

Mesial Temporal Sclerosis in a Recently Diagnosed SLE - Scleroderma Overlap Syndrome: A Case Report



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ABSTRACT

Systemic lupus erythematosus (SLE) is the most common form of lupus and a chronic autoimmune disorder that can affect multiple organ systems including the joints, skin, the cardiovascular system and even the central and peripheral nervous system. Although rare, these patients may present with neuropsychiatric symptoms. This patient presented initially with an SLE flare associated with sudden focal to generalized tonic-clonic seizures. Further rheumatologic workup was done which revealed that the patient also has scleroderma, an autoimmune connective tissue that causes inflammation of the skin and other key internal organs. Due to the seizure occurrence, cranial magnetic resonance imaging (MRI) was done which showed incidental mesial temporal sclerosis, which is the scarring of the medial part of the said lobe of the brain. Her overlap syndrome was managed with Hydrocortisone and

she was given Valproic acid as her anti-epileptic drug with no recurrence of seizure afterwards.

Key Words: Systemic lupus erythematosus, Scleroderma, Mesial temporal sclerosis, Overlap syndrome, Valproic acid

INTRODUCTION

Systemic lupus erythematosus (SLE) is a common autoimmune disease. These have multiple manifestations including constitutional symptoms like fatigue, musculoskeletal symptoms like arthralgia, dermatologic manifestations such as malar rash and discoid lupus, cardiovascular complications and other syndromes including interstitial lung disease and nephritis. The main mechanism of SLE is the production of autoantibodies directed toward an individual's own cells. Antinuclear antibodies or ANA is present in almost 95% of the cases. Other autoantibodies include anti double-stranded DNA (dsDNA) and anti-Smith antibodies (anti-Sm).[1]

There are 19 SLE related-neuropsychiatric syndromes (NPSLE) according to the American College of Rheumatology. Diseases affecting the central nervous system include aseptic meningitis, cerebrovascular disease, demyelinating disease, headache, movement disorder, myelopathy, seizure disorders, acute confusional state, anxiety disorders, cognitive dysfunction, mood disorders and psychosis; while those affecting the peripheral nervous system include acute inflammatory

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demyelinating polyradiculoneuropathy, autonomic disorders, mononeuropathy, myasthenia gravis, cranial neuropathy, plexopathy and polyneuropathy. [2]

According to a retrospective cohort done by Zhu, et.al. in 2009, out of the 306 patients included in their study, a total of 108 neuropsychiatric SLE events were recorded.[3] In a multiethnic cohort done in 2009 which included 600 SLE diagnosed patients, 40 of the participants or (6.7%) developed seizures of different semiology.[4]

Scleroderma, like SLE, is also an autoimmune disease. It affects the connective tissues and is usually characterized by thickening of the skin. Abnormal interactions between endothelial cells, fibroblasts and lymphocytes (B and T cells) lead to microcirculatory vascular involvement, like SLE. There are two types of scleroderma: localized scleroderma and systemic scleroderma (or systemic sclerosis).[5] In localized scleroderma, seizures (41.58%) and headache (18.81%) were the predominant neuropsychiatric symptoms while in systemic scleroderma, headache (23.73%), seizures (13.56%) and cognitive impairment (8.47%) were the most common neurologic symptoms.[6]

Temporal lobe epilepsy (TLE) is the most common form of focal type of seizure.[7] Mesial temporal sclerosis (MTS) is one of the variants of TLE which involves scarring of the median part of the said lobe due to multiple etiologies. Hippocampal sclerosis is pathologically seen as segmental pyramidal atrophy in segments of hippocampus in CA1, CA3 and CA4 areas of the hippocampus.[8] Medial temporal lobe epilepsy is a type of epilepsy that often becomes drug-resistant.[9] In a case report done by Nobrega Jr, et.al. in 2018, regular seizures began at an average age of 14 years with a mean duration of epilepsy ranging at 27.2 ± 13.4 years. Seizure type of patients with MTS was primarily focal-onset with impaired awareness in almost 93% of cases and only four of the patients included in the study had a history of autoimmune disease (two cases of multiple sclerosis, one systemic sclerosis and one ulcerative colitis).[10]

CASE

A 38-year-old female was admitted due to generalized weakness, febrile episodes and productive cough. She was initially managed as

a case of pneumonia. The patient has a one-year history of joint pain affecting the bilateral distal and proximal interphalangeal joints, as well as the knees. Other symptoms included alopecia, excoriations and cutaneous thinning around the perioral and lip areas.

She also presented with proteinuria and minimal pericardial effusion, as noted on a 2D echocardiogram. Her ANA titer was 1:320 with a speckled pattern, along with elevated anti-dsDNA and strongly positive anti-Sm antibodies. Hypocomplementemia (low C3) was noted, along with low levels of anti-SSA and anti-SSB antibodies. Her symptoms and presence of these antibodies are consistent with SLE.

Interestingly, erythematous patches with a "salt and pepper" appearance were noted on the forehead, neck and nape areas. A concomitant elevation in systolic pulmonary artery pressure was observed during cardiac testing. The patient also complained of claudication pain, which was aggravated by prolonged walking and relieved by rest. Further investigations were conducted. Although her anti-RNA polymerase III was negative, her anti-ScI-70 antibody was positive.

Based on clinical findings and serology, the patient was diagnosed with SLE-scleroderma overlap syndrome.

After being treated with Meropenem and Azithromycin for pneumonia, the patient was also managed for the recently diagnosed SLE-scleroderma overlap with intravenous Hydrocortisone 100 mg.

However, on the fifth day of hospitalization, the patient experienced sudden episodes of blank stares with preserved awareness, each lasting about five seconds and associated with dizziness. Postictal symptoms included fatigue and a pulsatile bifrontal headache. Approximately one hour later, she had another episode characterized by upward rolling of the eyeballs lasting about five seconds, without any noted jerking of the extremities. This was followed by postictal confusion. A similar seizure episode occurred 30 minutes later, now accompanied by upward eye rolling, stiffening of all extremities and perioral cyanosis. This episode lasted for approximately 10 seconds.

The patient was initially treated with the antiepileptic medication Valproic acid 500 mg intravenously every 12 hours.

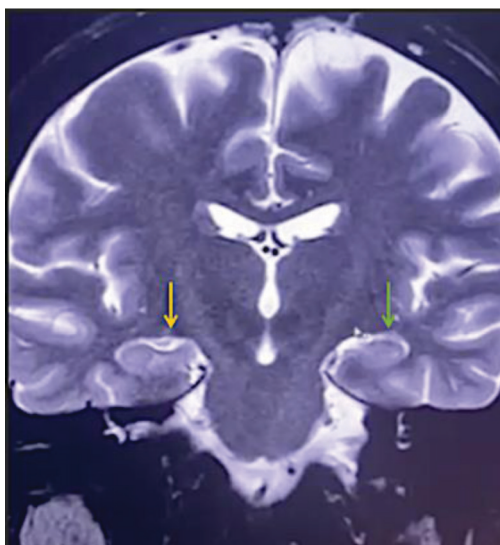


Figure 1: T2 weighted/FLAIR image-coronal cut; There was noted reduced volume or atrophy on the left hippocampus in contrast with the right, with increased T2W/FLAIR signal signifying sclerosis on both bilateral mesial temporal areas with generalized cerebral atrophy.

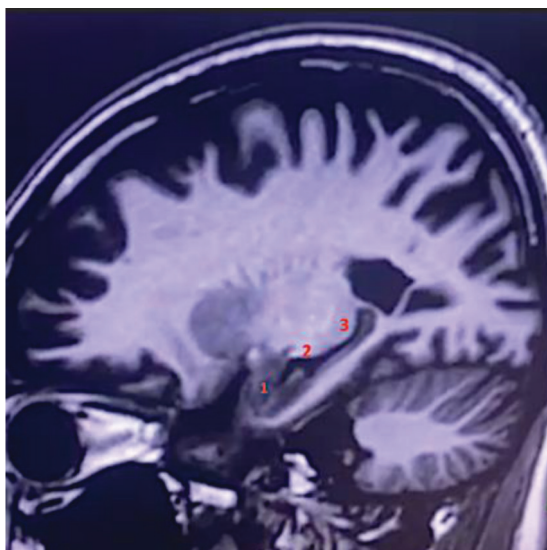


Figure 2: T1 weighted image sagittal cut. 1=hippocampal head, 2=hippocampal body, 3=hippocampal tail

Asleep-deprived 21-channel electroencephalogram (EEG) was performed but showed no epileptiform discharges and was deemed normal. Given the inconclusive EEG findings, neuroimaging was warranted. Cranial MRI revealed subtle atrophy of the right hippocampus with increased T2-weighted/FLAIR (Fluid-Attenuated Inversion Recovery) cortical signals, consistent with subtle right mesial temporal sclerosis. Additionally, a few tiny T2W/FLAIR hyperintensities were noted in the periventricular and subcortical white matter bilaterally, as shown in Figures 1 and 2.

Her steroids were eventually shifted to a more potent preparation; thus, Methylprednisolone

pulse therapy was initiated. For her seizures, she was started on Valproic acid 500 mg twice daily as maintenance therapy, since Carbamazepine—commonly used—can potentially cause lupus-like adverse effects.

DISCUSSION

Overlap syndrome is an entity that satisfies the classification criteria for at least two distinct connective tissue diseases which may include SLE and scleroderma. The patient was able to satisfy the criteria for both diagnoses and was managed accordingly. Her first neuropsychiatric manifestation

was seizure which is very unusual. The average dose of steroids (HR = 1.03; 95% CI 1.01 to 1.05; $p < 0.0001$) was associated with a shorter time-to-seizure occurrence in patients with neuropsychiatric SLE (NPSLE).[11] MRI imaging was done which revealed bilateral MTS for her case. In a retrospective study done in Japan by Toyota, et.al. in 2013, the prevalence of medial temporal lobe epilepsy in SLE was 2.9%.

Interleukin 1 and 6 and tumor necrosis factor- α lead to the activation of the hypothalamic pituitary adrenal axis, which lowers the threshold for seizure occurrence. Ischemic events including infarcts are also contributory in the development of seizures in SLE.[12] Research also has looked into autoimmune reactions affecting the limbic system resulting in medial temporal lobe epilepsy. Glutamic acid decarboxylase (GAD) and γ -aminobutyric acid (GABA)-B receptors have been identified as neuronal antigens in limbic encephalitis. This suggests a possible involvement of disturbed inhibitory GABAergic signaling in the etiology of seizures.[13]

In general, long-term prognosis of pharmacological therapy in patients with MTS is generally considered poor,[14] however, not all patients with MTS are medically intractable; 25% of the patients achieved complete control while receiving anti-epileptic drugs. Poor seizure control was related to early age of seizure onset, a history of febrile convulsions and epileptiform discharges on the EEG,[15] which fortunately was not seen with the patient.

Carbamazepine and Lamotrigine are avoided to treat seizure in SLE patients because its adverse effects include SLE like-syndromes, specifically skin hypersensitivity. Hence most SLE patients with epilepsy are mostly treated with Valproic acid,[12] which is done for the patient. Currently the patient is maintained on Valproic acid and has no recurrence of seizures for almost a year.

CONCLUSION

Overlap syndromes can present with neuropsychiatric manifestations and treatment to such should be tailored based on the patient's clinical profile. For this case, Valproic acid is chosen as the main antiepileptic drug and Carbamazepine and Lamotrigine are avoided due to the associated adverse effects of the latter.

Ethical considerations

This study complies with the ethical principles set out in relevant guidelines as specified in the certificate of agreement and compliance in this research; as well the National Ethical Guidelines 2017 edition.

Informed consent process

A clearly written informed consent form was obtained, understood and signed by the legally acceptable representative, securing their consent for presentation, publication of the case, taking of photographs and videos, including other diagnostic results and images. The primary investigator, not the primary physician of the patient, obtained consent.

Vulnerability

The subject in this research was a patient of the secondary investigator of this research. Nevertheless, vulnerability was reduced with the primary investigator obtaining the consent from the legally acceptable representative. The decision maker should be a legally acceptable representative, should be of sound mind, have appropriate judgement and without hindrance to any cognitive skills which may be possible in cases with MTS or any seizure disorders. Any first degree relative or spouse, in this case, may act as the legally acceptable representative for participation in this case report.

Privacy and confidentiality

Patients' confidentiality is protected by removing patient identifiers in the case report, with full compliance with the Data Privacy Act and its implementing rules and regulations. The raw data collected in this study will be stored for up to five years only.

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None

Authors' contributions

Conceptualization - FMT and JAC and JTL; Data curation - FMT and JAC and JTL; Formal analysis - Not applicable; Funding acquisition - Not applicable;

Investigation - FMT and JAC and JTL; Methodology - Not applicable; Project administration - Not applicable ; Resources - FMT and JAC and JTL; Software - Not applicable; Supervision - FMT and JAC and JTL; Validation - FMT and JAC and JTL; Visualization - FMT and JAC and JTL; Roles/Writing - original draft - FMT and JAC and JTL; Writing - review and editing - FMT and JAC and JTL. All the authors have read and approved the manuscript.

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Data Availability

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Declaration of generative AI and AI-assisted technologies

None

Declaration of interests

None of the authors has any conflict of interest to disclose. We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Consent for publication

The consent for publication of the collected data is secured as part of the informed consent of the participant. It was reassured to the participant that all data will be anonymized and that privacy will be upheld.

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