Neurological Manifestations In A Patient With SLE Complicated By TTP: A Case Report

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Citation

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Abstract

Neurological involvement in Systemic Lupus Erythematosus (SLE) is common, occurring in up to 14 to 75% of patients in different series.1 We describe a case of active SLE complicated by thrombotic thrombocytopenic purpura (TTP) in a 21-year-old woman and discuss the neurological and radiological findings. The significance of early diagnosis of SLE complicated by TTP and its aggressive treatment with plasma exchange and concomitant cyclophosphamide therapy is emphasized.

CASE REPORT

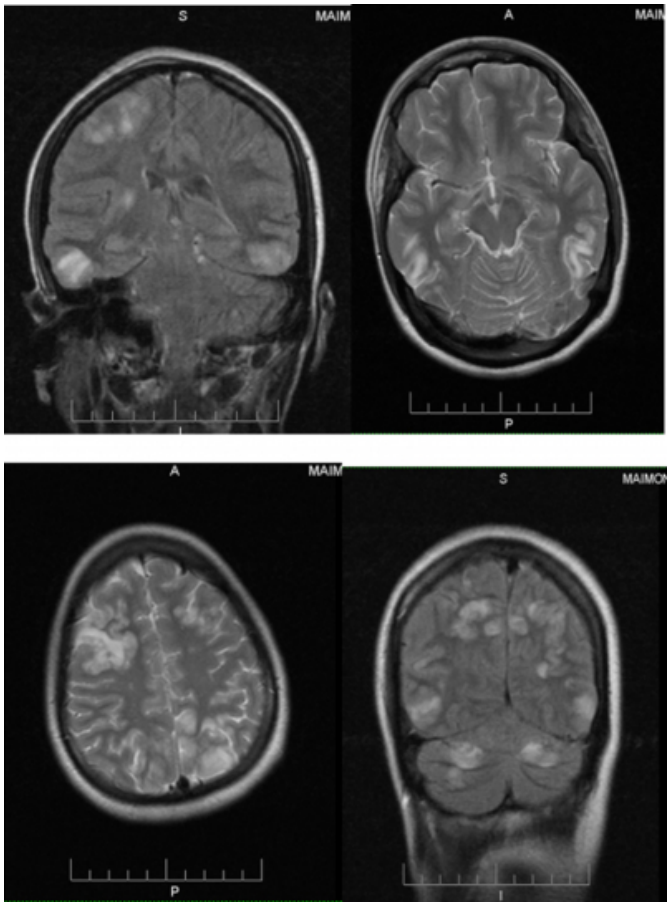
A 21-year-old African American woman was admitted to our hospital with complaints of bilateral lower extremity edema and reduced urine output for the past 2 weeks. She had been diagnosed with SLE one year previously and was maintained on 20 mg of oral prednisolone daily. She was found to have a blood urea nitrogen (BUN) of 63 mg/dL and a serum creatinine of 2.5 mg/dL. A renal biopsy was scheduled to document the pathologic nature of her lupus nephritis. While awaiting the renal biopsy, the patient had two focal seizures starting from the right hand with rapid secondary generalization. Neurological examination immediately after the ictal event revealed a conscious woman with post-ictal confusion. She followed simple commands and had right sidedright-sided focal weakness with a right pronator drift. Power was 4/5 Medical Research Council (MRC(MRC) grade in the right arm and 5/5 MRC grade in the other limbs. Deep tendon reflexes were 3+ in the knees and ankles with well-sustained bilateral ankle clonus and bilateral extensor plantar response. Following the seizure the patient's condition decompensated necessitating transfer to the medical intensive care unit, where she was intubated for airway protection

Laboratory evaluation revealed a WBC count of 1.8/ mm^3, hemoglobin=9.7g/dl, hematocrit of 28.1 % and platelet count of 18000/ mm^3. Reticulocyte count was 7.6% and peripheral smear showed abundant schistocytes cells along with some tear drop cells (1%). LDH was 1249 IU/L, serum haptoglobin was less than 8 (normal 43-212 Units) and ANA titer was positive at1:80: 80. Massive proteinuria, hematuria and urinary casts were present.

MRI of the brain revealed multiple areas of T2 hyperintensity in the right and left cerebellar cortex and subcortical areas as well as the right and left frontal, parietal, temporal and occipital cortex and subcorticalsub cortical areas. Similar findings were noted in the right and left lentiform nuclei, anterior and posterior limbs of the internal capsule with prominent gyral and irregular sub-cortical enhancement after intravenous gadolinium suggestive of sub-acute infarcts and vasculitis (Fig. 1a-d). Normal enhancement of the cortical veins and venous sinuses was visualized on MRV. MRA of the circle of Willis was normal.

Figure 1

Figure 1a-d: MRI of the brain showing multiple areas of T2 hyperintensity in the right and left cerebellar cortex and sub cortical areas, the right and left frontal, parietal, temporal and occipital cortex and sub-cortical areas. Prominent gyral and irregular sub-cortical enhancement after intravenous gadolinium is seen suggestive of sub-acute infarcts and vasculitis.



A diagnosis of SLE complicated by TTP was made and the patient underwent plasmapheresis with plasma exchange and was treated with pulse cyclophosphamide. With these intensive therapies her consciousness level improved, schistocyte numbers diminished and the anemia and thrombocytopenia significantly improved. Proteinuria persisted and the patient at this time is receiving monthly cyclophosphamide therapy and prednisolone. Renal biopsy revealed membranous lupus nephritis (WHO class V). (see WHO classification below)

WORLD HEALTH ORGANIZATION CLASSIFICATION OF LUPUS NEPHRITIS

Class I: normal glomeruli (~8% of biopsies)
Class II: pure mesangial alterations (~40% of biopsies)
Class III: focal glomerulonephritis (~15% of biopsies)
Class IIIA: focal segmental glomerulonephritis (~12% of biopsies)
Class IIIB: focal proliferative glomerulonephritis
Class IV: diffuse glomerulonephritis (~25% of biopsies)
Class V: diffuse membranous glomerulonephritis (~8% of biopsies)
Class VI: advanced sclerosing glomerulonephritis

DISCUSSION

TTP is a rare and occasionally fatal hematological disorder that can coexist with SLE and other autoimmune diseases. TTP characteristically presents with the pentad of microangiopathic hemolytic anemia, fever, thrombocytopenia, renal and neurological manifestations, though symptoms at first may be subtle starting with malaise, fever, and headache. TTP is characterized by platelet aggregation causing microvascular occlusion. This results in tissue ischemia and platelet destruction. TTP is caused by defective cleavage of ultralargeultra large von Willebrand factor due to deficiency of cleaving protease (ADAMTS13). This deficiency may be genetic or acquired. Adult onset TTP is a rare condition and affects 1-3 per million per year. It is most common among the 20 to 40 year old age group and affects women: men in the ratio of 2:1. Most often TTP develops spontaneously but factors like drugs (ticlopidine, clopidogrel, quinine) infections including HIV, malignancy and SLE have been implicated. The diagnosis rests on the clinical picture and presence of fragmented red cells in the peripheral smear.

The course of TTP concomitant with SLE generally unfolds, as progression of both diseases in a parallel fashion, as evidenced by the clinical manifestations in the TTP pentad and the SLE Disease Activity Index.

The onset of SLE may precede TTP and in some cases, TTP may appear first. TTP and SLE have been known to occur simultaneously [2,3,4,5].TTP associated with SLE may present with similar clinical features and hence differential diagnosis between them is difficult. Our patient had her course of SLE complicated by rapidly developing TTP, which presented with the neurological manifestation of seizures. The recognition of schistocytes, rarely seen in SLE, led us to the diagnosis of TTP. Neuroimaging was suggestive of CNS vasculitis and her condition stabilized with plasmapheresis and plasma exchange and concomitant cyclophosphamide therapy. This case report emphasizes the fact that early concomitant therapy may play a role in the treatment of patients with active SLE complicated by TTP and may prove life saving in these critically ill patients [6,7]. Further on TTP

should be considered in the differential diagnosis of any SLE patient with rapid neurological abnormaliiesabnormalities.

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References

1. Sanders EACM and Hogenhuis LAH. Cerebral vasculitis as a presenting symptom of systemic lupus erythematosus. Acta Neurol Scand 74, 75-77 (1986).
2. Starck M, Abedinpour F, Dendorfer U, Wagner-Czekalla J, Pachmann M, Mann JF, Nerl C. Acquired thrombotic thrombocytopenic purpura as the presenting symptom of systemic lupus erythematosus. Successful treatment with plasma exchange and immunosuppression-report of two cases.
Eur J Haematol. 2005 Nov; 75(5):436: 436-40.
3. Kapoulas S, Liakos S, Karkavelas G, Ageloudi M, Grekas D, Giannoulis E. Thrombotic thrombocytopenic purpura associated with rapidly progressive lupus nephritis: report of two cases.
Clin Nephrol. 2005 Apr; 63(4):297: 297-301.
4. Hamasaki K, Mimura T, Kanda H, Kubo K, Setoguchi K, Satoh T, Misaki Y, Yamamoto K. Systemic lupus erythematosus and thrombotic thrombocytopenic purpura: a case report and literature review.
Clin Rheumatol. 2003 Oct; 22(4-5):355: 355-8.
5. McHenry M, Meenagh G, Wright GD. Thrombotic thrombocytopenic purpura associated with cerebral SLE.
Ulster Med J. 2003 May; 72(1):52: 52-4.
6. Akaogi J, Akasaka N, Yamada H, Hama N, Satoh M, Nichols C, Ozaki S. Intravenous cyclophosphamide therapy in a case with refractory thrombotic microangiopathic hemolytic anemia and SLE.
Clin Rheumatol. 2004 Dec; 23(6):541: 541-3.
7. Guvenc B, Unsal C, Gurkan E, Canataroglu A, Saritas B, Evran M. Systemic lupus erythematosus and thrombotic thrombocytopenic purpura: a case report. Transfus Apher Sci. 2004 Aug; 31(1):17: 17-20.

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