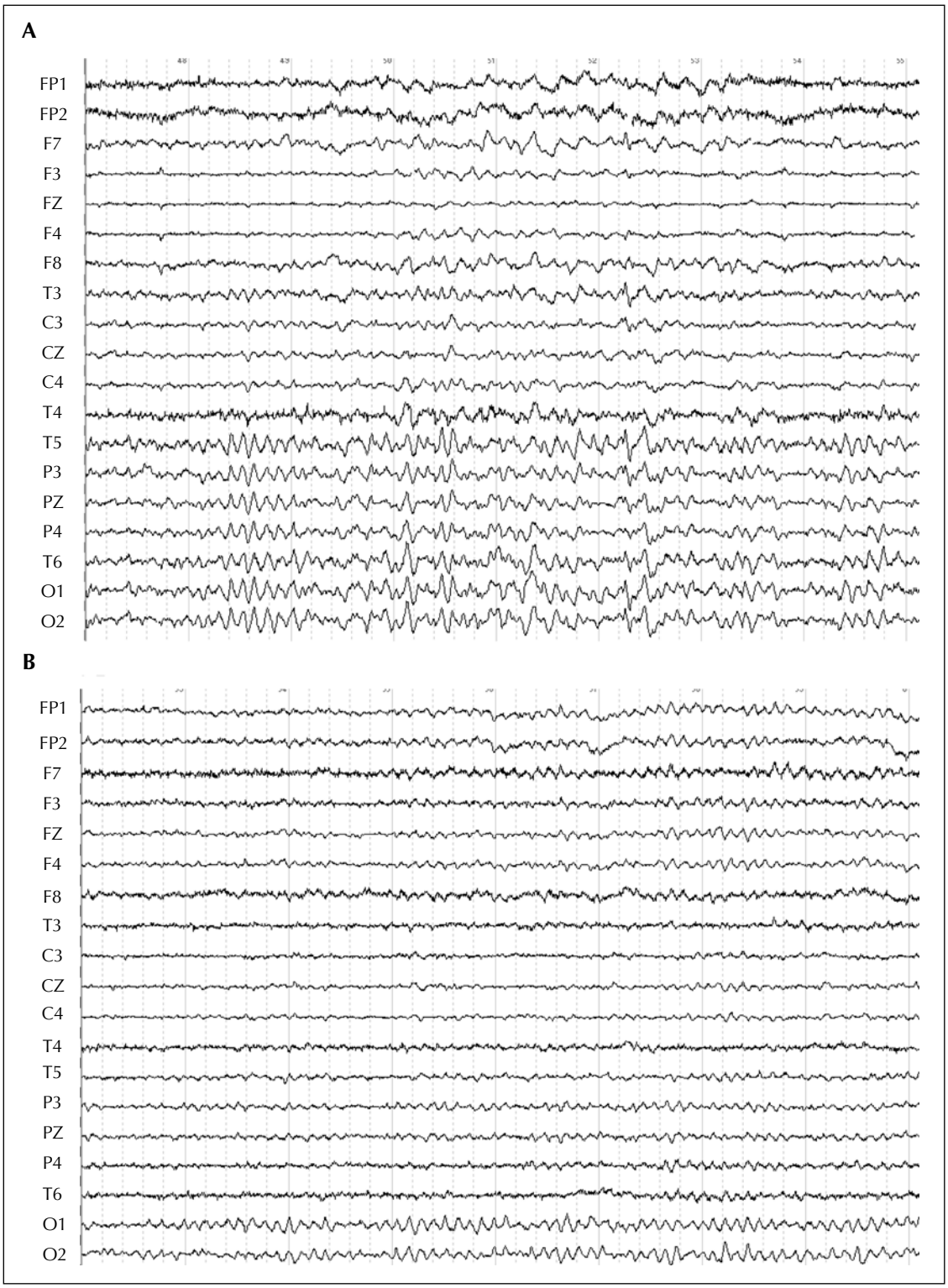

Figure 1. A) EEG performed in January 2005 showing sharp waves bifrontotemporally in this recording against a common reference in F7 and T3 on the left and in F8 on the right and a triphasic wave in T5 (medication topiramate 100 mg/d). **B**) EEG performed seven months later (August 2005) showing a normal 8-9 hertz alpha rhythm (medication - topiramate 100 mg/d and prednisolone 100 mg/d). A routine, digitized EEG (Nihon Kohden, Neurofile V2.91, Japan) with a sampling rate of 256 Hertz, a time constant of 0.3 seconds and a low pass filter of 70 Hertz, was performed. Eyes were closed during recording. Gain was 3.5 µV/mm, period of time is eight seconds.

and continued this regimen for 18 months. Within six months, the epileptic activity had ceased completely. Tapering topiramate after nine months and prednisolone after 14 months did not lead to a recurrence of seizures. In addition, cognitive impairment improved. This was most likely due to successful treatment of the HE, but possibly also because of the removal of topiramate, which is known to cause impaired cognition in some patients (Duncan *et al.* 2006). At the follow-up visit six months later, the patient remained stable without antiepileptic drugs or a glucocorticoid.

In summary, our report alludes to HE as a relevant differential diagnosis in intractable epilepsy in the elderly of obscure etiology. In these cases, evaluation of anti-thyroid antibodies should be performed, and long-term steroid treatment should be initiated if HE is suspected. □

References

Brain L, Jellinek EK, Ball K. Hashimoto's disease and encephalopathy. *Lancet* 1966; 2: 512-4.

Castillo P, Woodruff B, Caselli R, *et al.* Steroid-responsive encephalopathy associated with autoimmune thyroiditis. *Arch Neurol* 2006; 63: 197-202.

Cloyd J, Hauser W, Towne A, *et al.* Epidemiological and medical aspects of epilepsy in the elderly. *Epilepsy Res* 2006; 68S: S39-S48.

Duncan JS, Sander JW, Sisodiya SM, *et al.* Adult epilepsy. *Lancet* 2006; 367: 1087-100.

Ferlazzo E, Raffaele M, Mazzù I, *et al.* Recurrent status epilepticus as the main feature of Hashimoto´s encephalopathy. *Epilepsy Behav* 2006; 8: 328-30.

Hussain NS, Rumbaugh J, Kerr D, *et al*. Effects of prednisone and plasma exchange on cognitive impairment in Hashimoto encephalopathy. *Neurology* 2005; 64: 165-6.

Kothbauer-Margreiter I, Sturzenegger M, Komor J, *et al.* Encephalopathy associated with Hashimoto thyroiditis: diagnosis and treatment. *J Neurol* 1996; 243: 585-93.

Krämer G. Epilepsy in the elderly: Some clinical and pharmacotherapeutic aspects. *Epilepsia* 2001; 42(Suppl 3): 55-9.

Ramsay RE, Rowan AJ, Pryor FM. Special considerations in treating the elderly patient with epilepsy. *Neurology* 2004; 62 (Suppl 2): S24-S29.

Striano P, Pagliuca M, Andreone V, *et al*. Unfavourable outcome of Hashimoto encephalopathy due to status epilepticus. *J Neurol* 2006; 253: 248-9.