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Case Report

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A case of thrombotic microangiopathy and acute demyelinating central nervous system lesions as the first manifestation of systemic lupus erythematosus

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Abstract

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder with a relapsing and remitting course and multi- organ involvement which can present with a wide range of neuropsychiatric manifestations. Acute disseminating encephalomyelitis (ADEM) is an autoimmune demyelinating disorder of the central nervous system (CNS). Thrombotic thrombocytopenic purpura (TTP) is a medical emergency which manifests with microangiopathic haemolytic anaemia (MAHA), thrombocytopenia and neurological abnormalities and is known to be a rare association of SLE. We report a case of a 14 year old female who presented with fever and altered consciousness, subsequently diagnosed to have SLE with thrombotic microangiopathy and acute demyelinating CNS lesions in an ADEM-distribution

Keywords: SLE, ADEM, TTP, thrombotic microangiopathy, MAHA

INTRODUCTION

SLE is an autoimmune disorder with varying extents of organ involvement out of which nervous system involvement (Cerebral lupus) is considered as a major organ involvement needing vigorous and prompt therapy.

ADEM is a monophasic autoimmune demyelinating disorder of the CNS. ADEM like demyelinating CNS lesions are also recognized as rare neuropsychiatric manifestations of SLE[1].

TTP is a thrombotic microangiopathy (TMA) caused by severely reduced activity of a disintegrin and metalloproteinase with a thrombospondin type1motif, member13 (ADAMTS13)[2]. The exact aetiology of TTP is not known, but it is known to be associated with SLE[3].

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CASE PRESENTATION

A 14-year-old previously healthy female presented with a five-day history of fever, arthralgia, myalgia, nausea and vomiting. She had generalized headache, but no photophobia or phonophobia. She then developed altered level of consciousness over two days. There was no history of seizures. She had a significant non- scarring alopecia for three months with no oral ulcers, photosensitive rashes or inflammatory type joint pain or swelling. On examination, she was febrile, moderately pale and drowsy. The Glasgow coma scale was 14/15. There was no neck stiffness, lymphadenopathy, malar rash, oral ulcers or joint swellings. Neurological examination did not reveal papilloedema or focal neurological signs. Her weight was 56kg.

Her full blood count revealed marked thrombocytopaenia (Platelet count 8×10^9 /l) with normocytic anaemia (Haemoglobin: 4g/dl). Blood picture revealed MAHA. Lactate dehydrogenase level (1972 U/l) and reticulocyte count (4.9%) were elevated. Serum creatinine level was 104µmol/l (Normal range 44.2- 88.4µmol/l). Clotting profile and D- dimer levels were normal. Direct antiglobin test was negative.

Depending on the clinical scenario, a presumptive diagnosis of TTP was made and immediate therapeutic plasma exchange (TPE) was commenced along with oral prednisolone 1mg/kg/day. A total of seven cycles of daily TPEs were performed. ADAMTS 13 activity assay could not be carried out.

Considering her history of significant non-scarring alopecia, anti-nuclear antibody was arranged. It was highly positive (1: 1280). She had low C3 (78.2mg/dl) and C4 (7.2mg/dl) levels. Erythrocyte sedimentation rate was 30mm/1st hour, C- reactive protein was 2.4 g/dl and dsDNA was negative. 2D echocardiogram revealed a mild pericardial effusion.

Since she fulfilled four clinical and two immunological criteria [4], the diagnosis of SLE was made and was started on hydroxychloroquine 200mg daily(HCQ).

Despite the improvement of haematological markers with TPE, there was no improvement in her sensorium. On day four of admission, she developed right sided flaccid hemiparesis involving the arm and the leg. Over the next few days it progressed to spasticity. Magnetic resonance imaging (MRI) of the brain was in favour of ADEM like lesions distributed in supratentorial regions [Figure 1].

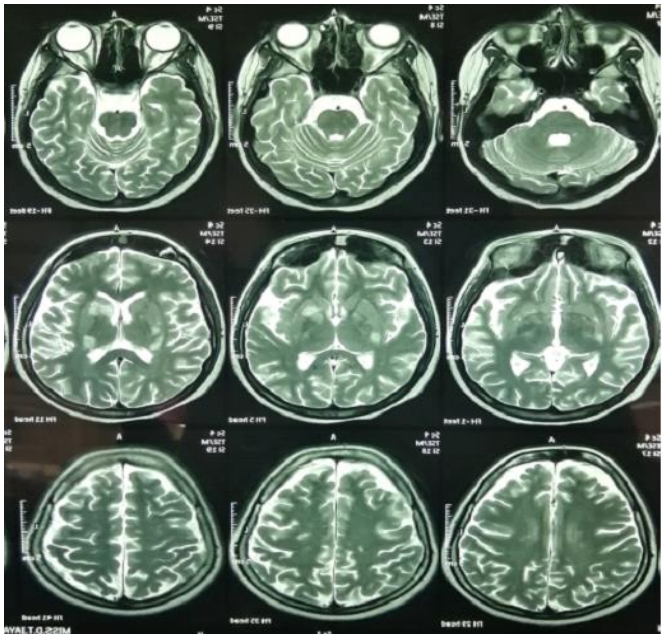

Figure 1: T2 weighted MRI showing bilateral asymmetrical hyperintense enhancements distributed in supratentorial regions of the brain which is compatible with radiographic evidence of ADEM like CNS lesions

Electroenchaphalogram revealed moderate cerebral dysfunction due to encephalopathy. Lumbar puncture revealed a normal full report, proteins and negative oligoclonal bands. Studies for cytomegalovirus, epstein-Barr, and human immunodeficiency viruses were negative. Both lupus anticoagulant and beta-cardiolipin antibodies were negative. Septic screen too was negative.

Since ADEM can rarely present as a neuropsychiatric manifestation of SLE, a tentative diagnosis of cerebral lupus was made. A total of five doses of intravenous (IV) methylprednisolone 1g/day were given followed by oral steroids 1mg/kg/day according to the standard guidelines[5]. IV immunoglobulin 0.4g/kg/day was given for a total of five days. As the improvement in the neurological state was not as expected, fortnightly IV cyclophosphamide 500mg/m^2 was commenced, to which she responded. Parents were acknowledged of the risk of subfertility and other major adverse effects prior to the commencement of cyclophosphamide and consent was obtained. A total of six doses of IV cyclophosphamide were given.

During the ward stay she was noted to have proteinuria with a urine protein to creatinine ratio of 9989 mg of protein/1g of creatinine. Urine full report didn't reveal any active sediment. Renal biopsy revealed a class II and class V SLE nephropathy. She was started on enalapril and mycophenolate mofetil (MMF) after cyclophosphamide pulsing.

The neurological weakness improved with vigilant physiotherapy. She was discharged from the ward with HCQ, MMF and prednisolone with the aim of tailing off the steroids.

DISCUSSION

The wide spectrum of clinical features of SLE and the lack of pathognomic features or investigations pose a diagnostic challenge and management dilemma for the treating clinician.

TTP and SLE may have overlapping features and may lead to a diagnostic dilemma [6]. MAHA and thrombocytopenia being recognized features of SLE[7], it was difficult for us to give a confident diagnosis of TTP. Another clue against TTP in this patient was poor response of neurological features to TPE. Hence other underlying systemic causes for secondary TMA were sought for. Concurrent CNS infection with abscess was initially thought of, but was safely excluded with lumbar puncture and MRI findings. Severe infection or antiphospholipid syndrome (APS) leading to secondary TMA was also excluded with negative septic and APS screening respectively. As such, TMA secondary to SLE was more favoured taking the clinical and investigation findings in constellation.

ADEM presenting as a neuropsychiatric manifestation of SLE has been reported in a few case reports and is a rare occurrence and it being the first manifestation of SLE is even rarer[8]. In this case, the dramatic response to IV cyclophosphamide favours the conclusion of cerebral lupus manifesting as ADEM like CNS pathology on brain imaging than pure ADEM.

To best of our knowledge there are not any published case reports of a SLE patient presenting for the first time with ADEM like CNS lesion on brain imaging and TMA simultaneously. This case report highlights the importance of considering the possibility of a broad spectrum of causes for neuropsychiatric manifestations in a patient with SLE. And in a patient with presumptive diagnosis of TTP and neurological manifestations who does not show an adequate response to TPE, an alternative or superadded aetiology for his/her neurological manifestations [9,10] should be thought of and investigated for. Lastly, it should be noted that prompt administration of more potent immunosuppressive therapy beyond the standard treatment in ADEM occurring in a background of an autoimmune condition like SLE, can be life saving like in the case of this young patient.

Author declaration

Author Contributions

1. Kithmini Dinushi Ellepola: Wrote the case report, drafted and edited the manuscript
2. Rakitha Atheendra Higgoda: Contributed to write the case report and edited the manuscript
3. Inoka Kumudini Jayasinghe: Contributed to write the case report, drafted and edited the manuscript and revised the final manuscript
4. Darshana Ranga Chamara: Contributed in editing the manuscript
5. Bhatiya Ganganath Premaratne: Contributed in editing the manuscript
6. Wasantha Dissanayake: Analyzed and edited the manuscript

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Ethics approval and consent to participate
Informed written consent was obtained from the patient and the mother for publication of this case report.

Competing interests
The authors declare that there are no conflicts of interest.

REFERENCES

1. Gil Alzueta MC, Erro Aguirre ME, Herrera Isasi MC, CabadaGiadás MT. Acute disseminated encephalomyelitis as a complication of systemic lupus erythematosus. Neurologia. 2016 Apr;31(3):209-11. doi: 10.1016/j.nrl.2014.02.001. Epub 2014 Apr PMID: 24703160.
2. Mannucci PM, Vanoli M, Forza I, Canciani MT, Scorza R. Von Willebrand factor cleaving protease (ADAMTS-13) in 123 patients with connective tissue diseases (systemic lupus erythematosus and systemic sclerosis). Haematologica. 2003 Aug;88(8):914-8. PMID: 12935979.
3. George P, Das J, Pawar B, Kakkar N. Thrombotic thrombocytopenic purpura and systemic lupus erythematosus: successful management of a rare presentation. Indian J Crit Care Med. 2008 Jul;12(3):128-31. doi: 10.4103/0972-5229.43682. PMID: 19742252; PMCID: PMC2738311
4. Gladman DD, Goldsmith CH, Urowitz MB, Bacon P, Fortin P, Ginzler E et al. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index for systemic lupus erythematosus international comparison. Journal of Rheumatology. 2000;27(2):373-376.
5. Fanouriakis A, Kostopoulou M, Alunno A, Aringer M, Bajema I, Boletis JN, Cervera R, Doria A, Gordon C, Govoni M, Houssiau F. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. Annals of the rheumatic diseases. 2019 Jun 1;78(6):736-45.
6. Aleem A, Al-Sugair S. Thrombotic thrombocytopenic purpura associated with systemic lupus erythematosus. Acta Haematol. 2006;115(1-2):68-73. doi: 10.1159/000089469. PMID: 16424653.
7. Allford SL, Hunt BJ, Rose P, Machin SJ; Haemostasis and Thrombosis Task Force, British Committee for Standards in Haematology. Guidelines on the diagnosis and management of the thrombotic microangiopathic haemolytic anaemias. Br J Haematol. 2003 Feb;120(4):556-73. doi: 10.1046/j.1365-2141.2003.04049.x. PMID: 12588343.
8. Bermejo PE, Ruiz A, Beistegui M, Zabala JA, Escamilla C. Hemorrhagic acute disseminated encephalomyelitis as first manifestation of systemic lupus erythematosus. J Neurol. 2008 Aug;255(8):1256-8. doi: 10.1007/s00415-008-0848-0. Epub 2008 Apr 23. PMID: 18425695.
9. Kim JM, Son CN, Chang HW, Kim SH. Simultaneous presentation of acute disseminated encephalomyelitis (ADEM) and systemic lupus erythematosus (SLE) after enteroviral infection: can ADEM present as the first manifestation of SLE? Lupus. 2015 May;24(6):633-7. doi: 10.1177/0961203314560426. Epub 2014 Dec 7. PMID: 25488421.
10. Ali D, Cardos B, Gorur Y, Lorenzo Villalba N, Janssen N, Bartha C et al. A Rare Case of Adult Acute Disseminated Encephalomyelitis Associated with Primary Epstein-Barr Virus Infection. EJCRIM 2019;6 doi:10.12890/2019_001094.