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Case Report Open Access

Acute cerebellitis in a case of systemic sclerosis overlap with systemic lupus erythematosus: Image study

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Systemic lupus erythematosus, and systemic sclerosis are chronic autoimmune diseases with symptoms with different degrees of severity and mechanisms. Hence, we present a 36-year-old female with a history of systemic lupus erythematosus which was later overlapped with systemic sclerosis. She complained of vertigo over three months before developing poor gait. She was diagnosed with truncal ataxia due to her ataxic gait and abnormal point motions. Based on the magnetic resonance imaging, a final diagnosis of acute cerebellar dysfunction in systemic lupus erythematosus was made. Cyclophosphamide was initiated with a single dose of 500 mg which continued for at least three more monthly cycles, and the methylprednisolone pulse was adjusted to 500 mg/day for three days. Due to measures taken to avert a renal crisis caused by scleroderma, the methyl prednisolone dose was deemed to be lower than the adjusted amount (1 g). A follow-up magnetic resonance imaging showed regression of the lesions after treatment, the cerebral lesion had shrunken, and corticomedullary lesion had resolved entirely. Cerebral ataxia could be developed in patients with sytemic lupus erythematosus in terms of vasculitis, diffusely infiltrating glioma, acute disseminated encephalomyelitis, and systemic lupus erythematosus itself. One of the uncommon signs of neuropsychiatric systemic lupus erythematosus is ataxia and cerebellar involvement. The prognosis is generally favorable while receiving immunosuppressive therapy.

eywords: Cerebellitis; Neuropsychiatric; Systemic Sclerosis; Systemic lupus erythematosus

Introduction

Systemic lupus erythematosus (SLE) and systemic sclerosis are chronic autoimmune diseases affecting almost every system, which develop symptoms with a wide range of severity, and some common and different mechanisms [1]. Neuropsychiatric SLE (NPSLE), also known as central nervous system (CNS) involvement, is estimated to be present in 80% of cases, with the cerebrum very infrequently implicated in 2% of the cases [2].

The cerebrum could be manifested in different forms, including cerebellitis, which is defined as “an acute neurologic condition characterized by cerebellar ataxia or dysfunction attributable to a recent or concurrent infective illness, a recent

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vaccination, or the ingestion of medication, and in which there is magnetic resonance imaging (MRI) evidence of predominantly cerebellar inflammation [3]. Skin thickening is the hallmark of systemic sclerosis (SSc), which affects many internal organs. This illness affects several areas of the CNS, including the cerebellum, and has micro- vascular lesions as the underlying etiology [4]. Hence, we present a known case of overlapping syndrome of systemic sclerosis and SLE who presented with severe cerebellar ataxia. As a rare finding, her MRI showed cerebellitis, and thus we initiated treatment with cyclophosphamide, and high-dose prednisolone. Our patient's symptoms subsided entirely upon treatment.

Case Presentation

The patient was a 36-year-old married woman 10 years ago diagnosed with SLE that later (four years ago) overlapped with SSc. The patient's primary signs and symptoms included arthralgia, weakness, arthritis of MCPs, and PIPs, and maculopapular non-pruritic skin rashes on the face, suggesting a malar rash. Initial laboratory tests showed WBC of 5800/mm3, Hb of 13.2 g/ dL, and PLT of 122000/mm3. The patient's CRP was zero and ESR was within normal ranges. Additional testing revealed low C3 and C4 levels, a positive antinuclear antibody (ANA), and a negative anti-double stranded DNA (anti-dsDNA). The patient was first diagnosed with SLE and was treated with prednisolone 10 mg/d and hydroxychloroquine 400 mg/d. Four years later, the patient developed cutaneous manifestations of SSc with positive anti-nuclear ribonucleoprotein/ Smith (RNP/Sm), anti-Sjögren's syndrome related (SS-A), anti-topoisomerase (anti-SCL70), and anti-ribosomal P (anti-Rib-P) antibodies. There was no other major organ involvement. Therefore, the patient's diagnosis was updated to SSc-SLE overlap, and treatment regimen changed to the prednisolone 5 mg/d, hydroxychloroquine 400 mg/d and azathioprine 100 mg/d until the recent admission in terms of 1.1 g/24h proteinuria and rapid rising of the serum creatinine to 2.1 mg/ dL. As a result, the patient was admitted to the hospital in November 2021 and a kidney biopsy was performed, which revealed proliferative glomerulonephritis, a class IV lupus nephritis. The patient complained of mild headaches over the past year with normal imaging that had exacerbated before recent admission, and interfered with her daily activities. Her headache was constant, vague, and sometimes pulsatile, accompanied by nausea and vomiting, and localized to the occipital and frontal areas. She denied having ever had diplopia or hazy vision. However, the patient had experienced genuine vertigo over the previous three months, three days before the last recent hospitalization, she experienced a poor gait. On neurological examination, her mental status, other cerebral functions, cranial nerves, sensory examination, motor system, and reflexes were normal, and she did not display nystagmus. However, her rapid alternating and point-point movements were abnormal, and she was found to have truncal ataxia. Moreover, her Romberg test was positive. Thus, we requested a brain MRI and Magnetic Resonance Venography (MRV), which showed normal superior sagittal, and transverse sinuses without thrombosis. Although cerebellum was not restricted or enhanced, MRI revealed specific regions of high density on T2 and FLAIR in the vermis and left cerebellar hemisphere. The rest of the brain MRI was normal. Therefore, a final diagnosis of acute cerebellar dysfunction in SLE was made, and we initiated cyclophosphamide, and methyl prednisolone pulse for the patient. However, since she had elevated creatinine and SSc, we adjusted cyclophosphamide to a 500 mg single dose and the methylprednisolone to 500 mg/day for three days. Based on kidney and CNS response, the treatment plan was to repeat cyclophosphamide at least for three more cycles. A follow-up MRI was conducted for the patient after a month, which showed the regression of lesions. Moreover, the cerebral lesion had shrunken, and corticomedullary lesion had entirely resolved. Finally, Based on the complications of CYC, as well as the patient's distance from the treatment center and the impossibility of monthly monitoring, we changed the treatment to mycophenolate mofetil.

Discussion

Neuropsychiatric SLE (NPSLE) refers to the neurological or psychiatric symptoms in a

patient with SLE for whom other diagnoses are ruled out. Previous studies reported headaches as the most prevalent of these symptoms. The headache could present in five forms, including tension headache and migraine, both of which were present in our patient. NPSLE increases mortality, and morbidity in patients [2,5]. Once NPSLE is suspected, it is recommended to assess antiphospholipid (APL), as well as anti-Rib-P, anti-neuronal and anti-ganglioside antibodies. Anti-Rib-P, antiDNA, and antiScl-70 were positive in our case. Previous studies reported that NPSLE mainly occurs in the active phase of disease [5]. Rheumatologists find it challenging to establish a diagnosis in such patients since there is no gold standard for identifying NPSLE and no serum marker shows a good link with the existence of NPSLE. Therefore, American College of Rheumatology (ACR) determined 19 symptoms, any of which could be a hint for diagnosing NPSLE. However, mentioned symptoms were not related to the condition of our patient who presented with ataxia [6]. Since, as mentioned earlier, a diagnosis of NPSLE necessitates ruling out other causes, we initially had to look for other etiologies for cerebral ataxia. Patients with SLE may develop cerebral ataxia owing to vasculitis, diffusely infiltrating glioma, acute disseminated encephalomyelitis, or SLE itself. These conditions have characteristic clinical and imaging findings, which, except for the latter, were absent in our patient. Ataxia could rarely develop in celiac patients. Our patient underwent laboratory, endoscopic, and biopsy evaluations, which were negative for celiac disease. Another etiology responsible for the ataxia includes paraneoplastic-related anti-Hu and anti-Yo antibodies that are most commonly associated with lung, breast, and ovarian cancers. Since we did not have access to kits for these antibodies, we had to rule out the cancer risk.

Nonetheless, several hypotheses, including cerebral infarction and vasogenic edema, have been proposed for the development of cerebral ataxia in SLE patients [7]. According to the cumulative data, our patient was experiencing an SLE flare. This was further corroborated by the fact that the patient's symptoms subsided upon receiving treatment. Various modalities could be used to study CNS in these cases.A brain CT scan is best to look for brain edema, hydrocephalus, and brain stem compression only in the acute phase. More commonly, MRI is used to evaluate CNS involvement in SLE. The advantages of MRI over other modalities are its sensitive detection of bleeding, infarction, and good response to therapy. However, in anomalies that do not need MRI examination, alternative modalities single-photon emission computerized tomography (SPECT) may be employed. Previous studies attributed this to the presence of a metabolic impairment rather than blood flow obstruction [8,9]. However, we used FLAIR and coronal T2-weighted MRI sequences in our patient, as presented in Figure 1 MRI showed ill-defined, hyperintense lesions at the bulbo-medullary junction without mass effect, and ill-defined hyperintense lesions in cerebellar vermis, suggestive of cerebellitis. We are yet unsure of the underlying etiology of scleroderma's cerebellum involvement, which is a rather uncommon symptom of the condition. After one month of treatment, the cerebellar abnormalities were likewise resolved in the control pictures. For the first time, we provided a summary of all cases of cerebellar involvement in SLE patients. Our search showed 24 cases of NPSLE, all of whom developed cerebellar symptoms and underwent imaging (MRI/CT scan). Diagnoses for the oldest and most recent instances were made in 1977 and 2022, respectively. All of the patients were female and ranged in age from 15 to 52. Various forms and frequency rates of cerebellar involvement were reported in these studies, including cerebellar atrophy (n = 9), no imaging finding (n = 8), an abnormal signal in the cerebellar hemispheres (n = 5), solitary lesion in the dorsal part of the junction between medulla and pons (n=1), a hyperintensity involving vermis (n = 2), a hyperintensity involving paravermis (n = 1), a hyperintense area in the peduncles (n = 1), and an isolated lesion in the brainstem (n = 1) [1-17]. One study had not reported its imaging finding [18]. As stated earlier, cerebellar involvement in NSPLE was rarely reported and a documented imaging involvement of the cerebellar vermis. On the other hand, SSc was reported to affect the CNS. A systematic review in 2013 reported the prevalence of different forms of imaging findings in SSc: white matter lesion

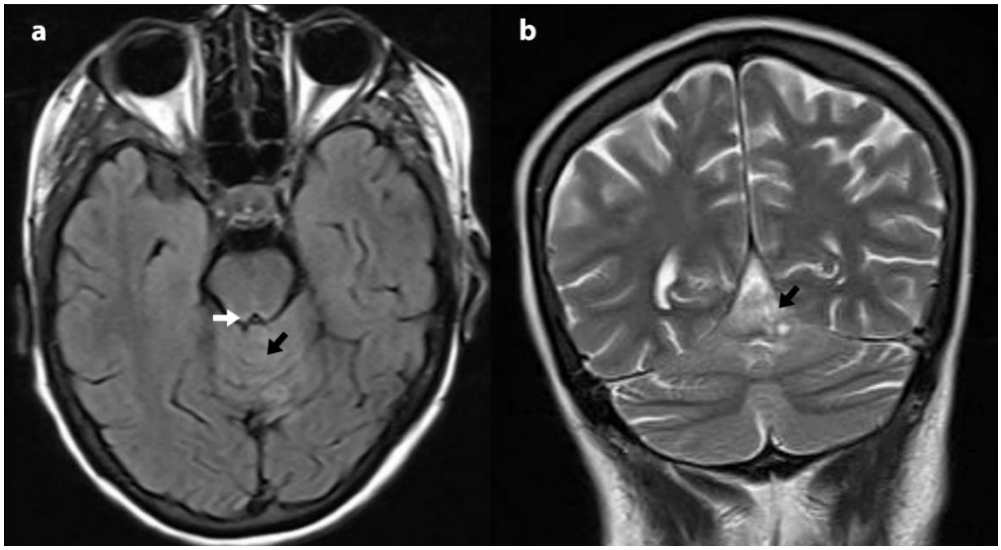

Figure 1. Axial brain magnetic resonance imaging (MRI) in FLAIR sequence (a) and coronal T2-weighted brain MRI showing ill-defined, hyperintense lesions at the bulbo-medullary junction without mass effect (white arrow in **a**). The presence of ill-defined hyperintense lesions in the cerebellar vermis (black arrows in **a** and (**b**) were suggestive of cerebellitis.

(25.51%), normal (15.3%), cerebellar hyperintense lesions (1.02%), and cerebellar infarction (1.02%) [19]. Therefore, the cerebellar involvement in the present case could be attributed to both SLE and SSc activities. We administered high-dose glucocorticoid and cyclophosphamide to our patient. After one month, the patient had a follow-up MRI, which revealed that the lesions had regressed. In addition, the corticomedullary lesion had completely disappeared and the cerebral lesion had reduced. The reversibility of imaging findings in NPSLE was attributed to acute blood-brain barrier changes [20]. Furthermore, we followed our patients clinically and with laboratory tests.

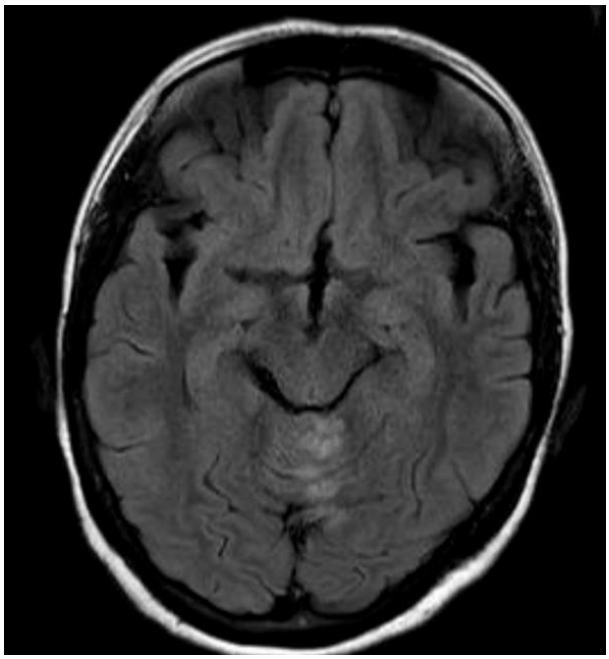

Figure 2. Axial brain magnetic resonance imaging in FLAIR sequence after one month of treatment shows the regression of the lesions. Bulbo-medullary lesions have resolved. Cerebellar junction lesions have smaller sizes and more conspicuous borders.

Table 1. Previously reported cases of cerebellar involvement in SLE

Cerebral involvement	Patient description	Year	Reference
Cerebellar atrophy	A 27-year-old Japanese female	2012	1
Cerebellar atrophy	A 22-year-old unmarried female	2011	2
A solitary lesion in the dorsal part of the junction between the medulla and pons.	A 28-year-old female	2000	3
Cerebellar atrophy	A 52-year-old female	2020	4
No findings	A 22-year-old, right-handed female	2021	5
Cerebellar atrophy	A 22-year-old female	2014	6
Cerebellar atrophy	A 40-year-old Egyptian	1995	7
An abnormal signal throughout the entire left cerebellar hemisphere	A 15-year-old Caucasian female	2010	20
Areas of T2/FLAIR signal hyperintensity involving the uvula and ventral pyramids of the cerebellar vermis as well as along the inferior margins of the left cerebellar tonsil and inferior margins of the bilateral cerebellar hemispheres	A 35-year-old female	2022	8
A hyperintense area in the posteroinferior portion of both mid-cerebellar peduncles extending to the cerebellar hemispheres.	A 47-year-old female	1992	9
Cerebellar atrophy	A 52-year-old Japanese female	2013	10
Cerebellar atrophy	A 42 years-old female	2018	11
An increased signal in cerebellar hemispheres, vermis, and paravermis	A 24-year-old black female	2017	12
No findings	A 34-year-old Caucasian patient	2008	13
An isolated lesion in the brainstem.	A 29-year-old non-Caucasian female	2008	13
An increased signal in the vermiscerebellaris	A 15-year-old non-Caucasian female	2008	13
No findings	A 14-year-old female	1988	18
Not reported	A 34-year-old unmarried female	1988	18
No findings	A 20-year-old female	1988	18
No findings	An 18-year-old male	1977	14
Brain MRV and MRA were normal.	A 22-year-old female	1977	14
Cerebellar atrophy	A 42-year-old female	1993	15
Cerebellar atrophy	A 27-year-old nulliparous female	1995	16
An equal-signal-intensity region in the T 1-enhanced image and a high-signal-intensity region with a diffuse undefined border in the T 2-enhanced image	A 24-year-old female	2002	17

SLE: systemic lupus erythematosus, T2/FLAIR: T2 and fluid-attenuated inversion recovery, MRV: Magnetic Resonance Venography, MRA: Magnetic Resonance Angiography

Conclusion

In conclusion, NPSLE presents with diverse symptoms, of which ataxia is the most infrequent symptom. CNS involvement in SLE usually occurs in females and is usually not limited to the cerebellum. The prognosis is generally favorable while receiving immunosuppressive therapy. Additionally, we must keep in mind that CNS symptoms, like the headache that is commonly reported by SLE patients, raise the possibility of CNS involvement and that additional research may be required. Although rarely, ataxia could be a primary symptom of SLE. Moreover, a severe scleroderma patient with recent onset of lupus overlap and cerebellitis makes the suspicion that scleroderma itself may be another underlying cause of cerebellitis in this case.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this study.

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References

1. Iwasaki Y, Okamoto A, Shoda H, Takahashi Y, Fujio K, Kawahata K. *et al*. Subacute cerebellar ataxia and atrophy developed in a young woman with systemic lupus erythematosus whose cerebrospinal fluid was positive for antineuronal cell antibody. ***Lupus*** 2012; 21(3):324-28. doi: 10.1177/0961203311418270.
2. Chattopadhyay P, Dhua D, Philips CA, Saha S. Acute cerebellar ataxia in lupus. ***Lupus*** 2011; 20(12):1312-15. doi: 10.1177/0961203311403346
3. Yaginuma M, Suenaga M, Shiono Y, Sakamoto M. Acute cerebellar ataxia of a patient with SLE. ***Clin Neurol Neurosurg*** 2000; 102(1):37-39. doi: 10.1016/s0303-8467(99)00078-5.
4. Kutlubaev MA, Idrisova RF, Zakirova EN, Hardy TA. Cerebellar ataxia as a first manifestation of systemic lupus erythematosus. ***Acta Neurol Belg*** 2020; 120(5):1241-43. doi: 10.1007/s13760-020-01376-5.
5. Sy MCC, Reyes NGD, Zamora GT, Fernandez MLL. Cerebellar ataxia as a primary manifestation of neuropsychiatric systemic lupus erythematosus. ***BMJ Case Rep*** 2021; 14(2). doi: 10.1136/bcr-2020-236825.
6. Ghosh K, Chatterjee A, Ghosh S, Chakraborty S. Cerebellar ataxia in a young patient: A rare path to lupus. ***J Neurosci Rural Pract*** 2014; 5(Suppl 1):S75-76. doi: 10.4103/0976-3147.145212.
7. al-Arfaj HF, Naddaf HO. Cerebellar atrophy in systemic lupus erythematosus. ***Lupus*** 1995; 4(5):412-14. doi: 10.1177/096120339500400513.
8. Appenzeller S, Cendes F, Costallat LT. Cerebellar ataxia in systemic lupus erythematosus. ***Lupus*** 2008; 17(12):1122-6. doi: 10.1177/0961203308093071.
9. Casciato S, Mascia A, Quarato PP, D'Aniello A, Scoppetta C, Di Gennaro G. Subacute cerebellar ataxia as presenting symptom of systemic lupus erythematosus. ***Eur Rev Med Pharmacol Sci*** 2018; 22(21):7401-03. doi: 10.26355/ eurrev_201811_16279.
10. Hanyuda M, Yoda Y, Shiozawa T, Hanaoka R, Miwa Y, Kaga S. *et al*. [A case with systemic lupus erythematosus presenting with reversible edematous lesion in cerebellum]. ***Ryumachi*** 2002; 42(5):801-06.
11. Kitching GB, Thompson JR, Hasso AN, Hirst AE. Angiographic demonstration of lupus cerebral phlebitis with communicating hydrocephalus. ***Neuroradiology*** 1977; 14(2):59-63. doi: 10.1007/bf00339960.
12. Kristoff TJ, Shoskes A, Claytor B. Lupus Cerebellitis Presenting With Ataxia: A Case Report. ***Neurohospitalist*** 2022; 12(1):117-20. doi: 10.1177/19418744211021221.
13. Lancman ME, Pomeraniec C, Norscini J. Magnetic resonance imaging findings in lupus ataxia. ***Acta Neurol Scand*** 1992; 86(4):425-26. doi: 10.1111/ j.1600-0404.1992.tb05111.x.
14. Manto MU, Rondeaux P, Jacquy J, Hildebrand JG. Subacute pancerebellar syndrome associated with systemic lupus erythematosus. ***Clin Neurol Neurosurg*** 1996; 98(2):157-60. doi: 10.1016/0303-8467(96)00013-3.
15. Nyo MT, Magazi D, Ally MM. Systemic lupus erythematosus: A possible cause of non-alcoholic Wernicke's encephalopathy. ***S Afr Med J*** 2017; 107(4):299-301. doi: 10.7196/ SAMJ.2017. v107i4.12053.
16. Shimomura T, Kuno N, Takenaka T, Maeda M, Takahashi K. Purkinje cell antibody in lupus ataxia. ***Lancet*** 1993; 342(8867):375-76. doi: 10.1016/0140-6736(93)91524-p.
17. Tsuruta D, Ohzono A, Ishii N, Ono F, Hamada T, Dainichi T. *et al*. Overlap syndrome comprised of systemic sclerosis and systemic lupus erythematosus associated with spinocerebellar ataxia type 6 and MALT lymphoma. ***Eur J Dermatol*** 2013; 23(1):117. doi: 10.1684/ejd.2012.1902
18. Singh RR, Prasad K, Kumar A, Misra A, Padmakumar K, Malaviya AN. Cerebellar ataxia in systemic lupus erythematosus: three case reports. ***Ann Rheum Dis*** 1988; 47(11):954-56. doi: 10.1136/ard.47.11.954.
19. Amaral TN, Peres FA, Lapa AT, Marques-Neto JF, Appenzeller S. Neurologic involvement in scleroderma: a systematic review. ***Semin Arthritis Rheum*** 2013; 43(3):335-47. doi: 10.1016/ j.semarthrit.2013.05.002.