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Mini Review

Epileptic Seizures in Patients with Neurodegenerative Diseases

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Abstract

The diagnosis of seizures in elderly patients can be difficult due to the high incidence of different concomitant diseases. The clinical presentation of seizures in patients with neurodegenerative diseases is often atypical. Post-ictal confusion and memory loss can particularly been prolonged in the elderly. The overall probability of developing seizures after onset of dementia is estimated at 11.5%. Unprovoked seizures start in the early stages of the neurodegenerative diseases, when the cognitive complaints are still mild or even minimal. The cognitive decline starts 6.8 years earlier In Alzheimer patients with epilepsy than in those without seizures. Epilepsy can coexist with Parkinson's disease although its association is questionable.

Levetiracetam and pregabalin are proposed as the safest anti-epileptic drugs, as they have fewer side effects. Levetiracetam improves performance on spatial memory and executive function tasks in Alzheimer patients with epileptic activity. The association of epilepsy and neurodegenerative diseases is nearly two-fold compared to their separate entities. Inflammation is considered as the most important common factor, linking both disease entities.

***Keywords**: Epilepsy; Neurodegenerative Diseases; Dementias; Anti-Epileptic Drug Treatment*

Abbreviations

AD: Alzheimer's Disease; DLB: Dementia with Lewy Bodies; FTD: Frontotemporal Degeneration; CBD: Corticobasal Degeneration; MSA: Multiple System Atrophy; PSP: Progressive Supranuclear Palsy; PD: Parkinson's Disease; AEDs: Anti-Epileptic Drugs

Introduction

Establishing the diagnosis of seizures in the elderly can be extremely difficult due to the high incidence of different concomitant diseases [1]. Cerebrovascular diseases are the most common causes of epilepsy in old patients with an incidence of 10.6% for intracerebral hemorrhages and 8.6% for ischemic strokes [2]. Early-onset seizures occur mainly in hemorrhagic strokes, while the late-onset ones mainly appear in ischemic strokes. The most common stroke presentation of the latter is an ischemic partial anterior circulation syndrome [3].

The most frequent types of seizures after ischemic strokes in the elderly are simple partial and complex partial seizures [4]. Generalized seizures and status epilepticus mainly occur in patients with hemorrhagic strokes [5].

Memory impairment as such is not a useful discrimination between the most frequent neurodegenerative dementia syndromes. Apraxia favors AD. Visual hallucinations mainly point to dementia with DLB while behavioral disinhibition and decline of executive functions are more frequent in FTD [6].

This article reviews the most recent publications concerning the occurrence of seizures and epilepsy in patients with neurodegenerative diseases and dementias.

Main core

In clinical studies without neuropathological confirmation the overall probability of developing seizures after onset of dementia is estimated at 11.5%. The highest incidences are found in AD with 13.4% and in DLB with 14.7%. The occurrence in FTD is as low as 3.0% [7]. However, in a more recent study with post-mortem neuropathological confirmed diagnosis the incidence of seizures in patients with neurodegeneration has been estimated to be higher. In this study the overall seizure prevalence is estimated at 31.3% for AD, 20% for CBD, 11.3% for LBD, 11.3% for FTD, 8.3% for MSA and 7.5% for PSP [8].

Overall, only 1.82% of the AD patients are treated with AEDs. For the behavioral variant of FTD the incidence is 1.28%, while for LBD it is 2.47% and for primary progressive aphasia 12% [9].

The clinical presentation of seizures in patients with neurodegenerative diseases is difficult to establish and often atypical, due to the memory disturbances and problems with the reconstruction of the anamnesis that these patients have [10]. The most recognized clinical presentations are simple partial and complex partial seizures. Post-ictal confusion and memory loss can particularly been prolonged in the elderly [11]. Unprovoked seizures consist to start in the early stages of the neurodegenerative diseases, when the cognitive complaints are still mild or even minimal with non-relevant neuro-imaging features [12]. AD patients with epilepsy present symptoms of cognitive decline 6.8 years earlier than those without seizures [13]. Some studies report an increase of seizure risk according to the severity of the dementia or with younger age of AD onset. Seizures may be difficult to distinguish from the common behavioral signs of dementia [14]. It is possible that the severity of the epilepsy could partially be responsible for the progression of the AD [15].

On 24-hour ambulatory scalp EEG's epileptic abnormalities are observed in 53% of AD patients. In the early stages of AD patients before the eventual occurrence of seizures the EEG shows a pattern of left temporal lobe hyperexcitability, while in AD patients with already confirmed seizures bitemporal hyperexcitability is observed [16].

In a study restricted to DLB a seizure incidence of 2.62% in clinical diagnosed patients is observed, while in a subgroup of neuropathological confirmed cases the frequency increases up to 3.8%. The two-year mortality in DLB patients with epilepsy is as high as 52.8% [17]. Idiopathic seizures can be responsible for psychotic symptoms and cognitive fluctuations in addition to the drug treatment and mimic DLB [18].

Difficulties can exist to distinguish DLB with status epilepticus from status epilepticus not associated to DLB [19]. Transient epileptic amnesia can be caused by DLB but also be an incidental association [20]. Also seizures must be differentiated from syncopes due to episodic hypotension, which is frequently observed in DLB [21]. On EEG frontal intermittent delta activity is only observed in 17.2% of DLB patients with and without seizures [22].

One study finds a greater incidence of seizures and myoclonus in patients with FTD than in the general population. 2.2% of seizures and 6.5% of myoclonus are observed in these patients. Some of the seizures are non-convulsive [23].

Epilepsy can coexist with PD eventually by chance. However, their co-existence may have an influence on the progression of the PD symptoms [24]. A more recent study suggests that PD is associated with an increased risk of epileptic seizures [25]. Some PD patients with acute episodes of cognitive changes can present as focal non-motor seizures with alteration of awareness. These cases can only be diagnosed by the demonstration of epileptic discharges on EEG [26].

Initially sporadic cases are described of action myoclonus and seizures in patients with PSP [27]. However, in a more recent study 7 cases are observed developing seizures, out of a series of 62 PSP patients, over a 9-year period [28].

The initial symptoms of MSA are mainly early autonomic symptoms that can mimic epileptic seizures [29]. Obstructive sleep apnea occurs frequently in MSA. It may induce seizures by means of sleep disruption and deprivation as well as cerebral hypoxemia with consequent oxidative stress [30].

Only one publication is found of seizure occurrence in a patient with CBD [31].

No studies are available on the incidence of seizures in patients with amyotrophic lateral sclerosis.

Because elderly patients require long-term medication for their neurodegenerative disease the addition of an antiepileptic therapy, can lead to a major interference [32]. The general guidelines for epilepsy treatment in elderly patients consist of starting at the lowest therapeutic doses and slowing the titration schedule [33]. It is important to start treatment after a first seizure when there is evidence of focal neurological involvement or a risk of recurrent seizures [34]. Levetiracetam and pregabalin have the most favorable pharmacological profile in elderly patients, followed by oxcarpazepine and lamotrigine [35]. Levetiracetam also improves spacial memory and executive function task in AD patients with epileptic activity [36]. Antipsychotic drugs should be avoided as much as possible in elderly demented patients with seizures. In particular the use of Clozapine should not been used as it can induce seizures [37].

Conclusion

There is a close link between dementia and the late occurrence of epileptic seizures in the elderly. This association is a nearly two-fold compared to their separate entities [38]. Inflammation is considered as the most important pathogenetic factor linking dementia and late-onset epilepsy [39].

Seizures occur infrequently in patients with neurodegenerative motor neuron diseases [40].

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