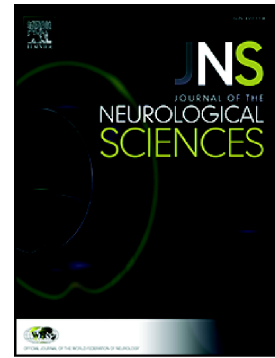


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Reversible sub-acute cognitive deterioration in cerebral amyloid angiopathy: a case report

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Introduction

The pathologies of cerebral small vessel disease (SVD) and Alzheimer's disease (AD) are the most important contributors to cognitive impairment and dementia in the elderly¹. However, the clinical trajectories of individual patients are affected not only by the underlying brain pathology but also by other reversible environmental factors². For instance, one population based study demonstrated that APOE ϵ 4 magnified the effect of physical inactivity, high dietary fat intake, alcohol drinking and smoking on dementia³. It is likely that the combination of pathological and environmental factors leads to the clinical phenotype in individual patients. Identification and removal of potential precipitating factors may have significant implications on the clinical course in patients. We present a case of reversible subacute cognitive deterioration in the context of probable cerebral amyloid angiopathy (CAA) and likely Alzheimer type neuropathology. In this case report we discuss the role of anticholinergic drugs as a precipitating cause of cognitive deterioration.

Case report

A 76-year-old female with a two years' history of subjective memory complaints presented to a local memory clinic for subacute worsening of cognitive function with a dramatic impact on her functional independence and social activities starting from December 2016. An extensive neuropsychological evaluation demonstrated an overall impairment in cognition with greater deficits in visuospatial processing and executive function. Blessed dementia scale (BDS) was 5/37. Global clinical dementia rating (CDR) was 1. Mild to moderate depression was present. Extensive work-up to exclude commonly reversible causes of dementia was negative. Thyroid-stimulating hormone and vitamin 12 levels were within normal range. Syphilis serology and the Mayo clinic autoimmune encephalitis panel were both negative (<https://www.mayomedicallaboratories.com/test-catalog/Overview/48404>). A brain MRI demonstrated diffuse cortical atrophy, extensive white matter hyperintensities (particularly in posterior areas) and more than 10 strictly lobar cerebral microbleeds (CMB), qualifying for a diagnosis of probable CAA⁴ (Figure). FDG-PET showed patchy decrease uptake in the parietal lobe and diminished activity within the posterior cingulate cortex. Lumbar puncture showed p-tau elevation and decreased A β -42 levels. During a memory clinic visit at this hospital for a second opinion in June, 2017, the patient was noted to be on dicyclomine (since December 2016) for irritable bowel syndrome. She was advised to discontinue the drug due to its anticholinergic effects. The patient's cognitive profile subsequently improved to the point that she had regained her baseline functional independence during a follow-up visit in September 2017 (BDS was 0 and CDR was 0.5).

Discussion

CAA is a common age-related cerebral SVD increasingly recognized as a contributor to vascular cognitive impairment and dementia in the elderly. Recent findings suggest a pattern of widespread cognitive changes in CAA patients which affect mainly executive function and processing speed⁴. The neuroradiological and neurocognitive profile of our patient is consistent with a diagnosis of probable CAA. CSF profile and FDG-PET also suggest some contribution of AD pathology in the overall clinical picture.

Despite clear neuroimaging evidence of CAA and AD pathology, this patient had been asymptomatic. This case reminds us that asymptomatic CAA and AD pathology is not uncommon^{1,5}. However, in isolation the detection of these pathologies does not constitute a diagnosis of disease⁵. A dramatic worsening only occurred after starting dicyclomine, a drug with anticholinergic properties. Anticholinergic drugs can cause or worsen cognitive impairment, based on evidence from cross-sectional studies in both healthy elderly population and patients with baseline cognitive impairment or dementia⁶. However, a regression of the cognitive symptoms after the discontinuation of the drug does not always occur⁷. These studies mostly calculated the total burden of anticholinergic drugs, instead of the effect of a single drug. In the case of dicyclomine, there have been 17 cases who experienced the side effect on cognition according to the FDA report so far

(https://www.druginformer.com/search/side_effect_details/Dicyclomine%20Hydrochloride/cognitive%20disorder.html), while no formal reports are available in the literature. The cognitive deficits that have been related to anticholinergic drugs also varies between studies,^{6,7} likely reflect the underlying pathologic process that was already present prior to initiation of drug. One plausible explanation in our patient is that the underlying asymptomatic mixed CAA/AD pathology has lowered the patient's cognitive reserve, making the patient more vulnerable to external factors. The patient's clinical deterioration could have also been influenced by the occurrence of a subacute mood disorder, known to be related with cholinergic system⁸.

In conclusion, we describe the reversal of cognitive impairment in a patient with probable CAA after dicyclomine discontinuation. Our case emphasizes the importance of detecting potentially reversible causes of cognitive impairment even in patients with known vascular and/or neurodegenerative pathologies. This case raises the question as to whether a reversible agent could be used diagnostically to identify those asymptomatic patients with underlying pathologies and low cognitive reserve who may be at increased risk to cognitively deteriorate.

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Figure 1 legend:

Panel A: Axial FLAIR showing posterior white matter hyperintensity (arrowhead) and widening of the sulci. Panel B: Axial T2*-weighted gradient-recalled echo showing lobar cerebral microbleeds (incepts) and absence of cerebral microbleeds in deep area. Panel C: Axial FDG-PET showing patchy decreased uptake in the parietal lobe (right [arrow] greater than left).

Authors Disclosures:

Marco Pasi reports no disclosures

Li Xiong reports no disclosures

Andreas Charidimou reports no disclosures

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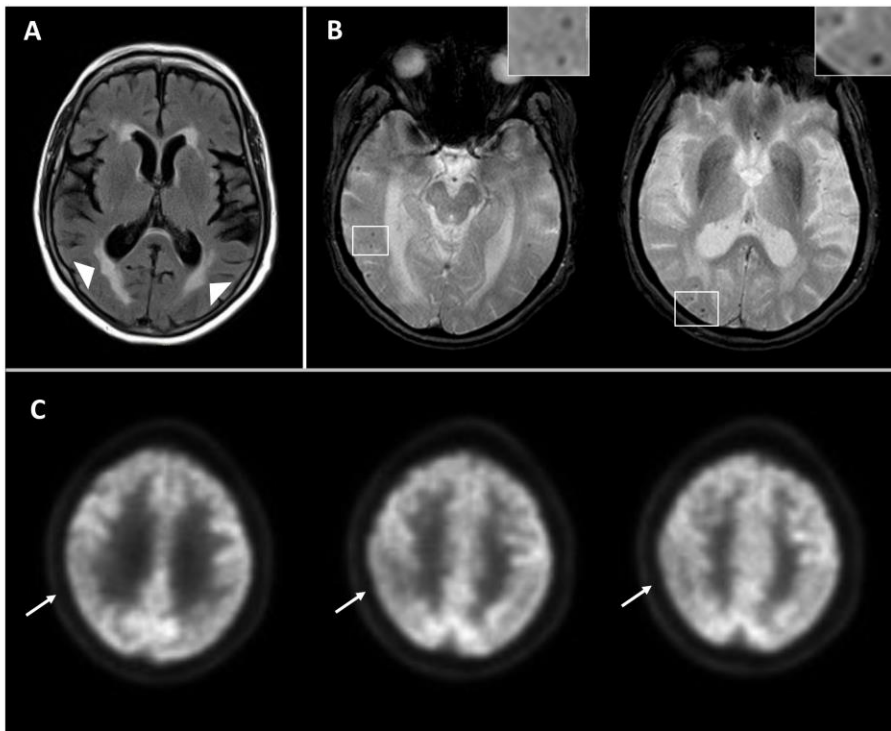


Figure 1