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MOVEMENT DISORDERS THAT OCCURRED AS LATE MANIFESTATIONS OF ALZHEIMER'S DISEASE CONTROLLED BY A LOW DOSE OF CARBAMAZEPINE

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ABSTRACT

Introduction: According to the World Health Organization, 44 million people worldwide suffer from Alzheimer's disease. Abnormal movements are atypical symptoms of Alzheimer's disease.

Case description: An 87-year-old woman, followed for Alzheimer's disease, experienced abnormal movements. The episodes lasted 30 minutes, were involuntary, uncontrollable, anarchic, predominantly in the upper limbs, and without loss of consciousness or bladder control. An electroencephalogram ruled out atypical epilepsy. Pharmacovigilance investigation ruled out a drug-related cause. Magnetic resonance imaging revealed abnormalities suggestive of Alzheimer's disease, with no other evidence to explain the abnormal movements. Apart from the presence of Alzheimer's disease biomarkers, cerebrospinal fluid analysis found no abnormality. Dopamine transporter scan rule out an atypical parkinsonian syndrome. Finally, abnormal movements associated with Alzheimer's disease were suspected. Abnormal movements disappeared within 72 hours on low-dose carbamazepine.

Conclusion: This case is educational both because of the clinical presentation and the management of symptoms.

KEYWORDS

Abnormal movements, Alzheimer's disease, management

LEARNING POINTS

- The number of people suffering from Alzheimer's disease, the leading cause of major neurocognitive disorders, is expected to reach around 78 million in 2030 and 139 million in 2050.
- The course of Alzheimer's disease may be punctuated by atypical symptoms, such as abnormal movements.
- In patients on carbamazepine, we observed a dramatic improvement in abnormal movements associated with Alzheimer's disease.

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INTRODUCTION

Alzheimer's disease is the leading cause of major neurocognitive disorders[1]. According to the World Health Organization (WHO), 44 million people worldwide suffer from Alzheimer's disease. This number is expected to reach around 78 million in 2030 and 139 million in 2050[1,2].

The clinical picture of Alzheimer's disease, characterized by progressive amnesia associated with either instrumental (aphasia, apraxia, agnosia) or behavioural (apathy, indifference, anosognosia) disorders depending on the location of the neuronal lesions, is well known[3]. However, this classic clinical picture can be punctuated by atypical symptoms, as in the clinical case we report here.

CASE DESCRIPTION

An 87-year-old woman followed for Alzheimer's disease was hospitalized for abnormal movements. The diagnosis of Alzheimer's disease was based on clinical, neuropsychological and biological findings. Cerebrospinal fluid analysis showed elevated levels of tau protein at 852 ng/l (normal <400 ng/l), phosphorylated-tau protein-181 at 102 ng/l (normal <60 ng/l), amyloid beta 1-40 peptide at 23298 ng/l (normal 4540-8480 ng/l) and amyloid beta 1-42 peptide at more than 1417 ng/l (normal <550 ng/l). The patient history included a violent traffic accident 55 years previously resulting in multiple complications, including skull fractures and injuries to both hips requiring prosthetics. The accident left the patient with a severe physical and psychological handicap. Her significant past medical history also included breast cancer 13 years previously, hypertension, familial hypercholesterolemia, and gastric haemorrhage.

Her usual treatment included bisoprolol, pantoprazole, acetyl salicylic acid for antiplatelet purposes, atorvastatin, paracetamol and oxazepam. She had a history of antidepressant use.

The patient had a high socio-educational status and continued to live at home with her spouse. She received assistance with bathing and housework. While Alzheimer's disease was in the mild to moderate stage, with a mini-mental-state-examination (MMSE) score of 23/30, the patient began to experience abnormal movements, 4 years after the identification of cognitive disorders suggesting Alzheimer's disease. The episodes started a year and a half before the hospitalization described here, initially occurring a few days per month before occurring daily or multiple times per day. These abnormal movements had no identified triggering factor (stress, alcohol consumption, etc.). They lasted around 30 minutes, mostly in the morning, were involuntary, uncontrollable, anarchic, very large, unilateral or bilateral and predominantly in the upper limbs, and without loss of consciousness or bladder control. Apart from the known chronic clinical signs and abnormal movements, the physical examination was unremarkable.

The first etiological hypothesis was epilepsy, even if the clinical picture was not suggestive. An electroencephalogram (EEG), both standard and with sleep deprivation, performed during abnormal movements, ruled out atypical epilepsy. It showed a background rhythm that was satisfactory, bilateral and symmetrical, but diffusing anteriorly, linked to aging. We observed a few bursts of diffuse slow theta waves, some of which were focused in the left temporal area, related to fluctuating alertness, but without pathological features. A drug-related cause was ruled out after a pharmacovigilance investigation and in the absence of signs of encephalopathy on the EEG. Magnetic resonance imaging revealed cortical atrophy *(Fig. 1)*, predominantly frontotemporal, bilateral grade 1 hippocampal atrophy on the Scheltens scale *(Fig. 1A)*, and score 1 leukoaraiosis on the Fazekas scale *(Fig. 1B)*, with no other abnormality (haemorrhage, tumour, etc.) that would explain the abnormal movements. Apart from the presence of Alzheimer's disease biomarkers, cerebrospinal fluid analysis found no markers of infection, inflammation or 14-3-3 protein. Dopamine transporter (DaT) scan showed no evidence of presynaptic damage of the nigrostriatal dopaminergic system, ruling out the hypothesis of an atypical parkinsonian syndrome. In parallel with the search for the aetiology of abnormal movements, a new cognitive assessment was performed, finding a

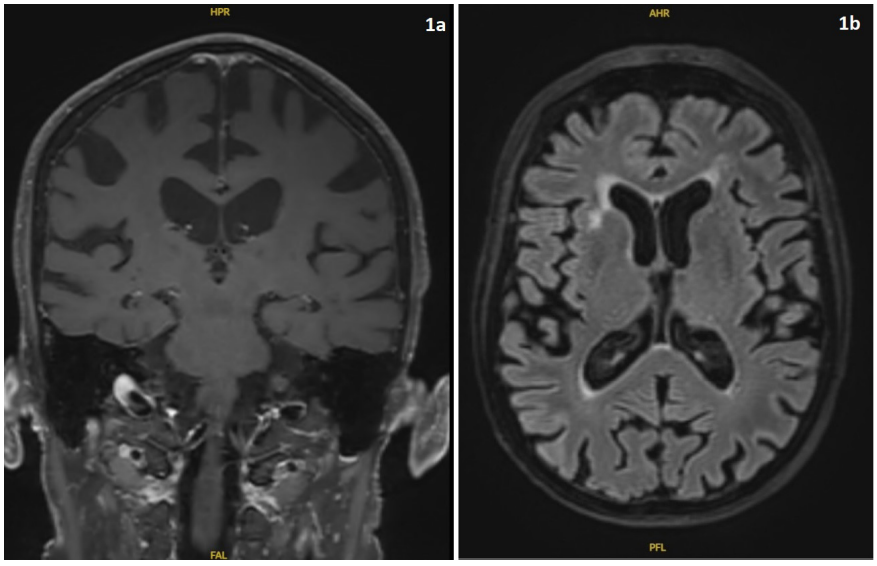


Figure 1. Magnetic resonance imaging showing cortical atrophy, predominantly frontotemporal, bilateral grade 1 hippocampal atrophy (A) on the Scheltens scale, and score 1 leukoaraiosis on the Fazekas scale (B).

decrease in the MMSE score to 15/30, which was possibly underestimated because performed during hospitalization. Another diagnostic hypothesis was raised, that of abnormal movements associated with Alzheimer's disease. The patient was started on low-dose prolonged-release carbamazepine (100 mg morning and night) as a therapeutic test. The result was highly favourable with the disappearance of abnormal movements within 72 hours.

DISCUSSION

The variable course of Alzheimer's disease can be punctuated by complications including the occurrence of atypical signs such as abnormal movements[4]. In addition to being very interesting from a semiological point of view, the novelty of this clinical case concerns the management of abnormal movements during Alzheimer's disease. Abnormal movements have already been described in patients with Alzheimer's disease. However, the motor disorders in these cases were myoclonus[4,5], which was not what occurred in our patient. The moderate dose of carbamazepine had a remarkable effect in our patient, resulting in the complete disappearance of the abnormal movements within a few days, and a clear improvement in quality of life. Carbamazepine has antiepileptic, mood-stabilizing and antimanic effects, and it is also indicated in the management of neuropathic pain[6]. In our case, epilepsy, which was clinically not compatible, was ruled out thanks to EEGs performed during the abnormal movements. Some cases of carbamazepine use for atypical symptoms during the course of Alzheimer's disease have been described in the literature. However, these symptoms tended to be behavioural disorders such as hypersexuality or problematic disinhibition (mood disorders, intrusion)[7,8]. Despite the fact that our patient was experiencing abnormal movements, we initiated carbamazepine based on the beneficial experiences in atypical symptoms in Alzheimer's disease reported in the literature. We were reinforced in our approach both a priori, the abnormal movements being very disabling for the patient, and a posteriori, since they rapidly resolved with treatment. In the literature, other molecules such as selective serotonin reuptake inhibitors have shown a benefit in the management of behavioural disorders in Alzheimer's disease[9]. Although these pharmacological alternatives appear promising, the evidence is not sufficiently robust to be able to recommend their use in routine clinical practice[10]. We feel that there is an interest in performing larger scale studies to investigate the value of these medications in atypical manifestations of Alzheimer's disease. In the immediate future, the prescription of these agents must be made on a case-by-case basis taking into account the benefit/risk ratio.

CONCLUSION

This case is novel both because of the clinical presentation (abnormal movements not associated with epilepsy or atypical parkinsonian syndrome, ruled out respectively by EEG or DaT scan, but appearing during the course of the Alzheimer's disease) and the management of symptoms (dramatic improvement in abnormal movements under carbamazepine). It therefore has great educational value.

REFERENCES

1. Bhatt A, Bhardwaj H, Srivastava P. Mesenchymal stem cell therapy for Alzheimer's disease: A novel therapeutic approach for neurodegenerative diseases. *Neuroscience* 2024;**555**:52-68.
2. Gauthier S, Webster C, Servaes S, Morais JA, Rosa-Neto P, 2022. Life after Diagnosis: Navigating Treatment, Care and Support. Alzheimer's Disease International, London, UK, pp. 1–416.
3. Pillon B, Dubois B, Agid Y. Cognitive deficits in non-Alzheimer's degenerative diseases. *J Neural Transm Suppl* 1996;**47**:61-71.
4. Mahmoudi R, Manckoundia P, Morrone I, Lang PO, Dramé M, Novella JL. Atypical case of Alzheimer's disease mimicking Creutzfeldt-Jakob disease: interest of cerebrospinal fluid biomarkers in the differential diagnosis. *J Am Geriatr Soc* 2010;**58**:1821-1823.
5. Li CH, Fan SP, Chen TF, Chiu MJ, Yen RF, Lin CH. Frontal variant of Alzheimer's disease with asymmetric presentation mimicking frontotemporal dementia: Case report and literature review. *Brain Behav* 2020;**10**:e01548.
6. Bialer M. Why are antiepileptic drugs used for nonepileptic conditions? *Epilepsia* 2012;**53**:26-33.
7. Ozkan B, Wilkins K, Muralee S, Tampi RR. Pharmacotherapy for inappropriate sexual behaviors in dementia: a systematic review of literature. *Am J Alzheimers Dis Other Demen* 2008;**23**:344-354.
8. Stewart JT. Carbamazepine Treatment of Hyperactivity and Intrusiveness in Dementia. *Clin Neuropharmacol* 2018;**41**:43-44.
9. Tosto G, Talarico G, Lenzi GL, Bruno G. Effect of citalopram in treating hypersexuality in an Alzheimer's disease case. *Neurol Sci* 2008;**29**:269-270.
10. Ballard C, Corbett A. Agitation and aggression in people with Alzheimer's disease. *Curr Opin Psychiatry* 2013;**26**:252-259.