Received: 30 January 2021 | Revised: 28 April 2021 | Accepted: 26 May 2021

DOI: 10.1002/ccr3.4454

CASE REPORT

Clinical Case Reports Open Access WILEY

Fatal cerebral venous sinus thrombosis as a manifestation of uncontrolled systemic lupus erythematosus in a young African female

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Funding information
There were no sources of funding

Abstract

In a young patient with systemic lupus erythematosus presenting with status epilepticus and neurological deficits, early brain imaging, risk factor identification and prompt treatment of underlying lupus flare-up and cerebral venous sinus thrombosis could significantly improve the management and prognosis.

KEYWORDS

brain infarction, intracranial hemorrhage, sub-Saharan Africa, systemic lupus erythematosus, venous sinus thrombosis

1 | INTRODUCTION

Systemic lupus erythematosus (SLE) is a relapsing and remitting autoimmune disease characterized by multi-organ involvement. The relapsing pattern is known as a lupus flare-up. Women have a higher incidence than men with a sex ratio of 9:1.[1] The disease can manifest as nonspecific symptoms and involve organs including musculoskeletal, dermatological, renal, neuropsychiatric, hematological, pulmonary, gastrointestinal, cardiac, vascular, ocular, endocrine, and obstetric.[2]

Having achieved remission status, flare-ups are estimated to occur in up to 25% of SLE patients within 1–2 years and up to 65% within 5–10 years. A quarter of the flare-up cases is classified as severe and the rest are of mild and moderate severity. An index for measuring lupus disease activity is the systemic lupus erythematosus disease activity index 2000 (SLEDAI-2K). Activity categories are defined based on the SLEDAI scores: 0 = no activity, 1–5 = mild activity, 6–10 = moderate activity, 11–19 = high activity, and ≥20 = very high activity.[3] A SLEDAI-2K score increase of more than 3 can be an outcome of a lupus flare-up. The commonly involved organs in flare-ups are the mucosa and skin, the musculoskeletal system (arthritis), the hematological system and kidneys (lupus nephritis). It can also affect the central nervous system causing neuropsychiatric symptoms, cerebrovascular disease, and seizure disorder.[4]

Neuropsychiatric involvement in SLE affects both the central and peripheral nervous system. Central involvement may be diffuse or localized. Diffuse disease includes cognitive decline, memory impairment, depression, and psychiatric disorders. Central disorders include seizures with or without cerebrovascular disease are reported in up to 50% of patients

presenting with neuropsychiatric SLE.[5] Cerebrovascular disease is further defined into stroke, transient ischemia, subarachnoid and intracranial hemorrhage, chronic multifocal ischemia, and sinus thrombosis.[6]

We present the case of a 22-year-old female with recently diagnosed SLE who stopped her maintenance immunosuppressive medication and presented in coma with status epilepticus. On recovering consciousness, she had multiple neurological deficits and died as a result if complications of her disease and immunotherapy.

2 | CASE REPORT

A 22-year-old female presented to the hospital with a history of new-onset episodes of generalized tonic-clonic seizures which started 24 h before admission each lasting 3–4 min, and accompanied by high-grade fever. She had been diagnosed with SLE 6 months previously with a positive serum antinuclear antibody (ANA) of 1:320, fever, oral ulcers, acute cutaneous lesions, and joint involvement. A negative antidouble-stranded deoxyribonucleic acid (anti-dsDNA) was reported. She was treated with prednisolone 60 mg once daily due to unavailability of other disease-modifying antirhematic drugs, and their high cost of acquiring them. She reported to have discontinued her medication 4 months before admission because of clinical improvement and high pill burden.

On admission, she was comatose with a Glasgow coma score of 3, febrile with temperature of 39.4°C, with a swollen face, malar rash, and alopecia. She had diffuse fine crepitations in both lungs fields. Neurological examination including fundoscopy revealed normal cranial nerves with generalized hypotonia and hyporeflexia in all four limbs. She was anemic with a hemoglobin of 7.8 g/dl with leukopenia of 3.25×10^9/L, platelet count of 193×10^9/L, elevated erythrocyte sedimentation rate of 115 mm/h, normal serum creatinine of 76 μmol/L, and elevated C-reactive protein of 8748 ng/ml (normal <700 ng/ml). An international normalized ratio and partial thromboplastin time were 1.16 and 22.4 s, respectively. Her SLEDAI-2K score on admission was 21 points. Screening for malaria and human immunodeficiency virus were both negative, and there was no growth on blood culture. A contrasted brain computed tomography scan showed no meningeal enhancement or pathological finding.

She was treated initially with intravenous diazepam and oral phenytoin without suppression of her seizures. Her care was continued in the medical intensive care unit where she was treated with an infusion of phenobarbital with suppression of her seizures after 48 h. On day 3 of admission, she regained consciousness and was found to be aphasic with no power in both lower limbs and diminished tone, power and reflexes in the left upper limb. The right upper limb was normal. A brain magnetic resonance imaging (MRI) scan and magnetic resonance venography (MRV) revealed right parietal and left fronto-basal lobe venous hemorrhagic infarction secondary to venous sinus thrombosis, shown in Figure 1 and Figure 2.

The venous sinus thrombosis was treated with low molecular weight heparin. And the lupus flare-up was treated with intravenous methylprednisolone 1 g followed by intravenous cyclophosphamide 825 mg on day 7 of admission. She was maintained on oral prednisolone, phenobarbitone, and warfarin, and as her overall condition improved, she was transferred to the general ward. However, she remained paraplegic with a dysphasia and left arm weakness. On day 18 of admission, she developed neutropenic sepsis with a leucocyte count of 0.82×10^9/L and platelet count of 219×10^9/L. She was given piperacillin-tazobactam and granulocyte colony-stimulating factor, but her condition continued to deteriorate and she died of sepsis 23 days after admission.

3 | DISCUSSION

The flare-up of SLE in this patient was most likely due to poor treatment compliance in the context of an active underlying disease. She presented in status epilepticus with multiple neurological deficits secondary to ischemic strokes as a result of the cerebral venous sinus thrombosis (CVST). While her seizures were controlled, anti-inflammatory and immunosuppressants were initiated because of the underlying SLE disease. However, she subsequently died of sepsis, a complication most probably of her flare-up and immunosuppressant medication.

The risk factors for SLE flare-up include African-American race, male gender, onset of disease less than 25 years of age, major organ disease, persistent disease activity, poor treatment compliance, low serum C3/C4, and high anti-dsDNA, and elevated serum B-lymphocyte stimulator.[4] In this case, the major risk factors were her age of onset at 22 years and poor treatment compliance, although her anti-dsDNA was negative at diagnosis. Serum C3/C4 and B-lymphocyte stimulator are not available in our setting.

A systematic review of SLE in Africa reported that the most frequent comorbid conditions are infections and cardiovascular diseases. The high hospital mortality rate of up to 43% which was reported in a series of hospital admissions was attributed to infections, renal disease, neuropsychiatric involvement, and lupus flare-ups.[7]

Specialized hospital services are limited in Africa. In Tanzania, it is estimated that there is one practicing neurologist per 8–10 million population,[8] while in sub-Saharan Africa, there is one per 3 million and 1 MRI scanner per 25 million.[9] It has been reported in our hospital setting that there is a recent increase in the number of stroke admissions, most

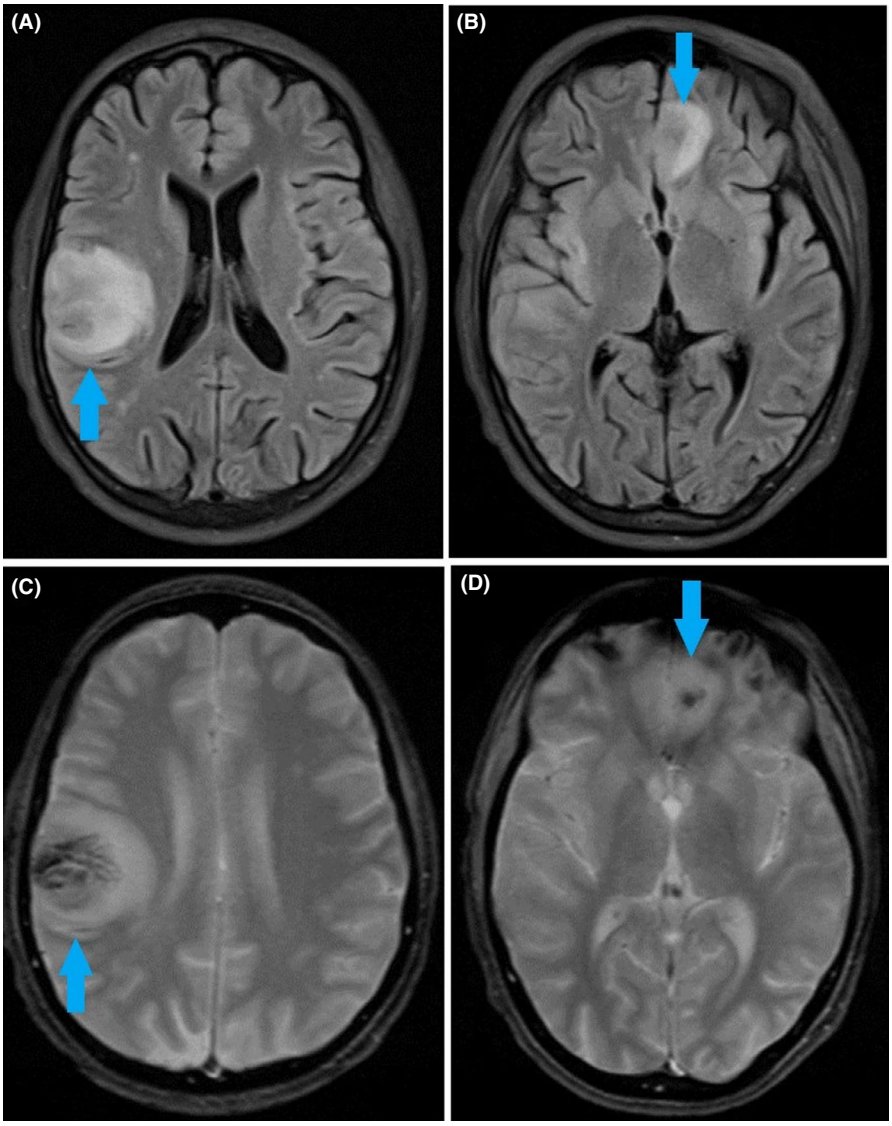

FIGURE 1 MRI axial flair (A and B) and axial T2 gradient echo (C and D) showing hemorrhagic infarction (blue arrow) in the right parietal lobe (A and C) and left fronto-basal lobe (B and D) with surrounding vasogenic edema

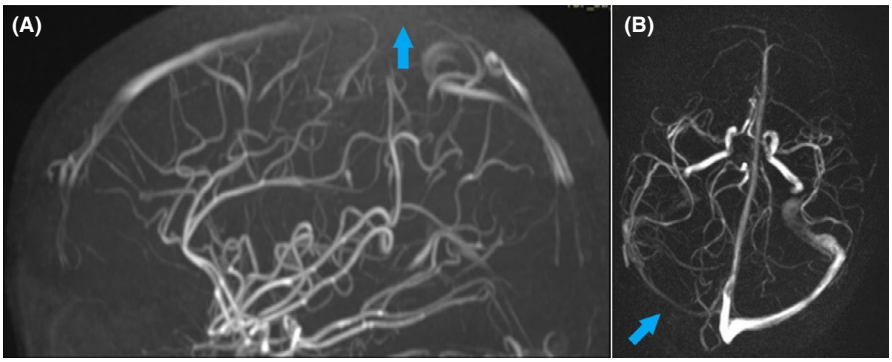

FIGURE 2 MRV showing a filling defect (blue arrow) in the superior sagittal sinus (A) and right transverse sinus (B) in keeping with right parietal and left fronto-basal lobe venous hemorrhagic infarction secondary to venous sinus thrombosis

likely related to a growing and aging population, greater access to health care, and western lifestyle factors particularly in urbanized females.[10] These factors greatly influence outcome of potentially treatable conditions such as SLE.

Neuropsychiatric features have been reported to occur in 12.9%–56.9% and cerebrovascular disease in 7.9%–41.5% of SLE patients.[6,11] Risk factors for developing neuropsychiatric symptoms are high levels of disease activity, positive antiphospholipid antibody at diagnosis, absence of anti-dsDNA antibody at diagnosis, and having a lower educational level.[12] The patient reported here had a high SLEDAI-2K with a negative anti-dsDNA at diagnosis. The presence of focal neurological disorders as occurred in this patient is known to increase the risk of mortality in SLE patients.[12]

The main mechanisms for increased risk of CVST in SLE include vasculitis causing endothelial cell injury; thrombosis secondary to antiphospholipid antibodies; and thrombophilia secondary to hyperfibrinogenemia and complications of lupus nephritis.[13] The use of prophylactic hydroxychloroquine as an immune modulator has been shown to decrease the risk of neuropsychiatric flare-ups and decreases the worsening of existing disorders by reducing blood viscosity, platelet aggregation, and red cell sludging.[5]

The treatment of CVST is based on the administration of antithrombotic therapy, removal of precipitating factors, immune suppression, and antiepileptic medication. The underlying cause of CVST in our patient was SLE. Anticoagulation is considered as the cornerstone of CVST treatment except for in patients with subarachnoid hemorrhage and thrombocytopenia.[14] The treatment of neuropsychiatric SLE by using intravenous cyclophosphamide and intravenous methylprednisolone as occurred in this patient, has been studied and results in a clinical improvement of greater than 20% from baseline as compared to methylprednisolone alone.[15] In this case, the patient's immunomodulatory treatment was complicated by neutropenia which resulted in sepsis and death.

4 | CONCLUSION

In conclusion, we present a case of CVST in SLE in a young female in Africa with a fatal outcome. The reported higher prevalence of SLE in Africa in combination with limited access to specialist care services and resources emphasizes the need for greater awareness, in particular of neuropsychiatric SLE. The case highlights the importance of specialist medical and neurological capacity building in sub-Saharan Africa. Early diagnosis, risk factors identification, and prompt management of underlying lupus flare-up and CVST could significantly improve its management and prognosis.

ACKNOWLEDGEMENTS

We thank the patient and her family for their patience and co-operation.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

AMS, EVA, AMS, and MCJD: involved with patient management. AMS and EVA: reviewed the inherent literature. AMS: prepared the manuscript and provided the images. MCJD and WPH: edited the manuscript. All authors approved the final version of the manuscript.

ETHICAL APPROVAL

The need for ethics approval for this case report was waived.

WRITTEN INFORMED CONSENT

Written informed consent was obtained from the patient's mother for publication of this case report and any accompanying images.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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How to cite this article: Sadiq AM, Assey EV, Sadiq AM, Dekker MCJ, Howlett WP. Fatal cerebral venous sinus thrombosis as a manifestation of uncontrolled systemic lupus erythematosus in a young African female. *Clin Case Rep*. 2021;9:e04454. https://doi.org/10.1002/ccr3.4454