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CASE REPORT

Late-onset temporal lobe epilepsy with unilateral mesial temporal sclerosis and cognitive decline: A diagnostic dilemma

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Summary We present a patient with new onset temporal lobe epilepsy and cognitive decline in his sixth decade with unilateral hippocampal atrophy on structural brain imaging, compatible with mesial temporal sclerosis. This unusual clinical scenario presented a challenging differential diagnosis since it may overlap with primary cognitive disorders, including early-onset Alzheimer's disease and some forms of frontotemporal dementia, and the recently elucidated syndrome of non-paraneoplastic limbic encephalitis associated with voltage-gated potassium channel antibodies.

Introduction

Symptomatic temporal lobe epilepsy (TLE) with the neuroradiological signature of hippocampal or mesial temporal sclerosis (MTS), namely hippocampal atrophy on coronal T_1-weighted magnetic resonance imaging (MRI), with or without high signal in the hippocampus on T_2-weighted or FLAIR images, is thought to be the commonest form of localization-related epilepsy.[1,2] The majority of patients, up to 90%, with TLE–MTS have a history of a precipitating incident such as febrile convulsions, brain trauma, ischaemia, or intracranial infection.[3] Genetic factors may also contribute: mutation of the alpha1 subunit of the voltage-gated sodium channel gene has been identified in a subgroup of patients with febrile convulsions and subsequent TLE.[4] In families with another inherited form of TLE, symptomatic and asymptomatic probands were shown to have MTS.[5]

In TLE–MTS, the first non-febrile seizure typically occurs between 4 and 16 years of age.[2] Onset after early adulthood is extremely unusual. We present a patient with late-onset TLE and focal cognitive deficits with neuroradiological evidence of unilateral MTS that fits into none of these recognised categories.

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Case report

A 60-year-old right-handed retired builder presented to the Epilepsy Clinic with several witnessed generalized tonic–clonic seizures over an 8-month period. Attacks occurred without warning, and were followed by 2–3 h of postictal confusion and irritability. They occurred in clusters of three to five, in the early hours of the morning, some arising directly from sleep. Two clusters led to hospital admission, one requiring a period of endotracheal intubation and ventilation on an intensive care unit for several days. During another seizure the patient sustained a shoulder injury which required reconstructive surgery. There was no prior history of events compatible with partial seizures or childhood febrile convulsions, and no family history of epilepsy. The only identified risk factor for epilepsy was alcohol consumption of 28 units over weekends, but the patient denied binge drinking prior to seizures.

In addition to seizures, the patient complained of being more forgetful in recent months. Examples recounted by him and his family included losing items (wallet, glasses), forgetting to pass on messages, and buying items already bought (e.g. newspapers). In addition, he reported difficulty recalling episodes from his earlier life, such as time spent in the armed forces, previous occupations, and foreign holidays.

Investigations included an interictal EEG which showed baseline alpha rhythm with occasional theta components but no epileptiform discharges. Non-enhanced MR brain imaging showed marked right hippocampal atrophy on coronal T_1-weighted sequences, compatible with right mesial temporal sclerosis; no signal change was seen on T_2-weighted or FLAIR images.

Neuropsychological assessment showed general memory functioning within the borderline range (WMS III score 75; 5th percentile) with evidence of significant decline when compared to predicted premorbid level of intellectual functioning (WTAR predicted 88). Impairments were evident in tests of both immediate and delayed memory (extremely low to average function), particularly in visual delayed memory (WMS II 68, 2nd percentile). Comparing delayed and immediate memory performance suggested a rapid rate of forgetting for visual but not auditory information.

He was treated with carbamazepine (600 mg/day) with cessation of seizures. He also felt that his forgetfulness improved after commencing antiepileptic drug therapy, an impression corroborated by family, but he declined a further neuropsychological assessment.

Discussion

This patient's presentation with secondarily generalised seizures, cognitive decline, and MR imaging evidence of unilateral hippocampal atrophy, was compatible with the diagnosis of TLE-MTS. However, the age of presentation (60) was unusual since most cases of TLE-MTS present between childhood and early adulthood. Late-onset TLE–MTS has been reported as a consequence of a meningitic illness due to neurocysticercosis,[6] but no precipitating illness was reported in our patient.

The precise role of MTS in our patient's clinical syndrome is uncertain: it may have been the common aetiology of both the seizures and cognitive decline, alternatively the acquired cognitive impairment may have resulted from the seizures per se. Repeat neuropsychological assessment following seizure cessation might have been helpful in deciding between these possibilities. The subjective impression of memory improvement may suggest that cognitive impairment was directly related to seizures.

In view of the age at onset and the clinical symptoms suggestive of both anterograde and retrograde amnesia, the differential diagnosis in this patient encompassed not only a seizure disorder but also a primary cognitive disorder of neurodegenerative or autoimmune aetiology.

Early-onset Alzheimer's disease (AD) is the commonest cause of amnesia at this age. Although seizures, usually secondarily generalised, become more prevalent with AD progression, nonetheless they may be present at the time of diagnosis without explanation other than symptomatic AD.[7] Cases of TLE with frequent seizures sufficient to cause memory decline simulating AD have been reported.[8,9]

Pure hippocampal sclerosis (PHS), an increasingly recognised cause of late-life cognitive decline sometimes associated with seizures,[10–12] also enters the differential diagnosis. This condition was initially defined on neuropathological grounds with neuronal loss in the hippocampal CA1 region. The appearances may look quite similar to seizure-associated MTS,[12] where the neuropathological substrate is neuronal dropout and astrocytosis in the granule cell layer of the dentate gyrus and hilar region with loss of pyramidal cells in the CA1 and CA3 regions, but with sparing of pyramidal cells in the CA2 region, subiculum, entorhinal cortex and temporal neocortex.[2] The neuroradiological signature of PHS is hippocampal atrophy.[13] In some cases, PHS may be strictly unilateral.[12] Initially, the clinical overlap between PHS and AD was emphasized, with a similar prevalence of seizures reported;[12] intractable seizures with cognitive decline was the presentation in one case.[14] More recently, however, many cases of PHS have been