

CASE REPORT

INTENSIVE CARE

Cerebritis as an initial presentation of systemic lupus erythematosus

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ABSTRACT

Systemic lupus erythematosus (SLE), an autoimmune disease with multi-system manifestations, has several clinical presentations varying from mild muco-cutaneous involvement to severe multi-organ involvement. We report the case of an 18-year-old girl who presented generalized tonic clonic fits. She gave a history of generalized headaches, recurrent painless oral ulcers, photosensitivity, joint pains and low-grade intermittent fever. Magnetic resonance imaging (MRI) scan of the brain revealed T2WI/FLAIR hyperintense signals in bilateral frontal, parietal and occipital regions and magnetic resonance angiography of the brain demonstrated mild areas of luminal narrowing in M1 and M2 segments of middle cerebral arteries bilaterally, suggestive of lupus cerebritis. Anti-nuclear antibody (ANA) and Anti-DsDNA antibodies were positive. She was diagnosed as SLE and was prescribed corticosteroids, cyclophosphamide and hydroxychloroquine. This case highlights cerebritis as initial presentation of SLE.

Abbreviations: ANA- Anti-nuclear antibody; CRP- C-reactive protein; FLAIR- Fluid attenuated inversion recovery; SLE- Systemic lupus erythematosus;

Key words: ANA; Cerebritis; Headache; Systemic Lupus Erythematosus

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1. INTRODUCTION

An autoimmune disease with multi-system manifestations, systemic lupus erythematosus (SLE) has several clinical presentations varying from mild muco-cutaneous involvement to severe multi-organ involvement including renal, cardiac, musculoskeletal and CNS disease.¹ Numerous immune-pathogenic pathways herald the development and progression of SLE and various pathogenic auto-antibodies such as anti-nuclear antibody (ANA), anti-double stranded DNA

(anti-DsDNA) antibodies have been identified.² In spite of the recent technologic advancements and understanding of etiologic factors of SLE, the specific pathogenesis is still not fully established, and diagnosing SLE remains a challenge. Several classification and diagnosis criteria for SLE have been postulated but their utility is a matter of debate in clinical setting.³ Treatment of SLE is dictated by the disease severity and the organ system involvement. Due to early detection of SLE and proper management, morbidity and mortality have improved dramatically. The 10-year survival rate of SLE was 63.2% in 1950s, which has now improved to 95% in

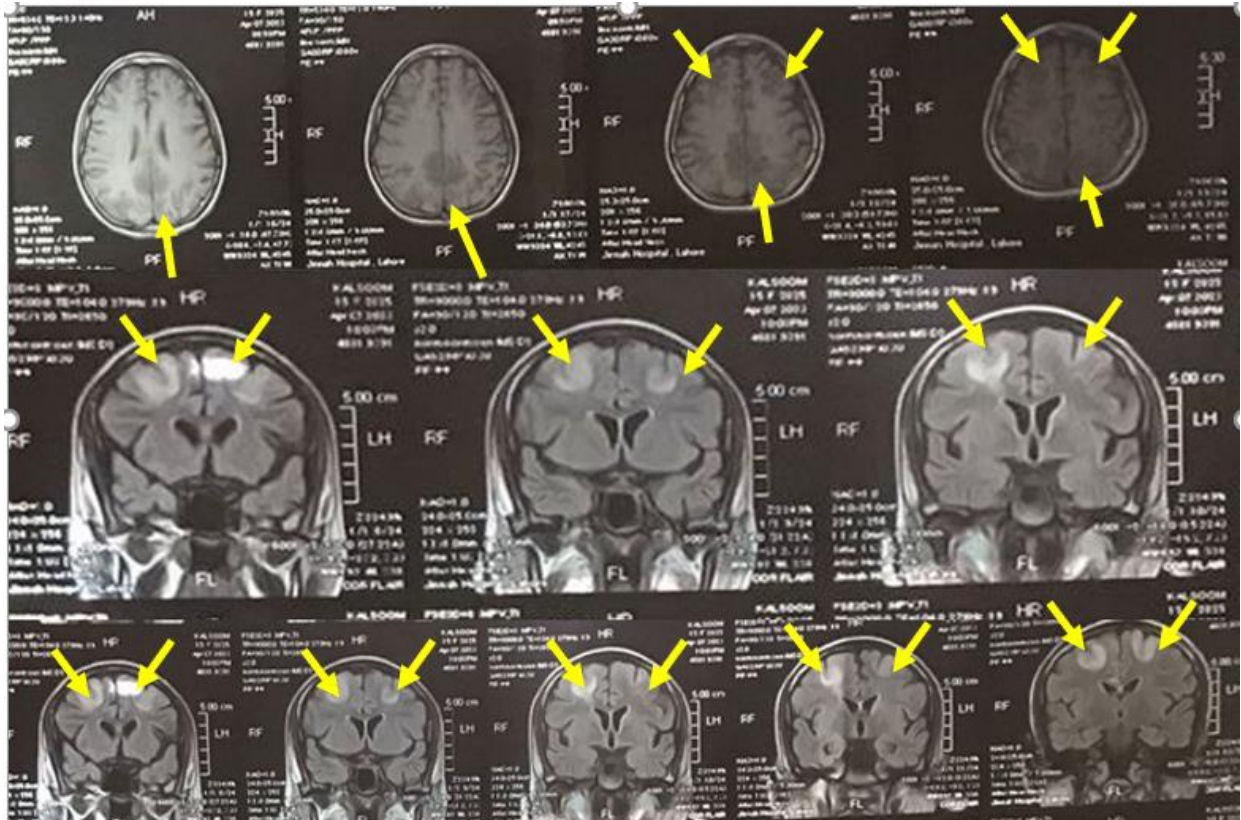


Figure 1: MRI-brain of the patient showing T2WI/FLAIR hyperintense signals in bilateral frontal, parietal and occipital regions

2000s.⁴ However SLE still poses a significant risk, if not timely diagnosed and adequately treated.

Herein, we report the case of an 18-year-old girl who presented with some unusual manifestations of SLE, especially generalized headaches. Magnetic resonance imaging (MRI) scan and MRI angiography of the brain were suggestive of lupus cerebritis (LC) with positive ANA and Anti-DsDNA antibodies. She was diagnosed as SLE and started on corticosteroids, cyclophosphamide and hydroxychloroquine.

2. CASE REPORT

We report the case of an 18-year-old girl who presented with three episodes of generalized tonic-clonic fits. Each episode lasted for 3-5 min and was associated with frothing of saliva, urinary incontinence and post-ictal confusion lasting for 10-15 min. There was a 3-month history of generalized headaches prior to this presentation, having no specific pattern, diurnal variation or aggravating factors. She had consulted various general physicians, multiple times and had been prescribed various pain killers with partial improvement. There was a history of recurrent painless oral ulcers, photosensitivity, joint pains involving small joints of

hands without swelling or morning stiffness and low-grade intermittent fever. She was unmarried and a student of A-levels. She did not smoke or use illicit drugs. On examination, she was vitally stable with a temperature of 99.8 °F. Once the seizure had ceased, there was no focal sensory, motor or cerebellar neurological deficit with a power of 5/5 in all four limbs. She had 2 oral ulcers and a malar butterfly rash. Joint examination revealed mild tenderness with no joint swelling or limitation of movements. Cardiovascular and respiratory examinations were normal.

On investigation, complete blood count revealed normochromic normocytic anemia with hemoglobin of 9.2 g/dl with normal total leukocyte count and platelet counts. ESR was raised at 68 mm/h with normal C-reactive protein (CRP). Serum albumin was low at 3.0 g/dl but urinalysis, liver function test and renal function tests were normal. Serologies for syphilis (TPHA), hepatitis B, hepatitis C and HIV were negative. Blood and urine cultures were negative. The patient and her attendants did not consent for lumbar puncture and cerebrospinal fluid analysis could not be done. MRI of the brain revealed T2WI/FLAIR hyperintense signals in frontal, parietal and occipital regions bilaterally, as shown in Figure 1 and MRI angiography of the brain

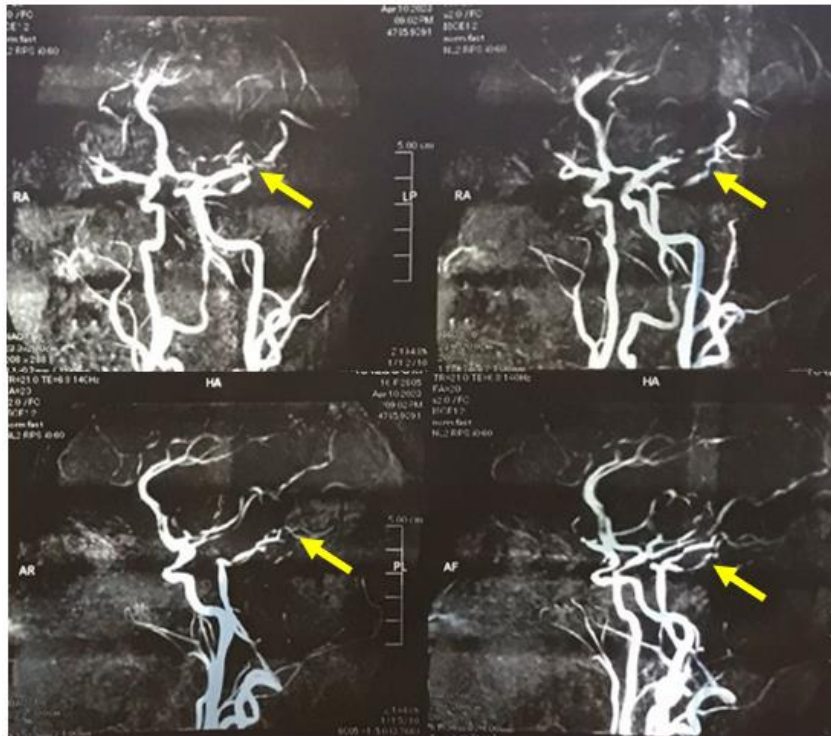


Figure 2: Magnetic resonance angiography (brain) of the patient showing mild areas of luminal narrowing in M1 and M2 segments of middle cerebral arteries bilaterally

demonstrated mild areas of luminal narrowing in M1 and M2 segments of both middle cerebral arteries suggestive of LC as shown in Figure 2. An autoimmune profile was done which showed positive ANA and positive Anti-DsDNA antibodies but negative RA Factor, Anti-Ro, Anti-La, Anti-CCP and Anti-Phospholipid antibodies with normal serum C3 and serum C4. Her echocardiography and abdomen-pelvic ultrasound were within normal parameters.

She was diagnosed as having SLE and was prescribed methylprednisolone 1 G/day IV for 3 days followed by oral prednisolone. After discussing the side effects, cyclophosphamide was prescribed as 500 mg infusion every 2 weeks for induction of remission (total dose 3 gm). In addition, she was prescribed hydroxychloroquine (5 mg/kg), topical steroids, sunblock SPF 60, oral omeprazole, and iron, calcium and Vitamin D supplements. At three months follow up, she was asymptomatic and azathioprine was started for maintenance of remission.

3. DISCUSSION

Although the prognosis of SLE has improved substantially over the years, SLE can still be a life-threatening disease and lead to premature mortality. According to Tselios et al.⁵ lupus patients were three

times more likely to die from any cause as compared to patients without lupus; especially SLE with onset before 40 y of age. Infections (24.5%), atherosclerosis (15.7%), lupus flare (13.3%) and malignancies (9.6%) were the leading causes of mortality in lupus patients.⁵ In China, Mu et al. reported substantial mortality in SLE; especially in the female patients with SLE, the leading cause of mortality was infections. Therefore, it is of pertinent importance that SLE be diagnosed timely and early treatment be initiated. With a sensitivity of 97% and specificity of 92%, the Systemic Lupus International Collaborating Clinics (SLICC) criteria is commonly used for diagnosing SLE.⁷ Requirement for diagnosis of SLE is ≥ 4 criteria (at least 1 clinical and 1 immunological criterion).⁷ Based on the SLICC criteria, our patient had a score of 5, including cerebritis, oral ulcers, malar rash, positive ANA and positive Anti-DsDNA antibodies.

Clinical presentation of LC is variable depending on the site and severity of the areas affected and may include headache, cognitive dysfunction, ataxia, anxiety, psychosis, depression, focal or diffuse seizures, mood changes, altered consciousness or hemiplegia.⁸ Our patient presented with diffuse fits and a history of headache and was subsequently diagnosed with LC. This is similar to the case reported by Leitao et al.⁹ of a patient with LC who presented with status epilepticus associated with respiratory failure requiring ventilator support. However, the patient had neurological sequelae causing significant morbidity. In India Goswami et al.¹⁰ reported 2 cases of LC presenting with seizures. The first patient had CNS involvement in the form of limbic encephalitis, making it difficult to diagnose and treat. The second case was diagnosed promptly as the clinical and laboratory findings were suggestive of SLE leading to targeted therapy and early recovery. Our patient had no history of psychiatric illness. However, patients of LC may present with psychiatric manifestations. Primary psychiatric disorder as presentation of LC was reported by Memon et al. in a patient presenting with nausea, vomiting and altered behavior (childish disinhibition) without seizures.¹¹ Cotard's syndrome, also known as Cotard's delusion or walking corpse syndrome, which is

characterized by fixed delusion that one is dead or dying, was reported by Luma et al. in a patient with LC.¹²

Management of SLE is complex and variability in clinical practice exists as the treatment is dictated by disease severity and organ system involvement. Medical therapy of LC incorporates immunosuppressive therapy with systemic steroids and cyclophosphamide.¹³ However, side effects of cyclophosphamide include infertility, bone marrow suppression, increased infection risk, gastrointestinal upset (nausea, vomiting, anorexia) and an increase in the malignancy risk.¹³ Corticosteroids are often used as first-line drugs because of their rapid onset of action and powerful anti-inflammatory action.¹⁴ The dose and duration of steroids depend on the disease severity. Hydroxychloroquine is especially useful to treat fatigue, muco-cutaneous and musculoskeletal manifestations in lupus and to prevent flares.^{15,16} Hydroxychloroquine is safe during all trimesters of pregnancy and also improves long-term survival by protecting against irreversible organ damage, thrombosis, and bone mass loss in SLE. Even with long-term hydroxychloroquine use, retinal toxicity is rare but should be monitored with ocular coherence tomography (OCT).¹⁵ Other agents used in SLE include simple analgesics, e.g., paracetamol and non-steroidal anti-inflammatory drugs, for pain relief; conventional disease modifying anti-rheumatic drugs, e.g., methotrexate, azathioprine, cyclosporine, mycophenolate, and biological disease modifying anti-rheumatic drugs, e.g., rituximab, belimumab, etanercept, abatacept, etc., with increasing disease severity and involvement of major organ systems especially renal system.^{17,18} Our patient was given intravenous cyclophosphamide and methylprednisolone, followed by oral prednisolone for induction of remission. In addition, she was prescribed hydroxychloroquine. At three months follow up, she was asymptomatic and azathioprine was started for maintenance of remission.

In conclusion, this case highlights cerebritis as initial presentation of SLE. It is necessary that the treating physicians keep SLE in their differentials when managing such patients so that timely diagnosis and early treatment may lead to reduction in morbidity and mortality.

4. Consent

Detailed informed consent was taken from the patient and her attendant prior to data collection and manuscript writing.

5. Conflict of interest

None declared.

6. Authors contribution

FA: Conception and design, data collection, assembly and patient assessment, critical review and corrections

NIB: Conception and design, literature research, data collection, assembly and patient assessment, manuscript writing

MBR: Literature research, data collection, assembly and patient assessment, manuscript writing

MSAG: Conception and design, literature research, critical review and corrections

AA: Data collection, assembly and patient assessment, critical review and corrections

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