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Case report

Early-onset dementia: diagnostic challenges

Bushra Elhusein, Omer Bakri Mahgoub, Abdalla Khairi

Psychiatry, Department of Medical Education, Hamad Medical Corporation, Doha, Ad Dawhah, Qatar

Correspondence to
Dr Omer Bakri Mahgoub;
Omeralshekh@hotmail.com

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SUMMARY

A 56-year-old man was brought to our hospital by his family, seeking medical treatment for the patient's long-standing progressive word-finding difficulties, forgetfulness, agitation and social withdrawal. After multiple previous physician consultations, the patient was mistakenly diagnosed with epilepsy and prescribed multiple anticonvulsants, to which his above mentioned symptoms were unresponsive. His condition progressed over the next 10 years, resulting in severe cognitive impairments and a complete dysfunctionality. An electroencephalogram (EEG) assessment revealed persistent spike and wave activity in the left temporal lobe. Brain MRI revealed multiple small bright T2 and fluid attenuated inversion recovery (FLAIR) foci within the white matter of both cerebral hemispheres surrounding the ventricular system, as well as some widening of extra-axial cerebrospinal fluid spaces. The patient was finally diagnosed with early-onset dementia and temporal lobe epileptiform abnormalities. This case emphasises the need for diagnostic consideration of dementia in cognitively impaired patients, even when they are not of an advanced age.

BACKGROUND

According to the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth edition), dementia (major neurocognitive disorder) is defined as significant acquired cognitive impairment in one or more cognitive domains (eg, learning and memory, language, executive function, complex attention, perceptual-motor function, social cognition) that represents a significant decline from previous baseline and interferes with independence in daily activities. Early-onset dementia usually refers to cases of dementia in adults occurring before the age of 65 years.

Dementia in young individuals can be a diagnostic challenge given its often non-specific symptoms and findings. As a consequence, patients with early-onset dementia are more often misdiagnosed than those with late-onset dementia.¹ Although there is a set of known clinical criteria for early-onset dementia, misdiagnoses can occur even in tertiary facilities.² The present case exemplifies these challenges. The patient presented here first experienced symptoms in his early 40s and, given his young age and unspecific clinical findings, received a seizure disorder diagnosis. Given this misdiagnosis, his treatment was delayed, and his condition further deteriorated.

CASE PRESENTATION

A 56-year-old man with no medical comorbidities who used to work as an electrician was initially

brought by his family to our psychiatry hospital-walk in clinic seeking help for memory loss over the past 10 years. During this time, the patient's family endorsed mood swings, social isolation, an unsteady gait, and word-finding difficulties.

Several months after symptom onset, the patient's family noticed that his memory loss became more prominent and that he was unable to follow passed event timelines, for instance arguing that long-ago events had happened only days prior. The patient also forgot the names of close relatives, maintained poor sleep (less than 3 hours per night) and altered his normal daily routines (eg, religious rituals). The family also endorsed increased agitation and anxiety at this time. The patient's functional skills began to gradually decline and he lost the skills required to do his job, which ultimately resulting in his being laid off. Furthermore, the patient's family reported that he lost his way home on two occasions and was ultimately brought home after 1 day by strangers both times. Finally, the patient's family reported one incident approximately 5 years prior to the current presentation, the incident happened during a family gathering when the patient lost consciousness for a few minutes. The patient was later taken to a neurologist in his home country.

An MRI and EEG were performed on the patient's first being examined by a neurologist. The MRI revealed some brain atrophy and the EEG was normal. The patient was started taking carbamazepine but according to his family his condition continued to progress. Medications, including quetiapine, which was later added to the patient's regimen to treat his sleep problems, were not efficacious.

A mental status examination revealed average grooming and hygiene, poor eye-to-eye contact, psychomotor retardation, a calm and quiet demeanour, irrelevant yet coherent responses to questions and blunted affect. The patient denied experiencing any hallucinations or other perceptual abnormalities and no overt delusions or obsessions were noted during his examination.

A cognitive assessment with the mini-mental state examination revealed a score of zero, as the patient was unable to complete any of the required tasks. While the patient registered three items correctly, he recalled none. He was unable to do the serial sevens or threes measures of attention and was unable to read or write.

The patient's medical history indicated significant iron deficiency anaemia, which required hospitalisation at the age of 18 years. He had no recorded history of hypertension, diabetes mellitus, dyslipidaemia, stroke, head trauma or any other chronic

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Figure 1 MRI of head.

illnesses. The patient was not on any regular medications before the treatment described above, though he was a smoker since the age of 18 years (quit 2 years prior to the current presentation) and denied any alcohol consumption or illicit drug use.

Finally, the patient's family, childhood and developmental history were unremarkable. He was educated through secondary school but did not complete his education for financial reasons. He completed professional electrician training and worked as an electrician for more than 20 years. He is married with four children. A physical examination revealed no further abnormalities.

INVESTIGATIONS

A complete blood count and urea, electrolyte and liver function tests were all within normal limits. The patient had normal levels of vitamin B₁₂ and folate and was negative for HIV and venereal disease (as per the Venereal Disease Research Laboratory test). Inflammatory markers were within normal limits. The patient's family refused a cerebrospinal fluid analysis.

An EEG assessment revealed persistent left-sided spike and wave activity over the temporal lobe region with an amplitude of 50–80 μ V, suggesting left temporal lobe epileptiform discharge.

A head MRI revealed multiple small and bright T2 and fluid attenuated inversion recovery (FLAIR) foci within the white matter of both cerebral hemispheres and surrounding the ventricular system, most notably in the frontal and occipital horns, with no corresponding areas of restricted diffusion on diffusion-weighted image sequences. This likely represented deep white matter ischaemic-related change.

Widening of the extra-axial CSF space, prominent sulci, and deepened gyri implicated both cerebral hemispheres and temporal lobes degenerative changes (figure 1).

DIFFERENTIAL DIAGNOSIS

The differential diagnoses in this case include Alzheimer's disease, vascular dementia, Lewy body dementia, multiple

system atrophy, Parkinson's disease, Huntington's disease and normal pressure hydrocephalus.

TREATMENT

Initially, 10 years prior to his latest presentation to our hospital, the patient was diagnosed with a seizure disorder. Accordingly, he started taking carbamazepine (200 mg once daily) and then donepezil 5 years later (5 mg later increased to 10 mg per day with carbamazepine). He did not show any improvement in his symptoms and a marked exacerbation of his forgetfulness, decreased functionality and increased agitation. He was assessed in an outpatient setting at our psychiatric facility and diagnosed with early-onset dementia after an initial assessment. He was subsequently started taking memantine (10 mg two times per day) and quetiapine (50 mg before bed) for the symptomatic treatment of insomnia. The patient's carbamazepine was discontinued given no evidence for clinical seizures.

OUTCOME AND FOLLOW-UP

One month after the initiation of his treatment, the patient's family reported improvement in his sleep quality and agitation, but not in his cognitive function. The patient's family travelled with him back to his home country and he became unavailable for follow-up.

DISCUSSION

In the present case, we discuss a 56-year-old male patient who sought medical help abroad for progressive word-finding difficulties, forgetfulness, agitation and social withdrawal. His history indicated chronicity, as he endorsed these symptoms for a period of more than 10 years. In general medical practices, the suspicion index for dementia at a young age is low and such cases usually represent a diagnostic challenge given the low presence of key manifestations, unspecific symptoms and the younger age at presentation. Collectively, these factors can result in a delayed diagnosis relative to older dementia patients.³

The challenges of early-onset dementia cases may relate to its aetiology. Here, a family history of similar conditions was denied, pointing against a genetic contribution to the disease aetiology. Furthermore, genetic testing was not done in this case for financial reasons. A history of metabolic disturbances, head trauma, alcoholism, drug misuse or vitamin deficiencies, all important aetiological factors in early-onset cognitive impairments, was excluded by interviewing the patient's family.

A head MRI revealed multiple small bright T2 and FLAIR foci within the white matter of both cerebral hemispheres and surrounding the ventricular system, most notably in the frontal and occipital horns. There were no corresponding areas of restricted diffusion for the diffusion-weighted image sequences, likely representing deep white matter ischaemic-related change. Unlike more acute lesions following stroke or multiple sclerosis, which may cause sudden sensorimotor deficits, white matter lesions due to ageing manifest in more subtle and gradual ways and are often cognitive in nature.⁴ The MRIs for people older than our patient often exhibit similar white matter lesions surrounding the ventricular system. Critically, this patient's gradually worsening cognitive symptoms may be, in part, explained by some particularly-located white matter lesions, for example, in the deep forebrain disrupting cholinergic projection fibres at their proximal origin.⁴ It is therefore plausible that frontal deep white matter lesions may result not only in cholinergic but also variable monoaminergic (eg, dopamine, serotonin and norepinephrine) neurotransmitters.⁴ The involvement of these

monoaminergic neuromodulators may also explain some of the non-cognitive symptoms that this patient experienced, such as mood swings, agitation, anxiety and sleep disturbances.

Starting with some difficulties in naming things and people, this patient's disease process involved progressive cognitive deterioration, a key characteristic of dementia. As the patient also experienced seizures, he was initially diagnosed with epilepsy, which was not confirmed via an initially normal EEG. An initial MRI, which was reported by the family, also indicated brain atrophy and lesions. Despite this, dementia was not considered. However, a follow-up EEG at our hospital revealed persistent spike and wave activity on the left side over the temporal lobe region with an amplitude of 50–80 μ V suggesting left temporal epileptiform activity. Widening of the axial CSF spaces, prominent sulci, and deepening of the gyri in both cerebral hemispheres as well as in the temporal lobes bilaterally was further evident on follow-up imaging. Collectively, the patient's imaging and EEG findings pointed towards both subcortical and cortical brain pathology and potentially epilepsy. Accordingly, mixed type dementia (cortical and subcortical) and co-morbid temporal lobe epilepsy were diagnosed.

Two observations are of note in the present case which indicate the primacy of dementia over epilepsy. First, antiepileptic

medication was of no benefit to this patient in his dementia symptoms, likely due to the progressive underlying pathology and resultant dementia. Second, age-related regression measures of memory in patients with epilepsy often show that amnesia/dementia is not a direct consequence of progressive epilepsy.⁵

Given the history, physical examination findings and brain imaging findings in this case, we reached a correct aetiological diagnosis of early-onset progressive cognitive deterioration. The clinical diagnosis of mixed cortical and subcortical dementia comorbid with temporal lobe epilepsy remains as a valid diagnosis. Reporting more cases with a similar presentation may ultimately result in case series and the identification of a specific pattern or clinical profile, which will lead to a better understanding of the aetiology and thus management of early-onset dementia cases.

Contributors All the authors were involved in the patients' care. BE was the primary author and the team leader, and was the clinical fellow who was assigned to the patients and saw the patients regularly in clinics. OBM is psychiatry resident who did the interview and cognitive assessment of the patient. AK is a consultant geriatric psychiatrist who helped the team to establish the diagnosis in dementia and contributed to the case discussion. All the authors met regularly to discuss and write the case report.

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REFERENCES

- McMurtry A, Clark DG, Christine D, *et al*. Early-Onset dementia: frequency and causes compared to late-onset dementia. *Dement Geriatr Cogn Disord* 2006;21:59–64.
- Mendez MF. The accurate diagnosis of early-onset dementia. *Int J Psychiatry Med* 2006;36:401–12.
- Elhusein B, Radwan A, Khairi A, *et al*. Atypical presentation of progressive young onset dementia. *BMJ Case Rep* 2018;11:pii: bcr-2018-225754.
- Bohnen NI, Bogan CW, Müller MLTM. Frontal and periventricular brain white matter lesions and cortical deafferentation of cholinergic and other neuromodulatory axonal projections. *Eur Neurol J* 2009;1:33–50.
- Helmstaedter C, Elger CE. The phantom of progressive dementia in epilepsy. *Lancet* 1999;354:2133–4.

Patient's perspective

The patient's wife described what she and her husband faced this way: a few years after the start of my husbands' symptoms he became dependent and required help carrying out daily tasks. This had a negative impact on our family, both socially and financially. Dementia is a life-changing experience.

Learning points

- To highlight the importance of healthcare professionals considering early-onset dementia for relevant patients.
- Increased public awareness of this condition is needed.
- It is critical that early-onset dementia diagnoses are made as expediently as possible to initiate a comprehensive management plan early in disease course.

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