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# Cerebrovascular disease, multiple sclerosis, or both? Case report and review of the challenging distinction between two potentially synergistic syndromes

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ABSTRACT

White matter changes (WMC) are frequently observed in clinical practice, but their clinical relevance is often obscured by radiology reports that do not clearly convey a likely diagnosis. In this regard, two attitudes contribute to diagnostic confusion: a tendency to dismiss findings as trivial (i.e., using vague characterizations such as "non-specific" or "normal for age"), and a gratuitous dilatation of the differential diagnosis (i.e., routinely adding rare diseases to the list, such as vasculitis). Very often, the finding of WMC presents physicians with a very practical problem, which is to determine whether the underlying etiology is an autoimmune demyelinating disease such as multiple sclerosis (MS), or a vasculopathy such as small vessel cerebrovascular disease (SVCVD). The implications of this distinction are great, because the treatment and prognosis of these two syndromes are very different. Here, we describe the challenging case of a relatively young woman with dementia due to a combination of MS and cerebrovascular disease.

## Case description

A 52 year old Chinese female presented with a 9-year history of gradual cognitive difficulties, dysphoric mood and altered sleep-wake-sleep cycles, starting after an otherwise uneventful surgery to remove uterine fibroids. Symptoms were intense enough to delay her return to work for several months. The patient improved, but not to her baseline, and was well until symptoms spontaneously worsened 5 years later, with difficulties concentrating and thinking that culminated in being laid off from work. The patient described her symptoms as "having a constant cloud in the brain." She had short-term recall difficulties and mental confusion, forgetting events, dates, and even the time of the day. She also had problems recognizing places, getting lost easily, while simple calculations became problematic, in spite of her background in economics. In parallel, she developed intermittent gait instability and left leg paresthesia. She was diagnosed with depression and anxiety, and started treatment with escitalopram, clonazepam, and quetiapine. While this treatment resulted in mood improvement, it exerted no effects on her cognitive symptoms, which continued to deteriorate.

Past medical history was relevant for hypertension and hyperlipidemia for 3 years, as well as asthma and allergic rhinitis. Interestingly, she reported an episode of "blindness" when she was a college student 20 years before, from which she recuperated completely within 48 hours. Unfortunately, she could not recall if this was monocular or binocular. She did not have symptoms of obstructive sleep apnea or obesity (BMI=21). Besides her psychiatric medications, she also took amlodipine and rosuvastatin. Her family history was significant for 2 maternal uncles with late-onset Alzheimer's disease.

The neurological exam revealed a fully alert patient, oriented to person, time, place and circumstance. Her registration was 3/3 and delayed recall was 3/3. Speech was fluent, and she was able to name, repeat, follow commands, write, and read. She had significant acalculia. She had a right afferent pupillary defect and pupillary hippus. Fundoscopy was normal. Motor exam and coordination were unremarkable. Deep tendon reflexes were 3+ symmetrically.

A comprehensive neurocognitive examination revealed a profile that was generally consistent with broad, non-dominant (right) hemisphere dysfunction, and deficits in visuospatial abilities, relative weakness in non-verbal memory, and lateralized motor testing (Table 1). In addition, several aspects of her testing and behavioral presentation (e.g., reduced inhibition, disorganization, impulsivity, stimulus-bound behavior, reduced comprehension, reduced confrontation naming, benefit from cuing) were suggestive of deficits with executive functions, comprehen-

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**Table 1**
Neuropsychological Data.

| Performance Validity Testing | | | |
|---|---|---|---|
| | Raw | Rating | |
| VSVT Easy: | 24 | Valid | |
| VSVT Hard: | 24 | Valid | |
| VSVT Total: | 48 | Valid | |
| Reliable Digit Span: | 9 | BR: >25 | |
| CVLT-II Forced Choice: | 16/16 | BR: 94.7 | |
| E-Score | 384.8 | – | |
| Cognitive Screening | | | |
| | Raw Score | Standard Score | |
| *MOCA (Chinese)* | 24/30 | – | |
| Functional abilities | | | |
| | Raw Score Dem Corr | Standard Score % | |
| *Texas Functional Living Scale* | 46 | *T* = 46 | |
| Time | 8 | – | |
| Money and calculation | 6 | – | |
| Communication | 28 | – | |
| Memory | 4 | – | |
| Intellectual Functioning | | | |
| | Raw Score | Standard Score | |
| *Test of Premorbid Functioning* | 26 | 84 | |
| Predicted TOPF | – | 121 | |
| *Wechsler Adult Intelligence Scale, 4th Ed.* | | | |
| Perceptual Reasoning Index | – | 98 | |
| Achievement Testing | | | |
| | Raw Score | Standard Score | |
| *Wide Range Achievement Test, 4th Ed.* | | | |
| Math | 51 | Std = 116 | |
| Attention / Working Memory | | | |
| | Raw Score | Standard Score | |
| *Wechsler Adult Intelligence Scale, 4th Ed.* | | | |
| Digit Span Total | | 22 | SS = 7 |
| Forward | Longest = 5 | 8 | SS = 7 |
| Backward | Longest = 4 | 8 | SS = 9 |
| Sequencing | Longest = 4 | 6 | SS = 7 |
| Processing Speed | | | |
| | | Raw Score | Standard Score |
| *Wechsler Adult Intelligence Scale, 4th Ed.* | | | |
| Coding | | 56 | SS = 8 |
| *D-KEFS Trail Making Test* | | | |
| Visual Scanning | | 17 | SS = 13 |
| Number Sequencing | | 26 | SS = 13 |
| Letter Sequencing | | 33 | SS = 12 |
| Motor Speed | | 39 | SS = 9 |
| *D-KEFS Color-Word Interference* | | | |
| Color Naming | | 31 | SS = 10 |
| Errors | | Self Corrected: | 0 |
| Word Reading | | 20 | SS = 12 |
| Errors | | Self Corrected: | 0 |
| *Color Trails Form A* | | | |
| Part 1 (Chinese) | Errors = 0 | 41 | Z = 0.48 |
| *Symbol Digit Modalities Test* | | | |
| Word Score, Chinese version Errors = 0 | | 49 | Z = 1.21 |
| Language | | | |
| | Raw Score | Standard Score | |
| *Wechsler Adult Intelligence Scale, 4th Ed.* | | | |
| WAIS-IV Verbal Comprehension Index | – | – | |
| Similarities | 33 | SS = 15 | |
| *D-KEFS Verbal Fluency* | | | |
| Letter Fluency | 30 | SS = 8 | |
| Category Fluency | 26 | SS = 5 | |
| *Expressive One-Word Picture Vocabulary Test, 4th Ed.* | | | |
| EOWPVT-4 Total (+0 Gain w/ access to Mandarin) | 109 | Std = <55 | |
| *Tokens Test* | 35 | – | |
| *Verbal Fluency, Chinese* | | Age Corr | |
| Character Fluency, Chinese | 8 | *Z* = -1.50 | |
| *Semantic (Animal) Fluency, Chinese | 15 | *Z* = -0.80 | |

**Normative sample is representative of Mandarin-speaking young adults (Mean age = 35.77, SD = 5.00) and should be interpreted cautiously.*

(*continued on next page*)

**Table 1** (*continued*)

| Performance Validity Testing | Raw | Rating |
|---|---|---|
| Visuospatial Functioning | | |
| | Raw Score | Standard Score |
| *Wechsler Adult Intelligence Scale, 4th Ed.* | | |
| Perceptual Reasoning Index | – | Std = 98 |
| Block Design | 33 | SS = 8 |
| Matrix Reasoning | 19 | SS = 11 |
| *Delis-Kaplan Executive Functioning System* | | |
| Condition 1: Filled Dots | 9 | SS = 10 |
| Errors | Set Loss: | 0 |
| Condition 2: Empty Dots | 9 | SS = 9 |
| Errors | Set Loss: | 0 |
| Condition 3: Switching | 8 | SS = 11 |
| Errors | Set Loss: | 0 |
| Total Correct Designs | 30 | SS = 10 |
| *Rey Complex Figure Copy Test* | | |
| Copy | 34 | – |
| **Hooper Visual Organization Test* | 20 | 62 |
| *Judgment of Line Orientation* | 28 | – |
| ** T-scores are inverted, with higher scores indicating greater likelihood of impairment* | | |
| Verbal Memory | | |
| | Raw Score | Standard Score |
| *California Verbal Learning Test, 2nd Ed.* | | |
| Trial 1 | 5 | z = -1 |
| Trial 5 | 12 | z = -0.5 |
| Total Trial 1 – 5 5/8/11/10/12 | 46 | 46 |
| Learning Slope 1 – 5 | 1.6 | z = 0 |
| List B | 3 | z = -1.5 |
| Short Delay Free Recall | 8 | z = -1 |
| Short Delay Cued Recall | 8 | z = -1.5 |
| Long Delay Free Recall | 8 | z = -1.5 |
| Long Delay Cued Recall | 10 | z = -1 |
| Semantic Clustering | -0.6 | z = -1 |
| Serial Clustering | 1.3 | z = 1 |
| % Recall from Primacy | 28 | z = 0 |
| % Recall from Recency | 35 | z = 1 |
| Across Trial Recall Consistency | 85 | z = 0.5 |
| Total Repetitions | 7 | z = -0.5 |
| Total Intrusions | 2 | z = 0.5 |
| Recognition Hits | 14 | z = -0.5 |
| Recognition False Positives | 2 | z = 0 |
| Total Recognition Discriminability | 2.7 | z = -0.5 |
| *Wechsler Memory Scale, 4th Ed.* | | |
| Logical Memory Immediate Recall | 21 | SS = 8 |
| Logical Memory Delayed Recall | 19 | SS = 9 |
| Logical Memory Recognition | 25 | — |
| *Flud Object Memory Test** | *(z)* | |
| Trial 1 | 8 | -1.26 |
| Trial 2 | 11 | -0.73 |
| Trial 3 | 11 | -1.45 |
| Trial 4 | 9 | -3.25 |
| Trial 5 | 10 | -3.79 |
| Storage | 63 | 0.06 |
| Delayed Recall | 11 | -1.60 |
| **Normative sample is representative of Mandarin-speaking young adults (Mean age = 35.77, SD = 5.00) and should be interpreted cautiously.* | | |
| Non-Verbal Memory | | |
| | Raw Score | Standard Score |
| *Rey Complex Figure Copy Test* | | |
| Immediate Recall | 6 | <20 |
| Delayed Recall | 6.5 | <20 |
| Recognition | 15 | <20 |
| *Brief Visuospatial Memory Test, Revised* | | |
| Trial 1 | 2 | 31 |
| Trial 2 | 3 | 23 |
| Trial 3 | 5 | 21 |
| Total Recall | 10 | 23 |
| Learning | 1 | 35 |
| Delayed Recall | 5 | 30 |

(*continued on next page*)

**Table 1** (*continued*)

| Performance Validity Testing | | | |
|---|---|---|---|
| | Raw | Rating | |
| Percent Retained | 100 | – | |
| Hits | 5 | – | |
| False Alarms | 3 | – | |
| Discrimination Index | 2 | – | |
| Response Bias | .55 | – | |
| Executive Functioning | | | |
| | Raw Score | Standard Score | |
| *Wechsler Adult Intelligence Scale, 4th Ed.* | | | |
| Matrix Reasoning | | 19 | SS = 11 |
| Similarities | | 33 | SS = 15 |
| *Delis-Kaplan Executive Functioning System* | | | |
| Letter Fluency | | 30 | SS = 8 |
| Category Switching | | 17 | SS = 15 |
| Category Switching Accuracy | | 15 | SS = 13 |
| Color-Word Inhibition | | 74 | SS = 7 |
| Errors (Self-Corrected/Uncorrected) | | 0/0 | SS = 12 |
| Color-Word Inhibition Switching | | 67 | SS = 11 |
| Errors (Self-Corrected/Uncorrected) | | 2/9 | SS = 7 |
| Trail Making Number-Letter Switching | | 97 | SS = 10 |
| Total Errors | | 1 | SS = 10 |
| Condition 3: Design Switching | | 8 | SS = 11 |
| Errors | | Set Loss: | 0 |
| *WCST* | # Trials: 111 | | *(Age Corr Std)* |
| Errors | | 30 | Std = 93 |
| Perseverative Responses | | 16 | Std = 94 |
| Perseverative Errors | | 12 | Std = 97 |
| Nonperseverative Errors | | 18 | Std = 88 |
| Categories Completed | | 6 | – |
| Trials to Complete 1st Category | | 30 | – |
| Failure to Maintain Set | | 0 | – |
| *Color Trails Form A* | | | |
| Part 2 *(Chinese)* | Errors = 0 | 125 | – |
| Motor Functioning | | | |
| | Raw Score | Standard Score | |
| *Grooved Pegboard* | | | |
| Dominant | Drops = 2 | 85 | SS = 6 |
| Non-Dominant | Drops = 5 | 100 | SS = 6 |

sion, and retrieval, which collectively implicated frontal-subcortical systems. It was concluded that some of her reported difficulties regulating mood were, at least, partly related to fronto-subcortical inefficiencies. The etiology of her neuropsychological profile at the time was considered to be vascular in nature, but the course, her significant mood symptoms, along with her considerable decline in overall cognition, raised concerns for a superimposed neurodegenerative process. Given the possible visuo-motor slowing contribution to visually mediated tasks, along with her fronto-subcortical involvement, MS was considered as part of the differential and a follow-up neurological evaluation was recommended.

Brain MRI revealed multiple, confluent and non-enhancing areas of prolonged T2 signal involving the subcortical white matter (Fig. 1). Contrast-enhanced MRA revealed multifocal luminal irregularity of intracranial arteries, mainly involving the right A2 and proximal upper and lower divisions of the right MCA. Neck MRA was normal.

The patient was diagnosed with vascular dementia and referred to the stroke clinic at UCLA, where detailed review of neuroimages and past medical history also raised concerns about MS. Importantly, MRI of the cervical spine revealed prolonged T2 cord signal extending from the C3 to C7 segments, indicative of a demyelinating process. The diagnostic work-up is summarized in Table 2. The patient was treated with ocrelizumab 150 mg IV every 6 months, resulting in stabilization of neurological symptoms. She expressed preference to not receive treatment with donepezil or memantine. Her blood pressure was kept < 140/80 mm Hg, while her LDL goal was < 70 mg/dL. She was counseled to take 81 mg of aspirin every day and a daily supplement of vitamin D, exercise daily, and adopt a Mediterranean-style diet.

## Discussion

We have described the case of a patient with early onset dementia associated with extensive WMC, who was initially considered to have vascular dementia but was subsequently diagnosed with MS after detailed review of past medical history, electrophysiology testing, and neuroimaging. The patient exhibited extensive abnormalities on brain MRI circumscribed to the white matter, with predilection for the corpus callosum, which had the typical appearance of “Dawson fingers” [1]. These WMC also involved the periventricular region and centrum semiovale, affecting juxta-cortical regions. This particular distribution is worrisome for a demyelinating disease rather than SVCVD, with MS being the most common culprit. The lack of gadolinium enhancement suggested an ostensibly quiescent process without active inflammation. At this stage, MS can still progress, indicating a neurodegenerative phase of the autoimmune disorder. Although the patient had cardiovascular risk factors, a right thalamic lesion consistent with a lacunar infarct, and evidence of intracranial atherosclerosis, the topography and features of white matter lesions was key to distinguish between cerebrovascular disease and demyelination. Cerebrovascular disease does not usually involve the corpus callosum, given redundant blood supply arising from both hemispheres [1]. Also, cerebrovascular disease does not typically involve the juxtacortical region, where u-fibers predominate, also due to rich collateral supply. There are exceptions to this rule, with CADASIL being the most pertinent example. Young CADASIL patients, in particular, are sometimes misdiagnosed with MS [2,3]. However, our patient did not carry mutations of the NOTCH-3 gene spanning the Epidermal Growth Factor (EGF) motifs (Table 2). In addition, she lacked other clini-

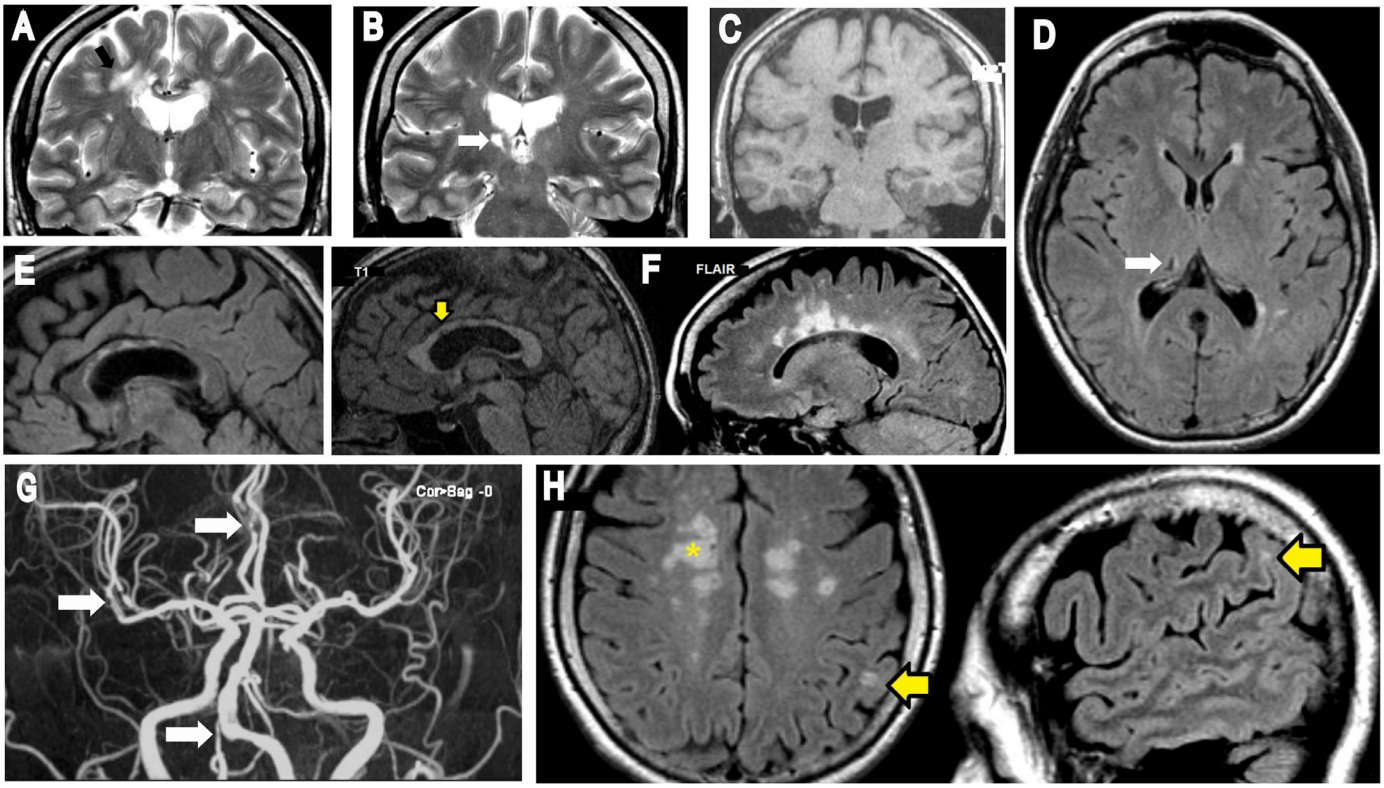


**Fig. 1.** MRI of the Brain with and without contrast. Panels A-B show coronal views demonstrating confluent T2 hyperintense lesions involving the periventricular white matter, mainly on the right side, which extend to the juxta-cortical region (black arrow). These images also reveal substantial atrophy of the corpus callusum and neighboring cerebral cortex. The white arrow in panel B points to a small fluid-filled lesion involving the right thalamus; Panel C provides a T1 coronal view of this lesion, while Panel D demonstrates a hyperintense rim on FLAIR indicating perilesional gliosis (white arrow), which is consistent with a lacunar infarct. Panel E shows T2 hyperintense lesions in the corpus callosum on sagittal FLAIR. Panel F shows indentations of the corpus callosum on T1 sequences (arrow), while the FLAIR sequence on the right shows typical Dawson fingers. Panel G shows multifocal intracranial stenosis (white arrows), predominantly involving the right A2, right MCA branches, and right intradural vertebral artery. Lumen irregularity suggests that atherosclerosis is the underlying etiology. Panel H again shows juxta-cortical lesions (arrows) on sagittal FLAIR involving the left parietal lobe, while the asterisk marks another instance of Dawson fingers extending into the centrum semiovale on the right side.

cal features of CADASIL, including a history of headaches, family history of stroke, or involvement of the temporal poles and external capsule, which were spared in her case (Figure). The presence of brain microhemorrhages and absence of optic nerve and spinal cord abnormalities can help distinguish CADASIL from MS. We also considered an adult-onset leukodystrophy in the differential diagnosis, but a more symmetric and diffuse involvement of the white matter would be expected with this syndrome [4]. We did not test very long chain fatty acids or the HTRA1 gene.

Clinically, some important clues are also worth considering. The patient reported an episode of reversible blindness in her 20's, and the neurological exam showed an afferent pupillary defect. While the evoked potentials were normal, the shape of the P100 peaks was doubled, which is suspicious for a post-chiasmatic conduction delay. Such episode could have represented optic neuritis, although the patient had difficulty remembering details. The symptoms of intermittent gait difficulties, together with the abnormal cervical spine imaging and somatosensory evoked potentials consistent with a demyelinating myelopathy, also point to a diagnosis of MS instead of cerebrovascular disease. An MS mimicking syndrome and a systemic vasculitis were entertained given the presence of faintly (+) ANA. However, the cardiolipin antibody panel was negative, as well as a comprehensive rheumatological work-up outlined in Table 2.

An important argument against the diagnosis of MS in this patient is that oligo-clonal bands (OCB) were not detected in the CSF. Although 1 out of 10 MS cases do not have OCB, the negative predictive value of this test is very high (~90%) [5]. We appropriately considered this a red flag, but could not ignore the other signs of demyelinating disease present in this patient. OCB-negative patients differ genetically from their OCB-positive counterparts, and also have less risk of clinical relapses and brain atrophy [6]. One may reasonably ponder whether OCB-negative MS represents a clinically distinct disease process. This said, no specific tests are currently available to diagnose MS, and physicians must rely on circumstantial evidence to make the diagnosis, using a combination of clinical findings, MRI, evoked potentials, and CSF analysis [7].

Cognitive impairment affects approximately 30–70% of MS patients, usually in association with older age of onset, progressive course, and larger burden of WMC on brain neuroimaging [8]. Jean-Martin Charcot himself noted memory *enfeeblement* and slowness of thinking in MS -a disease that he was the first physician to describe- during a lecture held at the Salpêtrière Hospital in 1877 [9]. The usual cognitive profile of MS patients includes defects in attention, executive function, information processing speed, visuospatial ability, and episodic memory [9]. MS can lead to dementia, but its true prevalence is unclear because an apparent resistance in the literature to use this term, which is otherwise familiar to all neurologists and neuropsychologists. MS is also associated with affective disorders which can exert a negative impact on patient's outcomes; a meta-analysis of 87,756 MS patients showed a pooled mean prevalence of 30.5% for depression, and 22.1% for anxiety [10]. Although depression can feature cognitive symptoms -sometimes referred to as pseudodementia- our patient's cognition did not improve with psychopharmacotherapy, in spite of improvement of dysphoria.

Cardiovascular risk factors, particularly hypertension and hyperlipidemia, are very frequent in the general adult population. These, in turn,

**Table 2**
Summary of diagnostic scrutiny.

| Test | Finding |
|---|---|
| Auditory brainstem evoked potentials: | Normal |
| Motor evoked potentials: | Normal |
| Somato-Sensory Evoked Potentials | Delayed central conduction of lower extremity testing, suggesting a myelopathy below the mid cervical level |
| Visual Evoked Potentials | Results within broad range of normal; P100 peaks shape was doubled, suggesting post-chiasmatic conduction delay |
| Abeta CSF | 749 pg/mL (Normal) |
| T tau CSF | 220 pg/mL (Normal) |
| P-Tau CSF | 74 pg/mL (AD is > 68) |
| ATI | 1.5 (AD is < 0.8) |
| ANA | (+) 1:40 |
| Oligoclonal bands CSF | 0 (Normal) |
| Albumin Index CSF | 5.9 (Normal) |
| IgG Index CSF | 0.5 (Normal) |
| IgG CSF | 3.6 mg/dL (Normal) |
| Albumin CSF | 25.5 mg/dL (Normal) |
| Total protein CSF | 42 mg/dL (Normal) |
| Myelin basic protein CSF | 1.61 (Normal) |
| Cardiolipin antibody | Negative |
| Beta 2 Glycoprotein 1 antibody | Negative |
| DRVVT (Lupus Anticoagulant) | Negative |
| Aquaporin 1 antibody | Negative |
| SSA/SSB antibody | Negative |
| RPR, HIV | Non-reactive |
| C-ANCA, P-ANCA, proteinase-3, Myeloperoxidase antibody | Negative |
| Rheumatoid Factor, thyroid peroxidase antibody, thyroglobulin antibody, Sm antibody, dsDNA antibody, centromere antibody | Negative |
| Homocysteine | 8 mcmol/L |
| Methylmalonic acid level | 0.15 umol/L |
| Vitamin B12 | 665 pg/mL |
| NOTCH 3 sequencing* | No mutations found |
| APOE genotype | e3/e3 |

* This was a next generation exome sequencing test performed in 2017 by Athena Diagnostics. It probes the majority of pathogenic variants involving a loss or gain of a cysteine in EGF motifs. Targets included coding regions in exons and 10 adjacent non-encoding regions. Resulting sequencing were analyzed using bioinformatics, including alignment to GRCh37/hg19 genomic build, and using the Genome Analysis Toolkit 2.3-9 for variant detection. A mean coverage of at least 30 sequencing reads was obtained within each target region with a minimum coverage depth of 20X. Target regions with coverage depths less than the minimum were not reported.

may lead to WMC [11,12], which can be observed in up to two thirds of persons older than 75 years of age [13]. Gradual WMC accrual, typically due to SVCVD, is associated with cognitive decline and stroke [13–16]. Aggressive control of cardiovascular risk factors is advocated to prevent stroke and dementia. There is good evidence that intensive control of blood pressure slows the accumulation of WMC, in addition to well-known reductions in stroke and myocardial infarction [17]. Intensive control of blood pressure also reduces the risk of mild cognitive impairment [18], which may represent the prodrome of dementia in many but not all cases. An intensive control of cardiovascular risk factors, on the other hand, should be a key component of MS management, as a general strategy to curb all potential factors capable of undermining the integrity of white matter tracts. Hypertension and other cardiovascular risk factors are common in MS patients, increasing WMC burden and brain atrophy, both markers of poor outcomes [19]. Specifically, systolic hypertension has been linked with heavier posterior white matter tract loss and greater frontal cortical atrophy in MS patients [20]. Our case is also a reminder that the presence of cardiovascular risk factors can delay the diagnosis of MS, to the detriment of functional status [21].

Our patient had evidence of intracranial stenosis, likely caused by large vessel atherosclerosis, given the observed luminal irregularity on brain MRA and history of vascular risk factors. The principal neuroimaging finding in intracranial stenosis is cortical infarcts within the affected vascular territory, a feature absent in the case we have described. Moreover, the distribution of WMC in our patient was independent from the vascular territories of affected arteries. There is an unclear relationship between intracranial stenosis and ipsilateral WMC in current medical literature [22], compounded by the fact that hypertension and other vascular risk factors -more typically associated with SVCVD- are prevalent in these cases. However, some studies suggest a correlation between intra-cranial stenosis and ipsilateral WMC, although this association does not depend on the degree of stenosis but instead on novel indicators of hemodynamically relevant intracranial atherosclerosis, such as post- to pre-stenotic signal intensity ratios (SIR) generated from time-of-flight MRA [23] and high-resolution MRI (HRMRI) estimates of vessel wall thickness using axial 3D fast spin-echo T1 imaging at 3.0 Tesla [24].

In conclusion, WMC caused by MS can be confused with SVCVD, leading to a wrong diagnosis of vascular dementia. Moreover, many patients with MS have coexisting cardiovascular risk factors and even clear-cut evidence of cerebrovascular disease that can further undermine the integrity of white matter tracts. Therefore, serious consideration should be given to aggressive control of coexistent cardiovascular risk factors in MS, particularly hypertension, hyperlipidemia, and diabetes mellitus. Careful review of neuroimaging and past medical history is needed in young individuals with a presumptive diagnosis of vascular dementia, and if doubts linger, the diagnostic work up should be supplemented with a spinal tap, spine imaging, and evoked potentials to rule out MS.

## Declaration of Competing Interest

None.

## Funding

None.

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