

CLINICAL CASE REPORTS

Late-onset nocturnal intractable seizure during sleep: what is the origin?

Skaidrius Miliauskas¹, Vanda Liesienė², Marius Žemaitis¹, Raimundas Sakalauskas¹

¹Department of Pulmonology and Immunology, Kaunas University of Medicine,

²Department of Neurology, Kaunas University of Medicine, Lithuania

Key words: nocturnal seizures; sleep apnea; treatment with positive airway pressure device; epilepsy.

Summary. A 54-year-old man was admitted to the Sleep Laboratory, Hospital of Kaunas University of Medicine, for assessment of nocturnal seizures of unknown origin during sleep. This patient complained of increasing daytime sleepiness, morning headaches. Before the admission to the Sleep Laboratory, the treatment with depakine and clonazepam had been prescribed. Despite the treatment, the frequency of nocturnal seizures and daytime sleepiness increased. Full night polysomnography was performed. Ten central apneas were registered during all night. Two central sleep apneas with deep desaturation followed by generalized tonic-clonic seizures were documented. First sleep apnea lasted for 180 seconds and was terminated by epileptic tonic-clonic seizures. The second central sleep apnea with oxygen desaturation of 65% was detected 20 minutes later. It lasted for 200 seconds and was also terminated by epileptic tonic-clonic seizures. The conclusion was drawn that the patient had epileptic seizures caused by central sleep apneas with deep oxygen desaturation. The treatment with nasal continuous positive airway pressure device was started. The seizures disappeared completely. Clonazepam was stopped. Depakine was gradually withdrawn during the two weeks. One-year follow-up showed very good compliance, no seizures, and diminished daytime sleepiness.

A 54-year-old man was admitted to the Sleep Laboratory of Department of Pulmonology and Immunology, Hospital of Kaunas University of Medicine, for the assessment of seizures of unknown origin during sleep.

Generalized tonic-clonic seizures began 6 years ago. The seizures were infrequent (1–2 per month) and were usually observed at night. The patient was not able to remember any episode but he could clearly define that the first event of seizures was triggered by vast alcohol consumption. This patient also complained of gradually increasing daytime sleepiness and frequent morning headaches during the last three years. He had been snoring for 20 years. However, there were no clear witnessed apneas. A neurologist of the same hospital assessed the patient in the outpatient clinic 6 months ago. Differential diagnosis included epileptic seizures (generalized tonic-clonic), partial epilepsy with secondary generalization, arousal epilepsy, and nocturnal paroxysmal dystonia. Routine EEG during wakefulness and daytime sleep was normal without any epileptic phenomenon. Brain

neurovisual evaluation (CT scan) showed no pathological changes. The treatment with depakine at a dose of 500 mg once daily every evening for 3 months was prescribed. Then the dose of depakine was increased to 500 mg twice daily, and such treatment had been continued for 3 months. Finally, clonazepam at a dose of 2 mg at night was added. Despite the treatment, the frequency of nocturnal seizures and daytime sleepiness increased.

The patient had no any known health problem in childhood and early adulthood. The score of Epworth Sleepiness Scale (ESS) was 10. The patient was in good general condition with no signs of impairment of the cardiovascular system. His height was 185 cm, weight – 68 kg. Body mass index was normal (19.8 kg/m²). No anatomical abnormalities were observed in the pharynx.

Full night polysomnography with the ALICE 4 system, USA, was performed (registration and analysis of electro-oculogram, electroencephalogram, electromyogram, ECG, heart rate, nasal air flow, thoracic and abdominal movements, pulse oximetry, snoring,

Correspondence to S. Miliauskas, Department of Pulmonology and Immunology, Kaunas University of Medicine, Eivenių 2, 50009 Kaunas, Lithuania. E-mail: skaidrius.miliauskas@kmu.lt

Adresas susirašinėti: S. Miliauskas, KMU Pulmonologijos ir imunologijos klinika, Eivenių 2, 50009 Kaunas
El. paštas: skaidrius.miliauskas@kmu.lt

body position). Sleep stages were determined according to the international recommendations (1). Definitions of respiratory events were as follows: 1) obstructive apnea, nasal flow cessation for minimum 10 seconds with spared thoracic or abdominal movements; 2) central apnea, nasal flow cessation for minimum 10 seconds without thoracic or abdominal movements; 3) hypopnea, reduction of air flow amplitude for 50% or more with desaturation at least 3% or microarousal at EEG; 4) microarousal, EEG acceleration for 3 seconds or more after respiratory event.

The second sleep stage occurred after 36 min; sleep efficiency was 72.1%. Ten central apneas were registered during night, with general respiratory disturbance index of 3.4 and arousal index of 10.7. No ob-

structive sleep apneas (OSAs) were detected.

Two central sleep apneas with deep desaturation followed by tonic-clonic seizures were documented. The first sleep apnea (Fig. 1) occurred during sleep onset. It lasted for 180 seconds and was terminated by epileptic tonic-clonic seizure (Fig. 2). The seizure began when deep oxygen desaturation (75%) occurred. The second episode of central sleep apnea (Fig. 3) with seizure was detected 20 minutes later. Desaturation reached 65% so far. Central sleep apnea lasted for 200 seconds and was also terminated by epileptic tonic-clonic seizures (Fig. 4). There were no additional episodes of seizures during the remaining sleep time. However, 8 additional central sleep apneas were recorded. The longest one lasted for 100 seconds

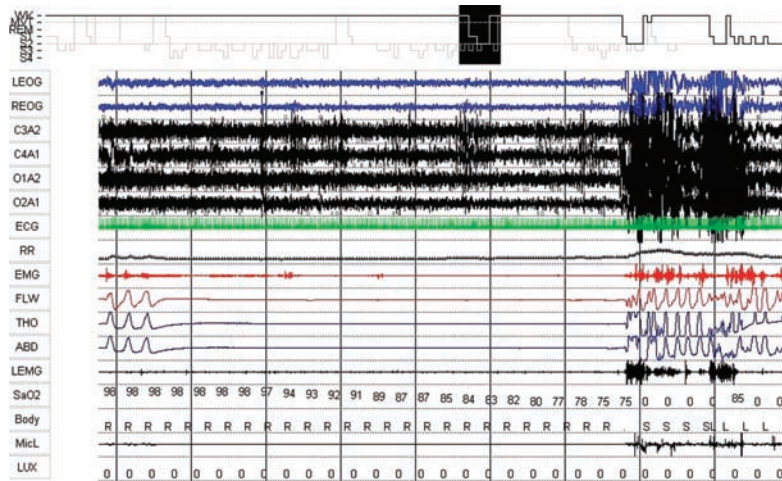


Fig. 1. Polysomnography (5 min), ALICE 4 system, just after the sleep onset

Central sleep apnea with duration of 180 seconds (no abdominal or thoracic cage movements during air flow cessation) can be clearly seen. Note that when oxygen desaturation reached 75%, epileptic seizures occurred (REOG, right electro-oculogram; LEOG, left electro-oculogram; C3–A2, C4–A1, O1–A2, O2–A1, four-channel electroencephalogram; EMG, chin electromyogram; LEMG, leg electromyogram; RR, heart rate, FLW, nasal air flow; THO, thoracic movements; ABD, abdominal movements; SaO₂, pulse oximetry; MicL, snoring; Body, body position).

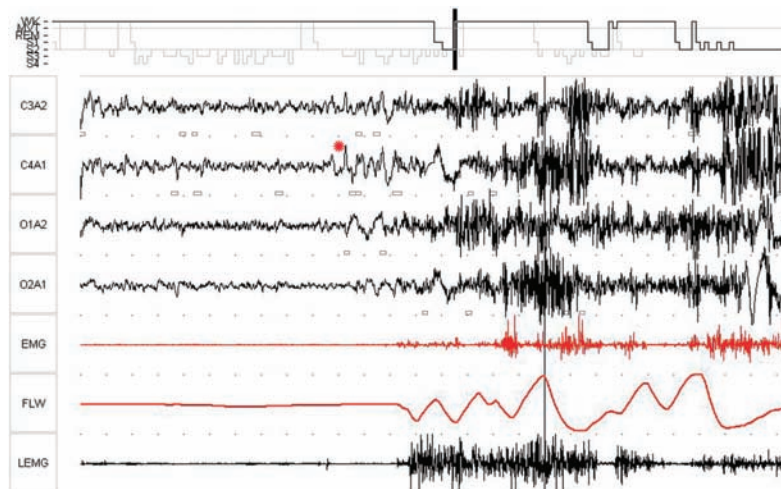


Fig. 2. Polysomnography (30 seconds)

The asterisk shows the beginning of epileptic paroxysm. Epileptic potentials (rhythmic theta sharp waves) are more prominent in the right side, followed by motoric activation more clear in the leg electromyogram (LEMG).

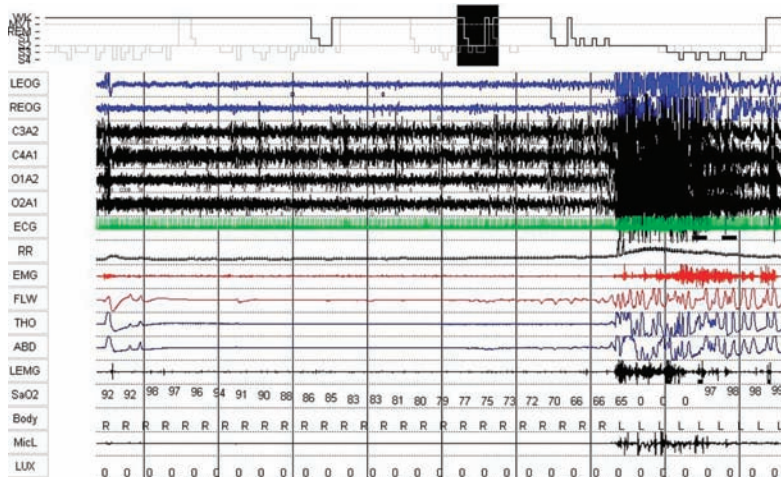


Fig. 3. The second central sleep apnea can be seen (duration, 200 seconds) Note that when oxygen desaturation reached 65%, epileptic seizures occurred.

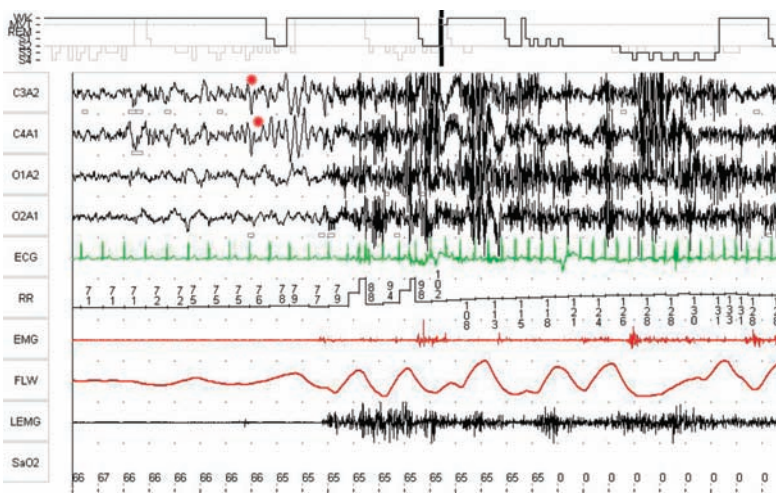


Fig. 4. Polysomnography (30 seconds), 20 min after sleep onset The asterisks show the beginning of epileptic paroxysm. Epileptic potentials (rhythmic tetra sharp waves) are more prominent in the right side, followed by motoric activation more clear in the leg electromyogram (LEMG).

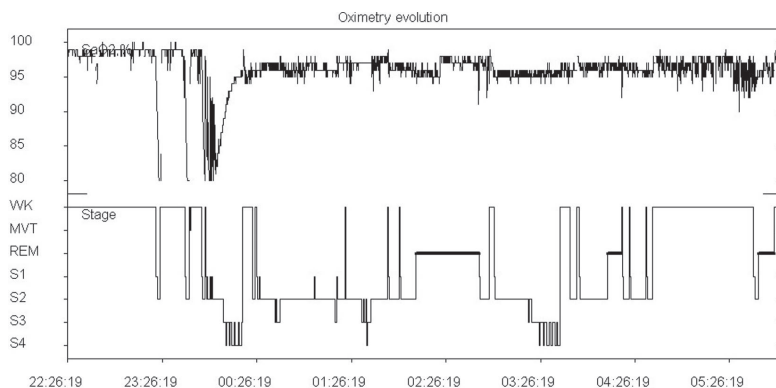


Fig. 5. All night hypnogram Note that deep oxygen desaturation can be seen in the first hour after sleep onset only.

and resulted in mild desaturation (83%). In the all night hypnogram (Fig. 5), we can notice that the lowest oxygen saturation was observed at the first sleep hour only.

We made the conclusion that the patient had epileptic seizures caused by central sleep apneas with deep oxygen desaturation. The treatment with nasal

continuous positive airway pressure (CPAP) device was started. Clonazepam was stopped immediately. The seizures disappeared completely. Depakine was gradually withdrawn during the two weeks. One-year follow-up showed very good compliance, no seizures, and decreased daytime sleepiness (ESS score, 5).

Discussion

The effect of sleep on seizures has been recognized since antiquity. In many cases, this epilepsy-sleep interaction has important implications for the diagnosis and treatment of seizures (2–7). Understanding the relationship between epilepsy and sleep is important for optimizing the management of a patient with epilepsy in several ways. First, sleep modulates the expression of epileptic seizures and interictal epileptiform discharges in EEG. Second, epilepsy and its treatment influence sleep organization and daytime alertness, and may contribute to, or ameliorate, sleep disorders. Most important, treatment of a coexisting sleep disorder may improve seizure control, daytime alertness, and health-related quality of life.

Late onset of epileptic seizures is often of unexplained origin and with complicated treatment or poor nighttime seizure control. Although epileptic seizures occur more commonly in older adults, their occurrence in this age group is often unexplained. One unexplored precipitant of seizures in older adults is OSA, which is also more common in this age group (2, 3, 8–10). Chihorek et al. (10) performed polysomnography in 11 older adult patients with late-onset or worsening seizures and in 10 patients who were seizure-free or who had improvement of seizures. Patients in the former group 1 had a significantly higher apnea-hypopnea index than patients in the latter group ($P=0.002$). Patients with late-onset or worsening seizures also had higher ESS scores ($P=0.009$) and higher scores on the Sleep Apnea Scale of the Sleep Disorders Questionnaire ($P=0.04$). The two groups were similar in

regard to body mass index, neck circumference, number of antiepileptic drugs currently used, and frequency of nocturnal seizures. The authors made the conclusions that OSA is associated with seizure exacerbation in older adults with epilepsy, and its treatment may represent an important avenue for improving seizure control in this population. Höllinger et al. (11) retrospectively reviewed the database of one sleep center and identified patients with both sleep apnea and epilepsy. They stressed the importance of considering diagnosis and treatment of OSA in epilepsy patients with poor seizure control and/or reappearance of seizures after a seizure-free interval. Treatment with CPAP device was continued with good compliance in 12 patients and led to a significant reduction of both ESS scores and seizure frequency in 4 patients. Khatami et al. (12) assessed sleep-wake habits, and the presence of sleep disorders was assessed by means of a clinical interview and a standard questionnaire in 100 consecutive patients with epilepsy and 90 controls. They showed that in epilepsy patients, excessive daytime sleepiness was predicted by a history of loud snoring and symptoms of restless legs syndrome but not by sleep apnea or epilepsy-related variables (including type of epilepsy, frequency of seizures, and number of antiepileptic drugs).

Finally, there is no universally accepted method to determine effective therapy for central sleep apnea. The CPAP device applied acutely often does not eliminate apneas and hypopneas (13). However, in our case, we suggest that seizures were abolished by elimination of deep oxygen desaturation and probably by shortening duration of central sleep apnea. More importantly, it shows that the principles of sleep medicine should be integrated into the practice of epileptology. For the beginning, it is time for those who treat patients with epilepsy to start asking a few extra questions concerning the sleep apnea including snoring, daytime sleepiness, and sleep habits.

Vėlyvieji generalizuoti naktiniai traukuliai. Kokia priežastis?

Skaidrius Miliauskas¹, Vanda Liesienė², Marius Žemaitis¹, Raimundas Sakalauskas¹

¹Kauno medicinos universiteto Pulmonologijos ir imunologijos klinika,

²Kauno medicinos universiteto Neurologijos klinika

Raktažodžiai: naktiniai traukuliai, miego apnėja, gydymas nenutrūkstamos oro srovės aparatu, epilepsija.

Santrauka. 54 metų vyras atvyko į Kauno medicinos universiteto klinikų Miego laboratoriją išsirtinti dėl neišskios kilmės naktinių traukulių. Pacientas skundėsi padidėjusiu mieguistumu dieną, galvos skausmais rytais. Prieš tai, pacientas buvo gydomas depakinu ir klonazepamu. Nepaisant gydymo, naktiniai priepuoliai dažnėjo, progresavo mieguistumas. Atliktas polisomnografijos tyrimas. Per visą naktį rasta dešimt centrinių

miego apnėjų. Po dviejų centrinių miego apnėjų, esant gilaus deguonies įsotinimo sumažėjimui, užfiksuoti toniniai-kloniniai traukulių priepuoliai. Pirmoji miego apnėja atsirado užmigimo metu ir tęsėsi 180 sek. Ji baigėsi epilepsiniais generalizuotais toniniais-kloniniais traukuliais. Antrasis centrinės miego apnėjos epizodas užregistruotas po 20 min. Deguonies įsotinimas sumažėjo iki 65 proc. Centrinė apnėja tęsėsi 200 sek. ir taip pat baigėsi epilepsiniais toniniais-kloniniais traukuliais.

Išvada. Epilepsiniai traukuliai, sukelti centrinės miego apnėjos su giliu deguonies įsotinimo sumažėjimu. Skyrus gydymą nenutrūkstamos oro srovės aparatu per nosies kaukę, traukuliai išnyko. Nutrauktas gydymas klonazepamu ir depakinu. Po vienerių metų paciento būklė gera, traukuliai nesikartojo, mieguistumas dieną žymiai sumažėjo.

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