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The Comorbidity of Focal Epilepsy and Narcolepsy Type 1 – Two Case Reports

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Abstract

The aim of this study is to remind the possibility of co-occurrence of epilepsy and narcolepsy. In the first case report, narcolepsy type 1 was diagnosed in 29-year-old female. After one year of the treatment with modafinil a new episodes of automatic behavior appeared. Patient was reevaluated and the diagnosis of focal epilepsy with partial complex seizures was established. Patient was treated with modafinil and lamotrigine and became seizure-free. In the second case report a 21-year-old female was referred with a typical history of narcolepsy type 1, but also with atypical episodes of gazing and automatic behavior with amnesia for these episodes. Narcolepsy type 1 and focal epilepsy was diagnosed. Some clinical symptoms of narcolepsy (cataplexy, automatic behavior, episodes of sleep attacks) need to be carefully analyzed by EEG and video-EEG not to overlook the epilepsy.

CASE REPORT

INTRODUCTION

Narcolepsy is a rare and underdiagnosed disease. It may be misdiagnosed as epilepsy and there is also possible comorbidity of narcolepsy and epilepsy that may be overlooked. Primary manifestations of narcolepsy type 1 are excessive daytime sleepiness, cataplexy, hypnagogic hallucinations and sleep paralysis. Clinical variability of these symptoms needs to be carefully analyzed because the similarity with epilepsy is sometimes challenging. Attacks of imperative daytime sleepiness may manifest as repeated lapses of vigilance or atypical automatic behavior. Similarity with partial epileptic seizures is apparent. Cataplexy, episodes of brief loss of the muscle tone with preserved consciousness that are caused by emotions may imitate clinical manifestations of focal or generalized atonic epileptic seizures. Even other paroxysmal symptoms of narcolepsy, as sleep paralysis and hypnagogic/hypnopompic hallucinations are important to differentiate from epilepsy especially in pediatric and young patients (Baiardi *et al.* 2015). On the other hand epileptic seizures in patients with the diagnosis of narcolepsy may be misinterpreted as the attacks of daytime sleepiness, sleep myoclonus or cataplexy. Prevalence of comorbidity of epilepsy and narcolepsy is unknown and is expected to be rare. Nevertheless, physicians should keep this possibility in mind, particularly if the atypical symptoms appear. We report case studies of two patients with comorbidity of narcolepsy type 1 and focal epilepsy.

REPORT OF CASE 1

A 29-year-old female, teacher on maternity leave, has reported typical cataplexy since her childhood. It manifested as a repeated genuflexion or as an opening of her mouth that was provoked by laughter or other positive emotions. Consciousness was always preserved. Later, in the age of 25 excessive daytime sleepiness appeared. She was describing frequent attacks of imperative sleep during different activities, even conversation, with partial improvement after naps. Score of the Epworth Sleepiness Scale was 18, conclusive for excessive daytime sleepiness. Neurological examination was with the normal finding. Electroencephalography (EEG) showed predominantly N1 and N2 sleep activity. Polysomnography was physiological with respiratory disturbance index (RDI) of 1.1, with the absence of sleep-disordered breathing. Short average sleep latency of 3 minutes and 30 seconds and three sleep onset rapid eye movement periods (SOREMPs) were present in multiple sleep latency test. Her HLA type was DQB1 0602. These results confirmed narcolepsy type 1 and patient was treated with modafinil 100mg twice daily. She felt better and only sporadic episodes of cataplexy appeared. After one year of treatment the patient mentioned a new problem in form of frequent episodes of automatic behavior with a loss of consciousness, amnesia, but without any feeling of sleepiness at the beginning of these complaints. Further diagnostic workup was performed and EEG showed focal interictal epileptiform activity in left fronto-temporal region (Figure 1). Magnetic resonance imaging (MRI) excluded structural intracranial lesion of the brain. Diagnosis of focal cryptogenic epilepsy was established and the treatment with lamotrigine was started. Initial dose was increased to 100mg twice daily with a positive effect on the episodes of automatic behavior. Due to the persistence of excessive daytime sleepiness, modafinil was switched to sodium oxybate in a dose of 3g twice daily for six months. During this period patient saw no satisfactory effect and asked to terminate this treatment. Actually she is treated with modafinil in a dose of 100mg twice daily and with lamotrigine in a dose of 100mg twice daily with a good effect. The patient does not suffer any episodes of automatic behavior. Daytime sleepiness and cataplexy are not severe. A combination of modafinil and lamotrigine seems to be safe and effective.

REPORT OF CASE 2

A 21-year-old female, college student was referred due to excessive daytime sleepiness. She has suffered the sleepiness since the age of 8 years. She was sleepy at school with frequent attacks of imperative sleep during the lessons and naps at home. Once she even fell asleep while she was walking on the street. Later on, also the episodes of cataplexy appeared with a dropping of the head or even a fall of the whole body without a loss of

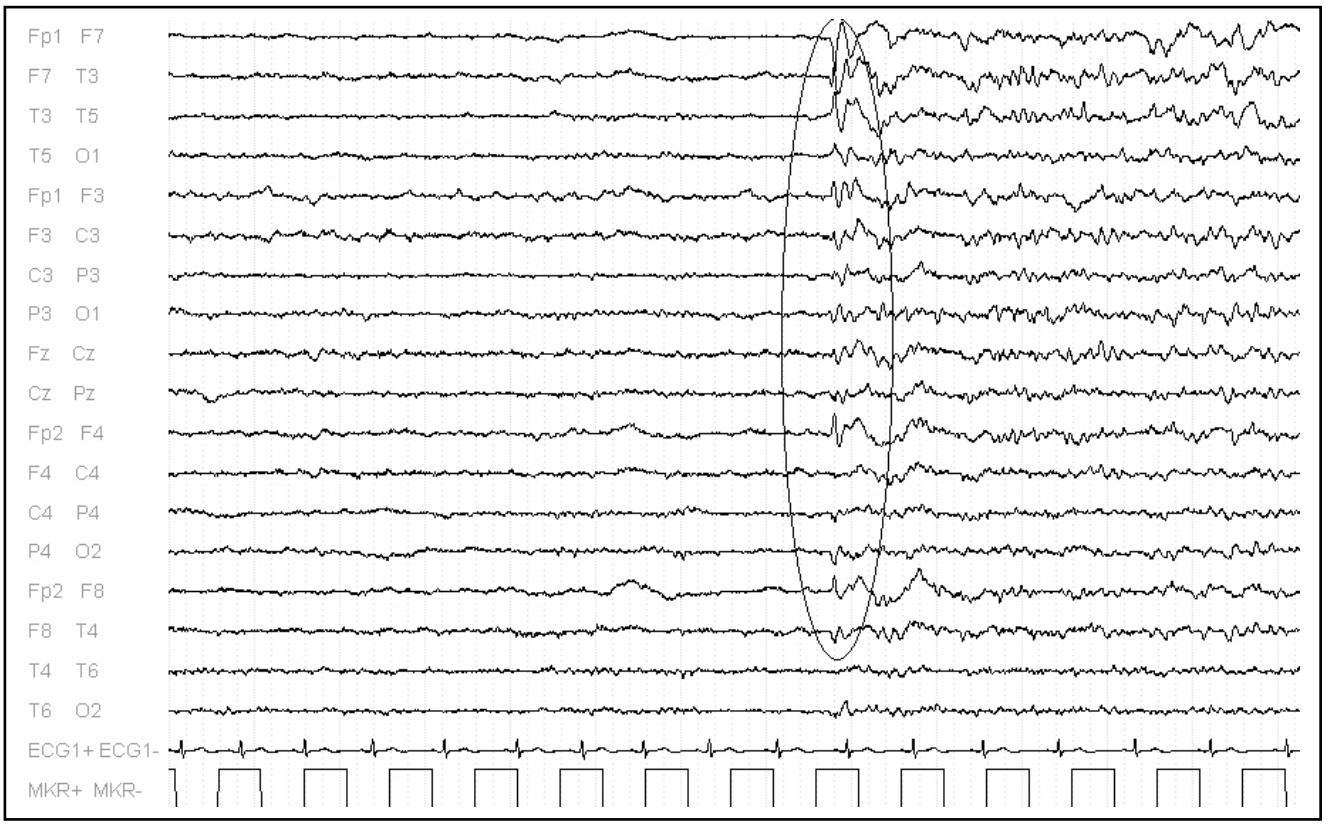

Fig. 1. Case 1. Electroencephalography. Short interictal generalized episode of complex activity with higher amplitude in the left temporoparieto-occipital region.

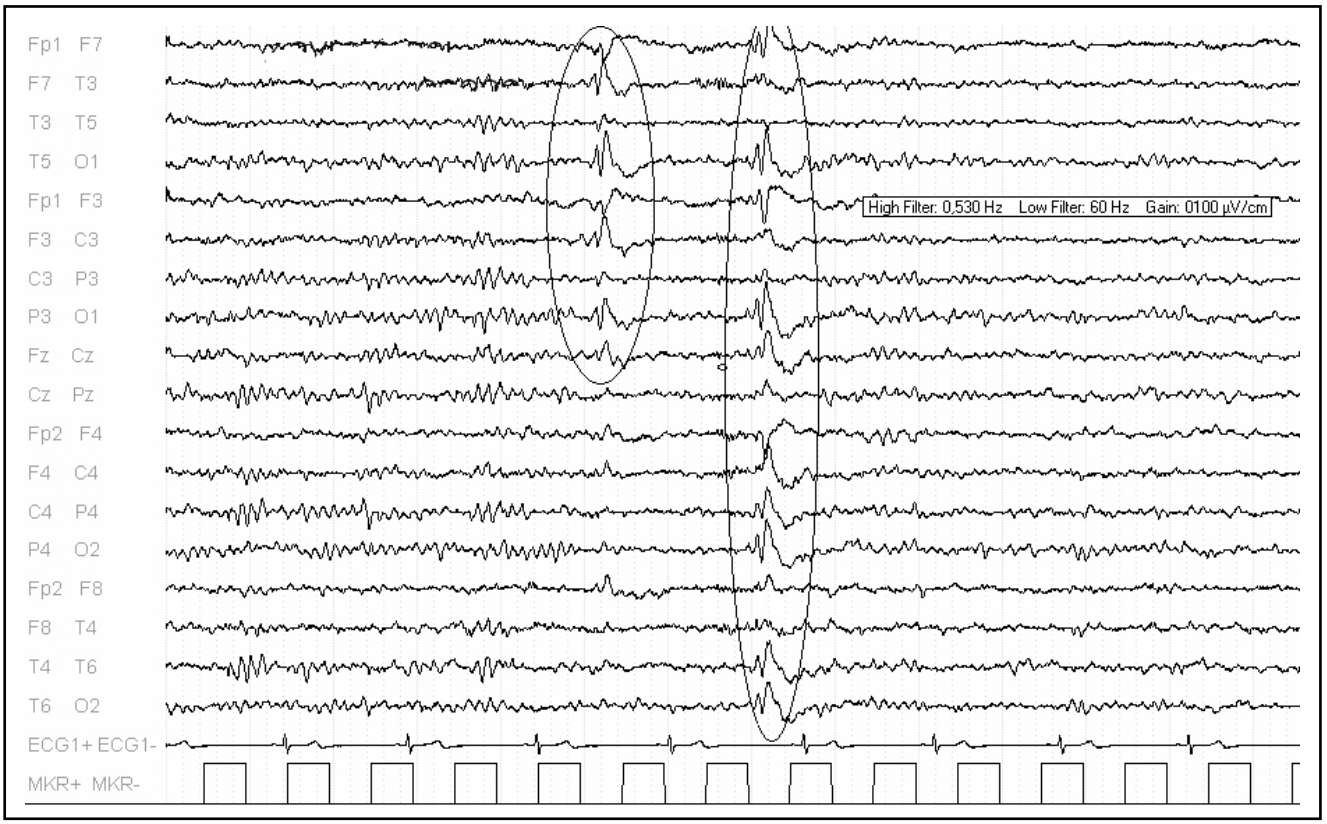

Fig. 2. Case 2. Electroencephalography. Repeated discharges of focal interictal epileptiform activity in the left fronto-temporal region with secondary generalization when eyes closed.

the consciousness. Symptoms were triggered by emotions. Another type of the episodes has been spotted by her mother for last three years. During these episodes, patient was starring, rolling her fingers, behaving automatic. She had amnesia for these episodes. Diagnostic workup was performed at the age of 16. MRI of the brain was without any pathology, as well as neurological examination. Score of the Epworth Sleepiness Scale was 15, conclusive for moderate sleepiness. Polysomnography was physiological with RDI 2.1. No signs of sleep-disordered breathing or periodic limbs movements were present. EEG examination showed interictal epileptiform activity in the left fronto-temporal region (Figure 2). Short average sleep latency of 1 minute and 30 seconds and two SOREMPs were present in multiple sleep latency test. Diagnosis of narcolepsy type 1 and focal cryptogenic epilepsy with complex partial epileptic seizures were established. Patient was treated with lamotrigine 100mg twice daily and modafinil 100mg twice daily with positive effect on sleepiness and automatic behavior.

DISCUSSION

Hypersomnolence is common in patients with epilepsy. It may be caused by antiepileptic medication or by nocturnal epileptic seizures (Cheng *et al.* 2013; Klobucnikova *et al.* 2014). In these patients, excessive daytime sleepiness may be also caused by sleep disorders as sleep apnea, sleep insufficiency or periodic limbs movements. Central disorders of hypersomnolence are quite rare in patients with epilepsy. Narcolepsy is a hypersomnia of the central origin caused probably by autoimmune selective damage of hypocretine neurons in the hypothalamus.

The main clinical features are:

1. Attacks of imperative sleepiness often manifested not only as sleep attacks but also as drops of vigility accompanied with automatic complex behavior.
2. Cataplexy is a transient condition caused by muscle atonia triggered by positive emotions. Consciousness remains preserved.
3. Hypnagogic or hyponopompic hallucinations are dreamlike visual, tactile or acoustic hallucinations. They occur usually upon falling asleep or upon awaking.
4. Sleep paralysis is characterized by an impossibility to move, by paralysis of skeletal muscles occurring upon awakening or at sleep onset. It usually lasts for several minutes and is very stressful (American Academy of Sleep Medicine 2014).

All of these clinical features could be easily misinterpreted as epileptic seizures (Zeman *et al.* 2001). On the other hand, according to this clinical similarity, epileptic seizures could be misdiagnosed as the sleep attacks, cataplexy or as a sleep paralysis, so epilepsy could be

overlooked. Narcolepsy has a broad spectrum of clinical manifestations, so every patient should be carefully evaluated to exclude or confirm the epilepsy. Comprehensive neurological and somnologic evaluation, EEG, video-EEG after the sleep deprivation, long-term EEG monitoring, full-EEG-polysomnography and multiple sleep latency test are helpful in diagnostic workup (Thorpy *et al.* 1992).

The prevalence of co-occurrence of narcolepsy type 1 and epilepsy is not high and may be easily overlooked. Only several case reports of this comorbidity were published. Joshi *et al.* refer three cases of young adult women with juvenile myoclonic epilepsy and coexisting narcolepsy (Joshi *et al.* 2015). Other four cases of idiopathic generalized epilepsy and narcolepsy type 1 were published by Baiardi *et al.* The co-occurrence was easily diagnosed in the case of tonic-clonic seizures. On the other hand, other types of epileptic seizures as absence seizures or myoclonic seizures led to misinterpretation (Baiardi *et al.* 2015). In other case report in a patient with narcolepsy, the episodes of impaired consciousness with automatism were registered and determined as complex partial seizures (Yang *et al.* 2013). In 2003 Lagrange *et al.* published case report of Rasmussen´s syndrome and new-onset narcolepsy (Lagrange *et al.* 2003). In this article, we present two case reports of young females with a history of narcolepsy since the childhood, who suffered also atypical episodes of automatic behavior with impaired consciousness. Focal epilepsy with complex partial seizures was recognized. Treatment with modafinil and lamotrigine was safe and effective in the both patients. According to the literature, different types of epilepsy (generalized, focal) may occur simultaneously with narcolepsy. Although some authors suppose possibility of a shared genetic predisposition to narcolepsy and generalized epilepsy, no common pathophysiological mechanisms between epilepsy and narcolepsy were proved (Joshi *et al.* 2015). Therapeutic combination of modafinil, sodium oxybate and antiepileptics seems to be safe in treatment of cataplexy and excessive daytime sleepiness in the patients with epilepsy and narcolepsy (Baiardi *et al.* 2015).

CONFLICT OF INTEREST

None.

ETHICAL APPROVAL

All procedures were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

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