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CNS SLE Vasculitis Mimicking Lewy Body Dementia: A Case Report Emphasizing the Role of Imaging with an Analysis of 33 Comparable Cases from the Scientific Literature

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ABSTRACT

Introduction: Neuropsychiatric symptoms occur in 30 to 40% of patients living with systemic lupus erythematosus (SLE). Brain imaging may play a pivotal role in determining the etiology as it did for the case presented here. **Methods**: A new case of central nervous system SLE is presented along with an analysis of 33 comparable cases from the scientific literature. **Results**: A 70-year-old female with subacute cutaneous lupus presented to a university-based geropsychiatry program after one year of benign visual hallucinations and several months of shuffling gait, recurrent falls, and forgetfulness. These symptoms were highly suggestive of Lewy Body Dementia, however, the patient's history of basal ganglia infarct, cognitive testing demonstrating inattention and executive dysfunction, and follow-up brain imaging, which did not reveal acute findings, aligned with cerebral pathology previously attributed to vasculitis and supported the diagnosis of subcortical dementia due to SLE CNS vasculitis. Oral prednisone 20 mg daily resolved her symptoms. Over the next 19 month her prednisone was tapered completely and her symptoms did not return. A systematic literature search identified 33 comparable cases. **Conclusion**: An analysis of previously published cases suggests that extending the duration of the prednisone taper beyond one year may decrease the risk of later occurring neuropsychiatric symptoms in this patient population.

Key Words: Case report; Lewy body dementia; lymphocytic angiitis; psychosis; systemic lupus erythematosus, vasculitis

Introduction

Neuropsychiatric symptoms (NPS) occur in 30-40% of patients with systemic lupus erythematosus (SLE) with the majority of these symptoms (40-50%) occurring within the first two years following diagnosis.[1] NPS may be due to primary neurological or psychiatric diseases, systemic disease, secondary complications and/or adverse effects of treatment.[2] It is unclear to what degree NPS are directly attributable to SLE, with estimates ranging from 13-38%.[3] Neuropsychiatric SLE (NPSLE) presents overtly with events such as seizure, psychosis, polyneuropathy, and cerebrovascular disease. Symptoms of milder forms of NPS characterized by symptoms such as headache, anxiety or depressive symptoms, and minor cognitive dysfunction often remain unrecognized[4] and usually cannot be attributed specifically to SLE, though they occur commonly in SLE patients.[1] Despite this, and as further discussed below, moderate to severe cognitive impairment in patients living with SLE is associated with antiphospholipid antibodies and is potentially due to multi-infarct dementia.[5]

Up to 3.5% of SLE patients will have psychosis due to recognized medical or physical disease and characterized by disordered/bizarre thinking, including delusions and hallucinations.[1, 2] While auditory hallucinations are often attributed to steroid therapy, visual and tactile hallucinations are thought to be due to SLE and are associated with antibodies to neuronal cells.[6]

Cerebrovascular disease in SLE patients can contribute to NPS, including psychosis and cognitive dysfunction. Up to 10% of SLE patients will experience cerebrovascular disease. Though SLE patients can present with thromboembolic or

hemorrhagic symptoms, 80% of patients present with ischemic stroke/TIA.[1] Antiphospholipid antibodies are associated with highly thrombotic states and can lead to multiple cerebral infarcts, causing recurrent stroke and multi-infarct dementia.[7, 8] Cerebrovascular events have high morbidity and mortality, particularly when associated with ill-defined cerebrovascular events and rare nervous system disease, such as cerebral vasculitis, which is demonstrated in less than 10% of postmortem studies.[9-11] One recent single-center study estimated that, compared to SLE patients without NPS, those with NPSLE had a three-times greater mortality and patients with CNS NPSLE, such as CNS vasculitis, had an almost eight-times greater mortality.[12] Brain biopsy remains the gold standard in the diagnosis of CNS vasculitis, but neuroimaging in conjunction with appropriate clinical examination and laboratory testing to exclude other potential causes can spare patients the risks associated with biopsy. Magnetic resonance imaging (MRI) and angiography (MRA) are highly sensitive for changes to the cerebral vasculature. Findings such as thickened or enhancing endothelium in cerebral vascular walls, vascular stenosis, multiple ischemic infarctions distributed across different vascular territories are the most pathognomonic MRI findings of vasculitis. High-intensity white matter lesions that appear bright on T2 and fluid-attenuated inversion recovery (FLAIR) imaging, though extremely nonspecific, are also suggestive of vasculitis.[13] In the proper clinical context, these findings can be deemed sufficient to initiate treatment for vasculitis, without need for biopsy.[13]

Psychosis and cognitive decline in SLE patients present diagnostic dilemmas. Differentiating psychosis due to steroid treatment from other medical or physical causes of psychosis requires a particularly thorough timeline of symptoms,

treatment doses, emergence of medication side effects, and changes on MRI.[14, 15] Similarly, understanding changes in cognitive function in SLE patients, especially in older adults, is challenging, as the frequency of cognitive dysfunction and cerebrovascular disease both increase with age, and subcortical vascular dementia can present with psychotic features.[16-19] A thorough review of neurocognitive testing, especially when coupled with cerebrovascular MR imaging, can help identify medical causes of psychiatric symptoms in these patients.

Methods

We present here a case of new-onset psychosis and cognitive impairment, mimicking Lewy Body Dementia, in a 70-year-old female with CNS vasculitis coupled with an analysis of all similar cases identified through a systematic literature search. All the case reports in the English literature of human patients with CNS vasculitis mimicking psychiatric conditions obtained by search of the PubMed and MEDLINE databases were reviewed. Specifically, reports were searched using the MeSH terms:

> ("case reports"[Publication Type] OR "case report"[All Fields]) AND ("vasculitis, central nervous system"[MeSH Terms] OR ("vasculitis"[All Fields] AND "central"[All Fields] AND "nervous"[All Fields] AND "system"[All Fields]) OR "central nervous system vasculitis"[All Fields] OR ("central"[All Fields] AND "nervous"[All Fields] AND "system"[All Fields] AND "vasculitis"[All Fields])) AND ("psychiatry"[MeSH Terms] OR "psychiatry"[All Fields])

Articles previously acquired by the authors not identified from this search were also reviewed.

Only case reports which met the following criteria were included:

(1) adult patient (>18 years)

(2) patient experienced new-onset NPS, defined as chronic headache, cognitive impairment, neuropathic pain, changes in behavior or vision, or impairments in language production or construction (with or without impairments in gait, balance, or strength)

(3) biopsy of a nerve or artery was consistent with vasculitis or, in cases where biopsy was not completed, imaging demonstrating thickened or enhancing endothelium in cerebral vascular walls, vascular stenosis, multiple ischemic infarctions distributed across different vascular territories, or high-intensity white matter lesions that appear bright on T2 and fluid-attenuated inversion recovery (FLAIR) imaging

(4) Report that the patient improved with steroid treatment and/or other immunosuppressants

Cases of transverse myelitis were excluded, as isolated spinal cord involvement is not expected to cause psychiatric symptoms. Further, this spinal cord disorder is estimated to affect 1-2% of lupus patients[20] and primary CNS angiitis is isolated to spinal cord in <1% of cases.[21]

Results

Case Vignette

A 70-year-old female with history of subacute cutaneous lupus (SCLE), hypertension, hyperlipidemia, and recurrent deep vein thromboses (DVTs) on warfarin who was brought to a university-based hospital emergency department by police officers for evaluation of dangerousness to herself and grave disability after she called the police to investigate intruders in her home. She was first diagnosed

with subacute cutaneous lupus (SCLE) in 2013, after development of an erythematous rash on her back, arms and face in 2012. The rash did not abate despite trial of trials of drug cessations and, hence, she was referred to dermatology for further evaluation. A biopsy in 2013 confirmed her diagnosis of SCLE. Her rash resolved with oral prednisone and topical clobetasol. Her rheumatologic laboratory findings at the time of her diagnosis are listed in Table 1. The police officers reported that when they arrived at the patient's home, the patient was found alone, though she adamantly pointed towards a location in the room where she believed two intruders stood. Rotten food, massive piles of trash, and insects were found throughout her home and she while with the police she denied all forms of psychosis including visual hallucinations.

During a review of symptoms conducted in the ED, she reported a one-year history of visual hallucinations and a few-month history of shuffling gait, recurrent falls, and forgetfulness. CT of the head on admission demonstrated no acute intracranial processes, though stable chronic sequelae of a previous right thalamic infarct were present. Her neurological examination revealed deficits in short-term memory, though her long-term memory was intact. Her motor exam was without significant tremor, rigidity, postural instability, masked face or bradykinesia. Her Montreal Cognitive Assessment (MoCA)[22] score of 19/30 prompted neuropsychological testing, which yielded a Mattis Dementia Rating Scale-2 Score[23] of 133/144 (low-average range), with pronounced deficits in construction and low-average performance with executive function, though recall was intact with prompts. Apathy and left visual field inattention affected her score on several tasks. She had no

evidence of cutaneous involvement of lupus at her time of presentation nor other signs of active lupus.

Medical History: Previous Imaging and Biopsy Suggesting CNS Vasculitis_

A review of the patient's medical history demonstrated a previous diagnosis of CNS vasculitis (lymphocytic angiitis). During an admission one year previously, the patient experienced left-sided neglect, which led to motor vehicle accidents. This prompted a brain MRI, demonstrating irregularity/beading of her right Middle Cerebral Artery (Figure 1, left panel, white arrow). MR angiography at that time revealed that the distal branches of her right Middle Cerebral Artery appeared smaller in number and caliber compared to the contralateral side (Figure 1, right panel, red arrow).

One month after the MRI and angiography, the patient developed left facial droop, left tongue deviation, and left hemiparesis. An MRI at this time demonstrated a right thalamic infarct and a brain biopsy demonstrated angiocentric and angioinfiltrative lymphocytes with macrophages and reactive gliosis. She was treated with rituximab and prednisone (20 mg daily) and demonstrated improvement in her neurologic deficits. She had not received treatment with anti-malarial agents as she declined an offer of hydroxychloroquine by rheumatology. Prednisone was tapered from 20 mg to 10 mg daily at her follow-up appointment three weeks later. The patient experienced worsening left-sided weakness over two weeks at 10 mg daily, so her dose was returned to 20 mg daily, and her deficits once again resolved. Subsequently, a slow prednisone taper, from 20 mg to 10 mg over three months, demonstrated no worsening of symptoms.

Follow-up Imaging

During the evaluation of her visual hallucinations, shuffling gait, recurrent falls, and forgetfulness, another brain MRI was obtained in order to explore whether an acute vasculitic flare had caused the patient's hallucinations, motor abnormalities and cognitive deficits. Although the contrast agent gadolinium improves the detection of inflammatory white matter lesions,[24] for unknown reasons it was not used for the patient's follow-up brain MRI. Nonetheless, this scan showed no evidence of vessel cutoff, focal vessel narrowing, beading, or aneurysms, though the right MCA changes were still present (Figure 2, blue arrow). Thus, no evidence for active or progressive vasculitis was seen on MRI.

Management

The patient's lack of acute findings on her follow-up MRI, history of basal ganglia infarct, and neuropsychological testing demonstrating inattention and frontal (executive) dysfunction made subcortical dementia due to SLE CNS vasculitis a possible explanation for her symptoms. Rheumatology was consulted at the time of admission, reviewed her neuroimaging described above, and expressed concern that an alternate explanation to her SLE may be contributing based on lack of evidence of active or progressive vasculitis on imaging as well as her lack of signs of active disease on exam. They recommended a neurology consultation, which also was obtained. Neurology felt that her previously documented cerebral pathology and lack of Parkinsonism on neurological examination made Lewy Body dementia less likely, and felt that her cognitive changes most likely reflected her CNS vasculitis, based on her history of response to prednisone and rituximab in the past. Despite her history of recurrent deep vein thrombosis, she did not have

evidence of multiple infarcts on neuroimaging to raise concern for a vascular dementia. Due to the only symptom or sign of disease being neuropsychiatric symptoms, with no evidence of imaging or exam findings to correspond with a more active flare of SLE, rheumatology recommended against re-trial of rituximab, and instead recommended an increase in prednisone from 10 mg daily to the previously effective dose of 20 mg daily. Additionally, she was maintained on risperidone 0.5 mg PO BID PRN for agitation which she required only infrequently, escitalopram 20 mg PO daily for depression and trazadone 50 mg PO nightly for insomnia. Her neuropsychiatric symptoms resolved with these medication adjustments.

After discharge from the geropsychiatry unit, she returned to her outpatient rheumatology clinic for ongoing oversight of her prednisone taper. Understanding that the 20-mg dose proved effective prior to and during her recent previous admission, the rheumatology consultant recommended a slow taper of 2.5 mg every 4 weeks, with careful attention to hallucinations. Six months post-discharge, the patient was tapered to a dose of 10 mg daily. Symptoms of adrenal insufficiency, in conjunction with a lack of hallucinations, led to continued tapering, until she was no longer taking prednisone about 19 months after her discharge from the geropsychiatry unit and her symptoms of hallucinations never returned. A repeat MRI and angiography demonstrated the expected interval evolution of her prior imaging findings without worsening.

Summary of Previously Published Case Reports of CNS Vasculitis Findings

Table 2 lists all of the cases which met the study criteria. In addition to age, whenever reported, gender, past medical and psychiatric history, presenting symptoms, and medications at presentation, are detailed. Duration of vasculitis, treatment of vasculitis, laboratory and imaging findings, biopsy findings, and recurrence of vasculitis are also summarized. Table 3 provides a summary of the available data including age at presentation, gender, and duration of symptoms. The frequency of the most common psychotic features is also provided.

Patients from the 33 case reports reviewed demonstrated a mean age of 52.85 years (range 18 – 90 years). Seventeen of the patients were male (51.51%), while 16 were female (48.48%). Symptoms lasted an average of 5.39 months (range 0.25-24 months). The most common presenting symptoms included speech impairment (aphasia, paraphasia, dysarthria, apraxia, or incoherent or abnormal speech, in 12 cases) and chronic headaches (eight cases). No patients demonstrated concomitant headaches and speech impediments. Vision deficits (simultanagnosia, loss of vision, or blurred vision) were reported in seven cases. Coordination difficulties (disorientation, clumsiness, dizziness, vertigo, and ataxia) were reported in 13 cases, though separating these symptoms from concomitantly reported symptoms such as hemiparesis, hemiplegia, paralysis, arm weakness proved difficult. Only five cases reported psychotic symptoms: auditory and visual hallucinations were present in one case each, erratic thinking was present in one case, and delusions were present in two cases.

Six cases reported cognitive deficits, with two patients demonstrating symptoms of dementia. Cognitive testing was not commonly performed, though Mini Mental State

Examination was performed in two reports: one patient demonstrated a score of 3/30, which improved to 14/30 after oral prednisolone for 12 days, while another scored 24/30.

Pre-existing medical or neurological conditions were included in 25 reports. Perhaps unsurprisingly, in seven patients, a history of hypertension was reported (four of these patients had giant cell arteritis (GCA) ischemic events). A history of SLE was present in six patients. Only five cases provided previous psychiatric history, with four patients suffering from depression.

Eleven cases included information about antibody test results and ten of these cases specifically reported on antiphospholipid antibody (APLS ab) test results. In these ten cases, the APLS ab was reported as normal (4) and negative (6). In the remaining case the report stated “antibodies were absent.” Imaging commonly demonstrated findings consistent with ischemia: CT and/or MR imaging demonstrated ischemic lesions in 30 of 33 patients, and subsequent angiography demonstrated an area of focal narrowing in nine cases.

Most patients (31 of 33) received therapy targeted towards their underlying vasculitis. All therapies administered consisted of high dose steroids. Though the steroid agent was not always explicitly stated, reported treatments typically included methylprednisolone. Initial treatment doses varied by report, with the highest initial dose of 1 g per day over 5 days. Discharge dosing varied from 2.5 mg to 1 g per day, with subsequent taper. Cyclophosphamide was given alongside steroid treatment in 12 cases and given as monotherapy in two cases, with IV doses

ranging from a single pulse of 500 mg/m^2 to pulses of 2 g per month for six months and oral doses ranging from 100-150 mg per day. Despite therapeutic steroid ranges, six patients either succumbed to their symptoms or experienced a recurrence of symptoms.

Discussion

Concomitantly occurring new cognitive impairment and psychotic features in SLE patients present a diagnostic dilemma, particularly in aging patients with vascular risk factors who are on maintenance steroid therapy. In this patient's case, the differential diagnosis included an acute vasculitic episode, subcortical dementia due to chronic vascular inflammation, steroid psychosis due to supra-therapeutic dosing, and underlying primary psychosis as potential causes for her neurocognitive changes. Understanding the temporal relationship between symptoms, treatment doses, side effects, and changes in her findings on serially obtained MRI helped elucidate the underlying cause.

Our review of literature of patients with CNS vasculitis mimicking psychiatric conditions demonstrated several important considerations for clinicians treating such patients. First, the most common psychotic symptoms found in our review of CNS vasculitis patients were delusions, followed by auditory/visual hallucinations and erratic thinking, though these were uncommon (3-6%). The low rate of hallucinations and delusions in these patients emphasizes the need for careful mental status examination during neuropsychiatric assessment to sense minor changes in mentation over time, as hallucinations and delusions are typically not present to help with diagnosis. A recent case series by Rodrigues et al. emphasized

the variety of presentations of CNS vasculitis in SLE patients. Their case series presented four patients with hypertension and/or dyslipidemia who went on to develop CNS vasculitis. Only one patient demonstrated cognitive deficits, including a language deficit (an inability to combine verbs). The other three patients presented with monoparesis, seizure, and demyelinating syndrome.[13]

Second, our review of the CNS vasculitis literature yielded only four cases reporting pre-existing depression at the time of presentation. Crucially, depression is under-recognized in patients with CNS vasculitis and could represent an early symptom.[52] Providers should thus screen SLE patients for depression as new depressive symptoms might suggest an opportunity to intervene prior to the development of further neuropsychiatric disease.

Several models have been proposed to describe dementia in CNS vasculitis patients, including a multiple-infarct model for vascular dementia. Vascular dementia can lead to severe cognitive dysfunction, impaired memory, impaired abstract thinking, and a decreased ability to perform simple manual tasks. Difficulty making decisions and controlling impulses are also common.[8] This patient's memory deficits were thought to be related to inattention related to frontal executive dysfunction, since she had difficulty with immediate recall but fared better with recognition and cued recall. Her executive dysfunction contributed to her grave disability, as the inability to carry out complex tasks clearly impaired her ability to perform activities of daily living.[16]

An older paradigm recognizes two patterns of cognitive impairment in SLE: impaired delayed recognition is associated with past or current nervous system involvement, and suggests residual neurological defect, whereas impaired immediate memory and concentration likely represent transient and diffuse CNS effects.[25] Though this patient appropriately fits the latter description, the pathophysiology of cognitive impairment is likely much more complex, as auto-antibodies, inflammatory mediators, endocrine factors, and vascular abnormalities have all been implicated in cognitive impairment in these patients.[26]

Hallucinations in this patient might have been affected by her previous thalamic injury, though her medications complicated the presentation. Whereas hallucinations in basal ganglia lesions are thought to occur due to frontal lobe dysfunction, causing an inability to utilize reality-checking pathways in the brain,[18] steroids typically cause dose-dependent psychosis within the first six weeks of treatment, with increased risk with prednisone-equivalent dose ≥ 40 mg/day. Crucially, discontinuation of the drug typically resolves NPS.[27] This patient's taper of her prednisone regimen from 20 mg to 10 mg daily was felt to be the precipitating factor in the flare of her vasculitis, that would go on to damage her cerebral vasculature, predisposing her to subcortical dementia. Improvement on 20 mg daily dose of prednisone further supported damaged vasculature as the cause of her dementia.

Imaging played a central role in understanding the pathophysiology of this patient's presentation. MRI and angiography in patients with cerebrovascular disease, represent important tools in the diagnosis of CNS vasculitis. Several characteristic

MRI findings have been identified in such cases. These include white and grey matter hyper-intensities, parenchymal defects, and abnormal DWI, as discussed previously. The latter three findings are especially common in patients with cerebrovascular disease or seizures.[28] Recent studies have shown SLE patients demonstrate a greater volume of white matter lesions compared to healthy controls, with corresponding cognitive dysfunction, particularly decreased verbal memory. Interestingly, bilateral hippocampal atrophy was also seen more commonly in patients with NPSLE than those with SLE without NPS.[29] Although imaging played a central role in the diagnosis of the vast majority of the cases included in this study, the allowance of three cases to be considered examples of CNS vasculitis in the absence of biopsy confirmation and with imaging revealing only white matter hyperintensities (Hirachi et al. 2015 and Rodrigues et al. cases 2 and 3) is a limitation of our study, given the well-known lack of specificity of white matter hyperintensities which has been acknowledged above.

The role of histopathology in the diagnosis of CNS vasculitis should not be dismissed, even as highly-sensitive imaging modalities continue to be developed, as imaging in CNS vasculitis is often non-specific, and some patients with NPSLE demonstrate normal MRIs. Though suggestive of NPSLE in the proper clinical context, diffuse vasculopathy, macro- and micro-infarction, and vasculitis are not specific to NPSLE. Despite this, sections of cerebral vessels demonstrating microthrombi with C4d and C5b-9 deposits have recently been identified as histopathologically unique to NPSLE. In one study, these small vessel injuries were not detectable, even with 7T MRI, but were highly-specific to NPSLE.[30] Positron emission tomography (PET) scanning using 18F-FDG radiotracer has demonstrated

the ability to identify minor neuroinflammation, such as microthrombi, but research into this technology is in the early stages of evaluation.[31]

Conclusion

The presentation of the patient we have described demonstrates the difficulty in differentiating the many causes of neurocognitive changes and psychiatric symptoms in patients with SLE. Careful attention to the pattern of cognitive deficits, the temporal emergence of cognitive and psychiatric symptoms and the neurological exam can help treating physicians build a proper differential diagnosis. This clinical suspicion guides utilization of imaging to ensure their patients receive optimal care.

The Authors declare that they have no conflicts of interest.

References

1. Bertsias GK, Boumpas DT. Pathogenesis, diagnosis and management of neuropsychiatric SLE manifestations. *Nat Rev Rheumatol.* 2010;6(6):358-367.

2. West SG. Neuropsychiatric lupus. *Rheum Dis Clin North Am.* 1994;20(1):129-158.

3. Hanly JG, Urowitz MB, Jackson D, et al. SF-36 summary and subscale scores are reliable outcomes of neuropsychiatric events in systemic lupus erythematosus. *Ann Rheum Dis.* 2011;70(6):961-967.

4. Tay SH, Mak A. Diagnosing and attributing neuropsychiatric events to systemic lupus erythematosus: time to untie the Gordian knot? *Rheumatology (Oxford).* 2017;56(suppl_1):i14-i23.

5. Tomietto P, Annese V, D'Agostini S, et al. General and specific factors associated with severity of cognitive impairment in systemic lupus erythematosus. *Arthritis Rheum.* 2007;57(8):1461-1472.

6. Bluestein HG, Williams GW, Steinberg AD. Cerebrospinal fluid antibodies to neuronal cells: association with neuropsychiatric manifestations of systemic lupus erythematosus. *Am J Med.* 1981;70(2):240-246.

7. Locht H, Wiik A. IgG and IgM isotypes of anti-cardiolipin and anti-beta2-glycoprotein i antibodies reflect different forms of recent thrombo-embolic events. *Clin Rheumatol.* 2006;25(2):246-250.

8. Asherson RA, Mercey D, Phillips G, et al. Recurrent stroke and multi-infarct dementia in systemic lupus erythematosus: association with antiphospholipid antibodies. *Ann Rheum Dis.* 1987;46(8):605-611.

9. Bernatsky S, Clarke A, Gladman DD, et al. Mortality related to cerebrovascular disease in systemic lupus erythematosus. *Lupus.* 2006;15(12):835-839.

10. Nguyen-Oghalai TU, Wu H, McNearney TA, Granger CV, Ottenbacher KJ. Functional outcome after stroke in patients with rheumatoid arthritis and systemic lupus erythematosus. *Arthritis Rheum.* 2008;59(7):984-988.

11. Weiner DK, Allen NB. Large vessel vasculitis of the central nervous system in systemic lupus erythematosus: report and review of the literature. *J Rheumatol.* 1991;18(5):748-751.

12. Ahn GY, Kim D, Won S, et al. Prevalence, risk factors, and impact on mortality of neuropsychiatric lupus: a prospective, single-center study. *Lupus.* 2018;27(8):1338-1347.

13. Rodrigues M, Galego O, Costa C, et al. Central nervous system vasculitis in systemic lupus erythematosus: a case series report in a tertiary referral centre. *Lupus.* 2017;26(13):1440-1447.

14. Chandra SR, Issac TG, Ayyappan K. New Onset Psychosis as The First Manifestation of Neuro-Psychiatric Lupus. A Situation Causing Diagnostic Dilemma. *Indian J Psychol Med.* 2015;37(3):333-338.

15. Murata M, Hashiramoto A, Yamaguchi T, et al. A case of central nervous system lupus in succession to lupus peritonitis: a difficulty in the differential diagnosis between lupus psychosis and steroid-induced psychosis. *Mod Rheumatol.* 2004;14(4):323-326.

16. Jeong JH, Kim E-J, Seo SW, Na DL. Cognitive and behavioral abnormalities of vascular cognitive impairment.In Miller BL, Boeve BF eds. *The Behavioral*

Neurology of Dementia. Cambridge, UK: Cambridge University Press; 2016: Chapter 19.

17. Dennis MS, Byrne EJ, Hopkinson N, Bendall P. Neuropsychiatric systemic lupus erythematosus in elderly people: a case series. *J Neurol Neurosurg Psychiatry.* 1992;55(12):1157-1161.

18. McMurtray A, Tseng B, Diaz N, et al. Acute Psychosis Associated with Subcortical Stroke: Comparison between Basal Ganglia and Mid-Brain Lesions. *Case Rep Neurol Med.* 2014;2014:428425.

19. Butler C, Zeman AZ. Neurological syndromes which can be mistaken for psychiatric conditions. *J Neurol Neurosurg Psychiatry.* 2005;76(Suppl 1):i31-38.

20. Quintanilla-Gonzalez L, Atisha-Fregoso Y, Llorente L, Fragoso-Loyo H. Myelitis in systemic lupus erythematosus: clinical characteristics and effect in accrual damage. A single-center experience. *Lupus.* 2017;26(3):248-254.

21. Benesh F, Pennington A, Fallon K, Rinker J. A Case of Primary CNS Angiitis Presenting as Longitudinally Extensive Transverse Myelitis *Neurology*. 2018, 90(15 Supplement) P6.228

22. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc.* 2005;53(4):695-699.

23. Jurica PJ, Leitten CL, Mattis S. *DRS-2 : Dementia rating scale-2: professional manual*. Lutz, FL: Psychological Assessment Resources; 2001.

24 Miller DH, Buchanan N, Barker G, et al. Gadolinium-enhanced magnetic resonance imaging of the central nervous system in systemic lupus erythematosus. *J Neuro* 1992;239:460-464.

25. Fisk JD, Eastwood B, Sherwood G, Hanly JG. Patterns of cognitive impairment in patients with systemic lupus erythematosus. *Br J Rheumatol.* 1993;32(6):458-462.

26. Kozora E, Hanly JG, Lapteva L, Filley CM. Cognitive dysfunction in systemic lupus erythematosus: past, present, and future. *Arthritis Rheum.* 2008;58(11):3286-3298.

27. Bhangle SD, Kramer N, Rosenstein ED. Corticosteroid-induced neuropsychiatric disorders: review and contrast with neuropsychiatric lupus. *Rheumatol Int.* 2013;33(8):1923-1932.

28. Jeong HW, Her M, Bae JS, et al. Brain MRI in neuropsychiatric lupus: associations with the 1999 ACR case definitions. *Rheumatol Int.*2015;35(5):861-869.

29. Cannerfelt B, Nystedt J, Jonsen A, et al. White matter lesions and brain atrophy in systemic lupus erythematosus patients: correlation to cognitive dysfunction in a cohort of systemic lupus erythematosus patients using different definition models for neuropsychiatric systemic lupus erythematosus. *Lupus.* 2018;27(7):1140-1149.

30. Cohen D, Rijnink EC, Nabuurs RJ, et al. Brain histopathology in patients with systemic lupus erythematosus: identification of lesions associated with clinical neuropsychiatric lupus syndromes and the role of complement. *Rheumatology (Oxford).* 2017;56(1):77-86.

31. Mauro D, Barbagallo G, D Angelo S, et al. Role of Positron Emission Tomography for Central Nervous System Involvement in Systemic Autoimmune Diseases: Status and Perspectives. *Curr Med Chem.* 2018;25(26):3096-3104.

32. Börnke C, Heye N, Büttner T. Rapidly progressive dementia. *The Lancet.* 1999;353(9159):1150.

33. Ampelas JF, Wattiaux MJ, Van Amerongen AP. [Psychiatric manifestations of lupus erythematosus systemic and Sjogren's syndrome]. *Encephale.* 2001;27(6):588-599.

34. Jacobs DA, Liu GT, Nelson PT, Galetta SL. Primary central nervous system angiitis, amyloid angiopathy, and Alzheimer's pathology presenting with Balint's syndrome. *Surv Ophthalmol.* Jul-2004;49(4):454-459.

35. Lukas C, Keyvani K, Bornke C. Primary angiitis of the central nervous system presenting with subacute and fatal course of disease: a case report. *BMC Neurol.* 2005;5:16.

36. Solans-Laque R, Bosch-Gil JA, Molina-Catenario CA, et al. Stroke and multi-infarct dementia as presenting symptoms of giant cell arteritis: report of 7 cases and review of the literature. *Medicine (Baltimore).* 2008;87(6):335-344.

37. Qu SB, Khan S, Liu H. Primary central nervous system vasculitis mimicking brain tumour: case report and literature review. *Rheumatol Int.* 2009;30(1):127-134.

38. Pires C, Foreid H, Barroso C, Ferro JM. Rapidly progressive dementia due to leukocytoclastic vasculitis of the central nervous system. *BMJ Case Rep.*2011;2011:bcr0820114619. doi:10.1136

39. Montefort M, Dashora U, Chowdhury M. Cerebral vasculitis presenting as a stroke. *BMJ Case Rep.* 2012;2012:bcr2012007194. doi:10.1136.

40. Coronel-Restrepo N, Bonilla-Abadia F, Cortes OA, et al. Primary angiitis of the central nervous system: a report of three cases from a single colombian center. *Case Rep Neurol Med.* 2013;2013 Article ID:940438. doi:10.1155.

41. Kalra S HS, Gutowski NJ. A Case of Isolated Central Nervous System Vasculitis. *ACNRM.* 2013.

42. Shiner EA, Zagami AS. An illustrative case of primary angiitis of the central nervous system. *SAGE Open Med Case Rep.* 2014. doi:10.1177

43. Holay MP, Game PD, Kharkar S, Chudalwar P. A case report: primary CNS angiitis. 2015;3(7):1813-1816. doi:10.18203.

44. Hirachi T. Mania occurring during systemic lupus erythematosus relapse and its amelioration on clinical and neuroimaging follow-up. Lupus. 2015;24(9):990-3. doi: 10.1177.

45. Bonstrup M, Ott K, Glatzel M, Magnus T. Frontal lobe dementia syndrome as a first manifestation of primary angiitis of the central nervous system (PACNS). *Clin Neurol Neurosurg.* 2016;141:92-94.

46. Johnson MA, Jakubek GA, Hawley JS. Unihemispheric cerebral vasculitis: Case report and review of literature. *J Neurol Sci.* 2016;368:32-34. doi:10.1016

47. Kumar A, Goel A, Lapsiwala M, Singhal S. Refractory rheumatoid vasculitis. *Oxf Med Case Reports.* 2016; 2016(11). doi:10.1093.

48. Xiao Y-D, Paudel RC, Zhou S-K, et al. Imaging findings of primary angitis of central nervous system: case report and literature review. *Int J Clin Exp Med*. 2016;9(6):12341-12344.

49. Hasan TF, Maraka S, Leeds NE, Loghin ME. A Rare Case of Primary Angiitis of the Central Nervous System (PACNS) Associated with Metastatic Prostate Cancer. *Neurology*. 2017; 88 (16 Supplement):155.

50. Kumar PP, Rajesh A, Kandadai RM, et al. Primary CNS vasculitis masquerading as glioblastoma: A case report and review. *Asian J Neurosurg.* 2017;12(1):69-71.

51. Lee JS, Jung TY, Lee KH, Kim SK. Primary Central Nervous System Vasculitis Mimicking a Cortical Brain Tumor: A Case Report. *Brain Tumor Res Treat.* 2017;5(1):30-33.

52. Chu L, Eustace M, Pittman N. Primary Angiitis of the Central Nervous System Presenting With Headache and Ataxia. *Can J Neurol Sci.* Aug 6 2018:1-2.

Figure 1:MRI/MRA prompted by Left-Sided Neglect One Year Prior to Admission: MRI demonstrates an irregularity/beading of the right Middle Cerebral Artery (left panel, white arrow). MR angiography demonstrates smaller/missing M2 segment and distal branches of the Middle Cerebral Artery on the right side (right panel, red arrow), compared to the left.

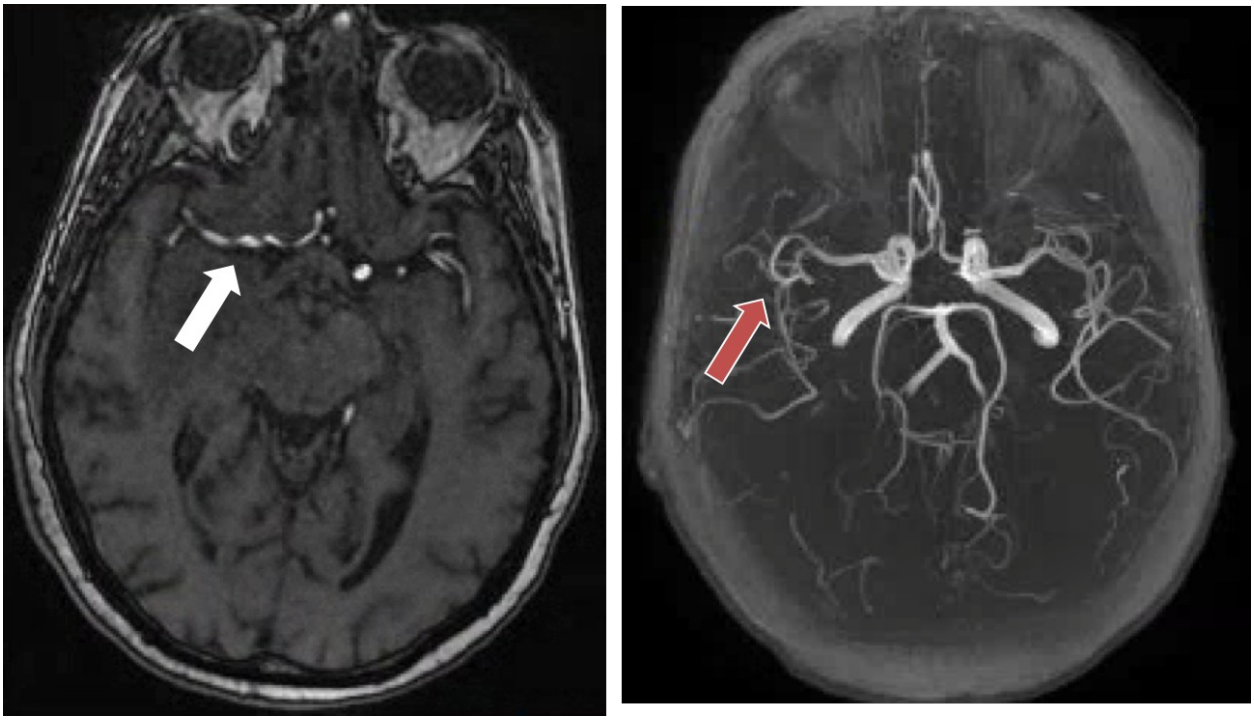

Figure 2: 3-D reconstruction of MRI at the Time of Presentation: Repeat MRI at the time of presentation to geropsychiatry demonstrated no focal narrowing or cutoff of cerebral vessels, to suggest an acute vasculitic episode. Distal right Middle Cerebral Artery branches remained reduced/absent, consistent with MRI one year prior.

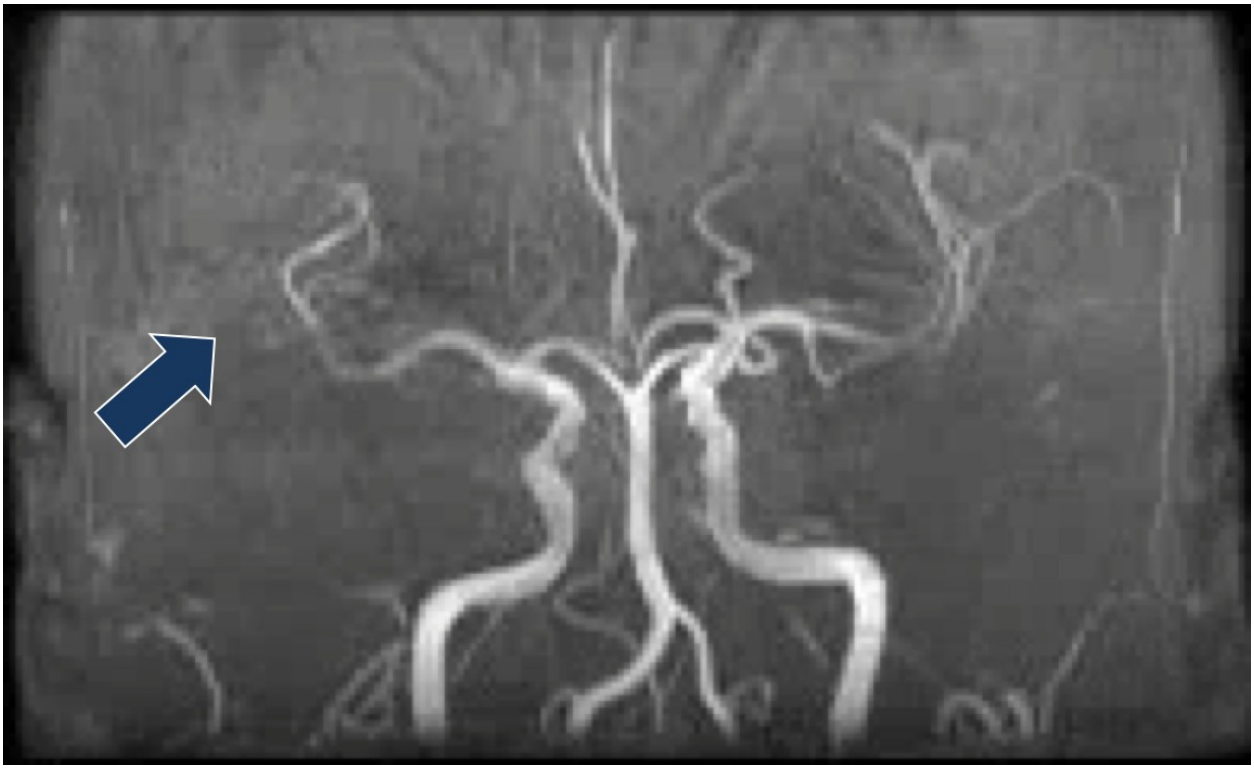

Table 1: Laboratory Findings at the Time of SCLE Diagnosis

	Time of Diagnosis of SCLE	Time of Diagnosis of CNS vasculitis
ANA	Positive >1:640, speckled	Positive >1:640, speckled
Anti-DSDNA	3	2
ANCA		Negative
C3		109
C4		16
Cardiolipin Ab IgM		3
Cardiolipin Ab IgG		<10
Cardiolipin Ab IgA		1
CCP Ab IgG		<8
Cryoglobulin		No precipitate
RF		<10
RNP		Negative
Serine Protease IgG		0
Smith Ab		Negative
SSA Ab	Positive, 1:4	Negative
SSB Ab	Negative	Negative
DRVVT Ratio		1.25
DRVVT 1:1 Mix Ratio		1.09

Table 2: Summary of 33 Published Cases of CNS Vasculitis Mimicking Psychiatric Conditions

Report	Age, Sex	Pre-existing Medical/ Neurological Conditions	Pre-existing Psychiatric Conditions	Presenting Symptoms	Medications at time of Symptoms	Duration of Vasculitis	Primary treatment of Vasculitis	Other Treatments (length of time)	Labs/ Imaging	Biopsy and Autopsy Findings	Recurrence
Börnke et al (1999)[32]	50F	Seizures for 7 months, 12 months progressive dementia	Not reported	Progressive dementia, disoriented, cognitive deficits, delusions, rigidity and myoclonus in arms and legs	Not reported	14 months	None	None	Antibodies were absent	Necropsy: central nervous system angiitis with irregular distribution in both hemispheres	Died
Ampélas et al (2001)[33]	38M	3 months of systemic lupus erythematosus	Depression, with suicide attempts	Sjögren's syndrome: auditory hallucinations, delusions of persecution, depression	Not reported	11 months	Cyclophosphamide (IV 2 g per month for 6 months)	Loxapine (400 mg per day for psychiatric symptoms), fluoxetine (40 mg daily for depression)	Labs: LP revealed blood cells CT: subarachnoid hemorrhage	No biopsy	No
Jacobs et al (2004)[34]	81F	Lyme Disease, breast cancer	No	Simultanagnosia, optic ataxia, and ocular apraxia	Doxycycline (for erythema chronica migrans)	1 month	IV corticosteroids, tapered gradually	None	MRI: bilateral parieto-occipital region signal abnormalities, with DWI abnormality in the right parieto-occipital region, and diffuse nodular leptomeningeal enhancement	Brain biopsy: granulomatous angiitis	Not reported
Lukas et al (2005)[35]	28M	Headaches for 3 weeks	Not reported	Acute hoarseness and tingling in left extremities; dysarthria, clumsiness, dysmetric finger-to-nose testing	Acidovir (suspected acute viral meningoencephalitis)	0.75 months	Steroids (2 x 1000 mg per day)	None	MR scans: hyperintensities of supratentorial grey and white matter; CCT: generalized brain edema	Postmortem examination: granulomatous inflammation with occlusion of leptomeningeal and cerebral arteries with infarction of cerebrum	Died
Solans-Laque´ et	63M	Mild hypertensi	Not reported	Daily Occipital headache,	Not reported	4 months	IV pulses of	Not reported	Labs: Anemia, elevated erythrocyte	Temporal artery biopsy	Not reported

al (2008)[36] Case 1		on		paroxystic vertigo			methylprednisolone (1 g) and IV heparin		sedimentation rate, lupus anticoagulant, anticardiolipin antibody IgG and IgM, protein S, and prothrombin were normal. CT and MRI: lesions of acute ischemic infarction of both hemispheres. MRA: bilateral stenosis at vertebral arteries.	consistent with GCA Necropsy revealed infarction of cerebellar hemispheres. Acute thrombosis of right vertebral artery.	
Case 2	67F	Hypertension	Not reported	Loss of vision in right eye, 3 months of headaches	Not reported	3.25 months	Methylprednisolone (1 g per day)	Prednisone (2.5 mg per day), aspirin (150 mg per day), and acenocoumarol daily (stopped after 5 years)	Labs: Anticardiolipin was negative. MRI: Ischemic lesions of cerebral arteries. MRA: bilateral clinoidal stenosis of internal carotid arteries, anterior cerebral arteries, occlusion of posterior cerebral arteries.	Temporal artery biopsy consistent with GCA	Not reported
Case 3	74M	Transient right hemiparesis and aphasia	Not reported	Transient ischemic attacks, progressive cognitive impairment, memory loss, confusion, disorientation	Not reported	2 months	Prednisone (1 mg/kg per day)	Clopidogrel after discharge	Labs: Normochromic normocytic anemia, elevated ESR. Clear CSF Ultrasonography at presentation: supra-aortic arteries showed occlusion of left ICA. CT: frontal and temporal cerebral atrophy with hydrocephalus MRI: multiple infarcts in basal ganglia and internal capsule. Color ultrasonography 2 months after presentation: stenosis and dark halo in left temporal artery	No biopsy could be completed due to patient's disorientation and agitation	No
Case 4	80M	No	Not reported	Temporal headache,	Not reported	2 months	Prednisone (80	None	Labs: Normochromic normocytic anemia,	Temporal artery	Died

				episodes of bilateral visual loss, diplopia, disorientation			mg per day)		elevated C-reactive protein MRI: multiple lacunar infarcts present in occipital lobes and cerebrum. MRA: stenosis of cerebral arteries.	biopsy: inflammation of elastic lamina, consistent with GCA	
Case 5	70F	Hypertension, TIA with right hemiparesis and blurred vision	Not reported	Loss of Vision in both eyes; headaches	Enalapril (5 mg per day)	3 months	3 pulses of IV methylprednisolone (1 g)	Discharged with prednisone and clopidogrel (75 mg per day)	Labs: Normochromic normocytic anemia, elevated ESR, fibrinogen, C-reactive protein, and alpha-2 globulin CT: no ischemic lesions; MRI: ischemic lesions in internal capsules	Temporal artery biopsy consistent with GCA	No
Case 6	90M	2 months of fever, facial pain, vertigo, nystagmus, dysarthria	Not reported	Ataxia, dysmetria, dysdiadokinesis of left arm	Not reported	2 months	Prednisone (1 mg/kg per day)	Discharged with prednisone, clopidogrel, aspirin (300 mg per day)	Labs: Normochromic normocytic anemia, elevated ESR, fibrinogen, C-reactive protein, and alpha-2 globulin CT: no signs of ischemia; Ultrasonography: occlusion of left ICA MRA: extracranial occlusion of left ICA	Temporal artery biopsy consistent with GCA	No
Case 7	85F	Hypertension	Not reported	Acute stroke with right hemiparesis, right upper limb paresis and blurred vision	Enalapril	6 months	3 pulses of IV methylprednisolone (1 g per day)	Discharged on prednisone and aspirin (300 mg per day)	Labs: Normochromic normocytic anemia, elevated ESR, fibrinogen, and C-reactive protein CT: frontal cerebral atrophy	Temporal artery biopsy consistent with GCA	No
Qu et al (2009)[37]	50F	Headaches	No	Sudden loss of vision; left side paralysis and quadriparesis; initial diagnosis of viral meningoencephalitis; frequent incoherent speech	Anti-tuberculosis therapy and daily dexameson	6 months	Methylprednisolone, cyclophosphamide, and methotrexate	None	Labs: Elevated lymphocyte count, antiospholipin antibodies within normal range. CT: Multifocal infarcts MRI: mass within right parietal lobe DSA: diffuse intracranial cerebral artery narrowing	Brain biopsy: extensive vessel inflammation (PCNSV)	No
Pires et al (2011)[38]	70M	No	Depression	Cognitive impairment,	N/A	0.5 months	Oral prednisone	None	Labs Elevated ESR MRI: confluent	Stereotactic brain biopsy:	No

				disorientation, memory deficits			lone (1 mg/kg)		hyperintense T2/FLAIR in periventricular and subcortical white matter	perivascular/ transmural small vessel inflammatory infiltrate, microglia activation, gliosis, sparse lymphocytes and neutrophils in brain parenchyma	
Montefort et al (2012)[39]	57M	Headaches	Not reported	Right arm weakness, decreased sensation, dyspraxia, left visual field impairment	Not reported	11 months	Dexame thasone; IV methylpr ednisolo ne (1 g for 3 days then 60 mg orally) with proton pump inhibitor.	None	Labs: Anticardiolipin antibody was negative. CT: blood in occipital horns of lateral ventricles, hypodensity in parietal, temporal, and occipital horns MRI: cortical infarction, blood present in ventricles, left capsule, and sulci MRA: irregularity in cerebral vessels (particular vessels not specified)	Biopsy within 4 weeks of presentation confirmed vasculitic changes	No
Coronel-Restrepo et al (2013)[40] Case 1	54M	No	No	Progressive headache and memory deficit; abnormal speech, disorientation, right hemiparesis and unstable gait	Not reported	1 month	IV methylpr ednisolo ne (1 g per day for 3 days), oral cyclopho sphamid e (100 mg per day), Aspirin (100 mg per day), and phenytoi n (300 mg per day)	Physical therapy for a month	Labs: Anticardiolipin antibody was negative. MRA: thinning at middle cerebral artery and anterior cerebral artery	Brain biopsy consistent with PACNS	No

Case 2	55F	No	No	Severe headache with syncope, left hemiparesis, aphasia, stupor	Not reported	0.25 months	IV methylprednisolone (1 g per day for 3 days), IV cyclophosphamide (1 g per month for 6 months)	Discharged with prednisolone (1 mg/kg per day) and oral phenytoin (300 mg per day)	CT: right frontal hematoma and vasogenic edema; cerebral angiography: cerebral vasculitis of posterior right carotid system and infundibular dilatation of left posterior communicating artery; MRI: intracerebral hematoma with right frontal edema	Brain biopsy: perivascular lymphocytic infiltrate with meninges	No
Case 3	35M	Arterial hypertension, left hip replacement due to avascular necrosis, chronic convulsive syndrome	No	Progressive memory impairment, left hemiparesis, language disorder	Enalapril, tegretol, phenobarbital	24 months	IV cyclophosphamide (1 g single dose), methylprednisolone (1 g per day for 3 days)	prednisone (50 mg per day) with gradual decrease at month 6 (12.5 mg per day); after 2 years, methylprednisolone (2 g/kg per day for 3 days), rituximab (2 doses of 1 g 2 weeks apart)	Labs: Anticardioplipin antibody was negative. MRI: lesions in left frontal lobe and periventricular region; After 2 years MRI showed lesions in fronto-parietal and left cerebellum	Brain biopsy: necrotizing granulomatous vasculitis	2 years after initial presentation
Kalra et al (2013)[41]	24F	Syncope	Mild depression	Collapsed at home; bilateral internuclear ophthalmoplegia, left hemiparesis, dysarthria, left ataxia	Not reported	3 months	Oral aspirin and IV methylprednisolone after oral prednisolone (steroids tapered gradually)	Therapeutic anticoagulation with warfarin due to progression of vasculitis after a month of prednisolone; Azathioprine daily; replaced steroids with aspirin (75 mg per day)	Labs: C-reactive protein and erythrocyte sedimentation normal, antiphospholipid screen within normal range. CT: multiple infarcts in left cerebellum, right thalamus, and left temporal lobe MRI: multiple infarcts in posterior and anterior circulation MRA: irregular narrowing of basilar artery and post	No biopsy completed. Clinical picture and work-up were deemed sufficient to diagnose isolated CNS vasculitis	No

									stenotic dilatation.		
Shiner et al (2014)[42]	62M	Type 2 diabetes; persistent headache for 2 weeks	Not reported	Dysphasia due to stroke	Metformin (for diabetes)	3 months	3 days IV methylprednisolone (1 g per day) then oral prednisone (70 mg per day); weaned by 10 mg weekly	Oral Cyclophosphamide (150 mg per day)	Labs: Anticardiolipin antibody was negative. MRI: regions of diffusion of restriction in left parietal and temporal lobes, areas of cortical fluid-attenuated inversion recovery	Meningeal and brain biopsy: patchy infarcts of vasculitic changes in vessels of left inferior temporal lobe	No
Holay et al (2015)[43]	35M	No	Not reported	Ischemic stroke and Left Hemiplegia	Not reported	3 months	IV Methylprednisolone (1 g x 3 days) with Tab omnacort (1mg/kg OD)	Discharged on tapering doses of steroids	Labs: Anticardiolipin antibody was negative. CT: acute infarct in right MCA MRI: lesion in right gangliocapsular, bilateral parieto-occipital and midbrain right cerebral peduncle region signal abnormalities. MRA: Right MCA along M1 and bilateral PCA irregularity with significant narrowing	No biopsy done: no provider capable of completing biopsy was available	No
Hirachi et al (2015)[44]	35F	4 years of systemic lupus erythematosus	No	Arthralgia, manic symptoms: hallucinations, radical mood swings, and affective incontinence (Young's mania rating scale: 29/60), depression	Prednisolone (20 mg per day discontinued a year before psychiatric symptoms manifested)	2.4 months	Methylprednisolone (pulse: 1000 mg for 3 days), prednisolone (50 mg per day)	Aripiprazole (6 mg per day increased to 24 mg per day), lithium (400 mg per day increased to 800 mg per day)	Labs: Anticardiolipin antibodies were within normal range; ESR was high. MRI: multiple white matter hyperintensities I-IMP SPECT: hypoperfusion in occipital area	No biopsy	No
Bönstrup et al (2016)[45]	47M	No	Not reported	Frontal lobe dementia syndrome: symmetric hyperreflexia, paraphasia, cerebellar dysarthria,	Not reported	24 months	IV methylprednisolone for 3 days (1g per day)	6 monthly doses of cyclophosphamide (750 mg/m^2) with weekly methotrexate (20 mg)	Labs: elevated C-reactive protein LP: Increased cell count and protein in CSF, MRI (6-9 months after initial symptoms): No	Brain biopsy: hemosiderin deposits around small blood vessels. Also, perivascular accumulation	Not reported

				weight loss. Social deficits: erratic thought, memory loss, disinhibited behavior.					abnormalities Repeat MRI (12-15 months after symptoms): Widespread, generalized cortical atrophy, especially in insular cortex and opercula, with ventricular widening, but also detectable in frontal and parietal lobes Contrast-enhanced MRA: No vascular irregularities	of inflammatory T-cells.	
Johnson et al (2016)[46]	30M	No	No	Aphasia, homonymous hemianopia, right hemiparesis, and retinal peri-phlebitis of left eye; developed seizures	Anti-epileptic medications for seizures	24 months	IV methylprednisolone (1000 mg per day for 5 days) followed by high dose prednisone taper	Cyclophosphamide (0.5 g/m^2) after re-exacerbation, re-dosed with solumedrol (5 days of high dose) and rituximab (2 cycles of 375 mg/m^2); mycophenolate (1000 mg twice a day)	CT: lesions in left parieto-occipital lobes; MRI: left medial frontal and parietal lesions; MRA: ipsilateral attenuation of left anterior, middle, and posterior cerebral arteries; EEG: left temporal seizures	Brain biopsy: cerebral gray and white matter changes within left ACA, MCA, and PCA - unihemispheric CNS vasculitis	Symptoms never remitted despite steroid treatment. Exacerbation occurred 1 year after initiation of treatment.
Kumar et al (2016)[47]	48M	Rheumatoid arthritis	Depression	Became refractory to DMARDs; developed neuropathic pain in limbs	Disease modifying anti-rheumatic drugs (DMARDS): methotrexate (15mg weekly), hydroxychloroquine (200mg daily), sulphasalazine (2000mg daily), leflunomide (20mg daily)	11 months	IV prednisolone (3 x 1000 mg per day, 3 x 500 mg per day, 3 x 250 mg per day, 3 x 125 mg per day) followed by oral prednisolone (60 mg per day)	Psychotherapy (functional component suspected) and antidepressants; infusion of rituximab after appearance of gangrene in hands.	CT: right thalamic hemorrhage with cerebral infarcts due to cerebral vasculitis	Sural nerve biopsy showed vasculitic neuropathy.	Died

Xiao et al (2016)[48]	40F	One episode of syncope; nephritis (treated and cured)	Not reported	Headache and dizziness	Not reported	6 months	Not reported	Not reported	MRI: lesion in fronto parietal region of left cerebrum; MRA: sudden termination of one branch of cerebral artery	Microscopy of lump in fronto parietal region: blood vessels containing numerous inflammatory cells (consistent with CNS vasculitis)	Not reported
Hasan et al (2017)[49]	66M	Metastatic prostate cancer	Not reported	Lower facial spasms and hand paresthesias; dizziness, dysarthria	Not reported	Not reported	IV immuno globulin; IV and oral methylpr ednisolo ne	Cytoxan	MRI: Ischemia in vascular territories	Brain biopsy: granulomato us angiitis	Not reported
Kumar et al (2017)[50]	56M	Hypertensi on and diabetes	No	Behavioral changes, urinary incontinence, difficulty walking; glioblastoma later excised and revealed CNS vasculitis	Not reported	2 months	IV cyclopho sphamid e (1000 mg per month for 6 months)	IV immunoglob ulin (in full dose) after progression of mononeuriti s multiplex	MRI: lesion in left frontal lobe; MRA: focal narrowing of vessels in left frontal region suggested vasculitis	Left frontal craniotomy and total excision of lesion. Biopsy: infiltrate of lymphonucle ar cells, perivascular granulomas, hemorrhages in adjacent brain parenchyma, gliosis	No
Lee et al (2017)[51]	25F	No	No	Cortical brain tumor; headache and right hemiparesis	Not reported	0.5 months	Steroid administ ration	None	Labs: Leukocytosis with neutrophil dominance, elevated C-reactive protein CT: low-density lesion in left frontal lobe	Biopsy: dominant lymphocytic infiltration in small vessels, arachnoid membrane showed fibrotic changes	No
Rodrigues Rodrigues et al (2017)[13] Case 1	67F	5 years of systemic lupus erythemat osus	Psychom otor retardati on	Subacute cognitive dysfunction, language deficit	Hydroxychlor oquine (400 mg)	1 month	Methylpr ednisolo ne (IV pulse 1g per day	Speech and language therapy	MRI: subacute infarcts in the left frontal parietal region. MRA: Focal stenosis	No biopsy	No

								for 3 days), Cyclophosphamide (IV 500/m^2/ month for 6 months)		in M2 branch of MCA.		
Case 2	Case 2	38F	12 years of systemic lupus erythematosus	Not reported	Left lower limb monoparesis	Hydroxychloroquine (400 mg)	0.75 months	Prednisone (1 mg/kg per day), cyclophosphamide (IV 750/m^2 per month for 6 months)	None	MRI: T2 hyperintense white matter lesions	No biopsy	No
Case 3C	Case 3	18F	5 years of systemic lupus erythematosus	Not reported	Tonic-clonic seizures	Hydroxychloroquine (300 mg), mycophenolate mofetil (2 g), prednisone (20 mg)	2 months	Methylprednisolone (IV pulse .5 g per day for 3 days), prednisone (1 mg/kg per day), IV human immunoglobulin (2 g/kg per day)	Anticonvulsants	MRI: fronto-parietal T2 hyperintense lesions	No biopsy	No
	Case 4	43F	16 years of systemic lupus erythematosus	No	Diplopia, lower limb dysesthesia	Prednisone (20 mg)	3 months	Prednisone (0.5 mg/kg per day), cyclophosphamide (1 pulse of 500/m^2), IV human immunoglobulin (2 g/kg per 5	None	MRI: subacute infarct in head of right caudate nucleus, lenticulostriate arteries	No biopsy (MRI supported vasculitis diagnosis)	No

							days for 6 months)				
Chu et al (2018)[52]	63F	3 years of headaches, osteopenia, reflux, thyroid nodule, femur and skull lesions	No	Gait disturbance, incoordination, vertigo, nausea, vomiting; bilateral appendicular ataxia	Rabeprazole and acetaminophen	0.5 months	Dexamethasone (4 mg per os/ IV every 8 hours)	Discharged with oral prednisone (60 mg per day), oral methotrexate (15 mg per week), prednisone tapered down	CT: right cerebellar edema; MRI: cerebellar leptomeningeal enhancement	Cerebellar biopsy: vasculitis and lymphocyte infiltration of meninges	No

Table 3: Summary of Demographic and Clinical Data from 33 Published Cases of CNS Vasculitis Mimicking Psychiatric Conditions

Age Mean (Range)	Gender: M:F Count (%)	Duration of Symptoms: Mean (Minimum-Maximum)	Most Common Psychotic Features
52.85 years (18 – 90 years)	17/33 (51.51%): 16/33 (48.48%)	5.39 months (0.25 months-24 months)	Erratic thoughts 1/33 (3.03%), auditory hallucinations 1/33 (3.03%), visual hallucinations 1/33 (3.03%), delusions 2/33 (6.06%)