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Systemic lupus erythematosus with Fahr's syndrome: A case report with review of literature

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ABSTRACT

Systemic lupus erythematosus (SLE) is a multisystem disease with autoimmune etiology. The neurological manifestations of lupus are diverse. We introduce a case of a 40-year-old male who presented with constitutional symptoms like low-grade fever, myalgia, and easy fatigability for one month. On examination, he had icterus, hepatosplenomegaly, and spasticity. Lab tests were suggestive of autoimmune hemolytic anemia with ANA positivity and low complements. Diagnosis of SLE was certain. CT brain showed bilateral symmetrical dense radial and punctate calcifications involving bilateral cerebral and cerebellar hemispheres suggestive of Fahr's syndrome.

Keywords: intracranial calcifications, Fahr's syndrome, SLE

Abbreviations (in alphabetical order):

AIDS	– Acquired immunodeficiency syndrome
ANA	– Anti Nuclear Antibody
AHA	– Autoimmune Hemolytic Anemia
BG	– Basal Ganglia
BSPDC	– Bilateral Somatopallido Dentate Calcification
CT	– Computed Tomography
DN	– Dentate Nucleus
MRI	– Magnetic Resonance Imaging
NPSLE	– Neuropsychiatric Systemic Lupus Erythematosus
SLICC/ SLEDAI	– Systemic Lupus International Collaborating Clinics/Systemic Lupus Erythematosus Disease Activity Index
SLE	– Systemic Lupus Erythematosus
WM	– White Matter

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem disease with autoimmune etiology. The neurological manifestations of lupus are diverse [1]. Fahr's Syndrome is a neurodegenerative illness commonly recognized as bilateral somatopallido dentate calcification (BSPDC), also referred to as idiopathic basal ganglia calcification [2]. Both Fahr's disease and Fahr's Syndrome are disorders marked by calcification in specific brain regions, which leaves patients with neurological and psychiatric aftereffects. Most commonly basal ganglia and dentate nuclei are involved. Fahr disease refers to primary basal ganglia calcifications with no known origin, while Fahr's syndrome is used when there is a secondary cause. There are clear, significant distinctions between the two illnesses regarding prognosis, therapy, location of lesions, and origin, even though their symptoms and signs may be similar [3].

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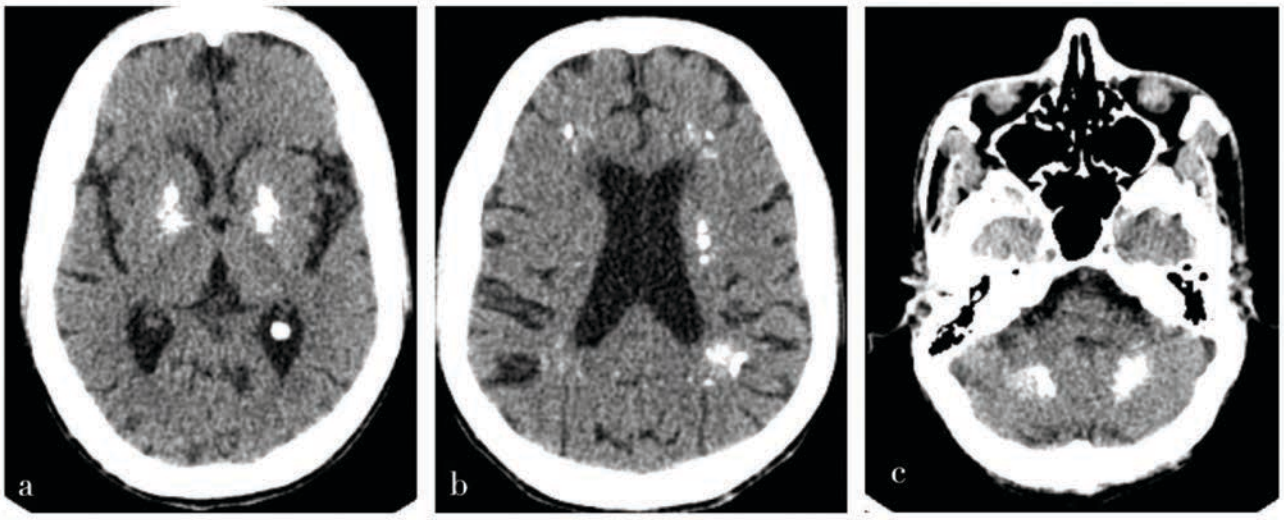

FIGURE 1. a,b - Cranial axial CT brain showing bilateral symmetrical dense radial and punctate calcifications involving bilateral cerebral; c- and cerebellar hemisphere

Seventy-five percent of SLE patients are often found to have nervous system involvement, ranging from mild, subtle symptoms like headaches and mood disorders to life-threatening illnesses including acute confusional state, Stroke, and myelopathy [4]. Clinicians frequently face a highly challenging diagnostic issue due to the vast diversity of appearances and differential diagnoses [5]. It is an uncommon manifestation of SLE since calcifications of the brain, basal ganglia, and cerebellum have only been recorded in a few individuals [6]. Although the exact cause of these calcifications in SLE is uncertain, they may be dystrophic after microinfarctions brought on by initial vascular injury and persistent venous inflammation. Around 5% of cases involved brain vascular involvement, and histological results pointed to non-inflammatory vasculopathy with subsequent infarcts [7]. The thalamus and cerebellum are less frequently involved in localized calcifications than the basal ganglia, the most common site [8].

This case report aims to increase awareness among clinicians that significant cerebral calcification can be seen in several rheumatological illnesses, including SLE, systemic sclerosis, and dermatomyositis. The exact mechanism underlying intracranial calcification in SLE is still unknown.

CASE PRESENTATION

A 40-year-old male presented with constitutional symptoms like low-grade fever, myalgia, and easy fatigability for one month. His Hb was 5.5 gm/dl, reticulocytes were 65%. His ANA (ELISA) was 1.62(1.1 positive). He was referred for a rheumatology consult. There was no history of joint pain, oral ulcers, or skin rash. He had difficulty waking for four years of age, which was attributed to poliomyelitis.

On examination, his BMI was 18 kg/m^2. He had icterus, facial dysmorphism with a high-arched palate, dental abnormalities, and a low hairline. He had a spastic diplegic gait, and deep tendon reflexes were brisk. Per abdomen examination had massive hepatosplenomegaly. Lab tests were suggestive of autoimmune hemolytic anemia (Table 1) with systemic lupus erythematosus. CT brain showed bilateral symmetrical dense radial and punctate calcifications involving bilateral cerebral and cerebellar hemispheres suggestive of Fahr's Syndrome (Figure 1). He was managed with high-dose steroids, Hydroxychloroquine, Azathioprine and Baclofen.

The final diagnosis was Systemic lupus erythematosus with autoimmune hemolytic anemia with Fahr's Syndrome with a SLICC/SLEDAI score of 2.

Table 1: Summarizing the lab parameters, the table shows the various laboratory parameters of the patient. The results indicate the presence of normocytic normochromic anemia with reticulocytosis and neutrophilic leukocytosis. The bone marrow aspiration and biopsy indicate an increase in the number of cells in the marrow, specifically in the erythroid and megakaryocytic cell lines. The patient has tested positive for both direct and indirect Coombs tests. The APLA Panel has a negative stance.

DISCUSSION

Systemic lupus erythematosus (SLE) is characterized by neurological involvement that can involve both the central and peripheral nervous systems. Varied manifestations include peripheral neuropathy, psychosis, depression, stroke, mobility disorders, and cognitive impairment [9]. MRI and CT brain imaging are predominantly normal in about 30-40% of patients while the rest can show either white matter hyperintensities or meningeal enhancement. Regardless of the cause, the distribution of calcified deposits is uniform, which could be explained by the brain's

TABLE 1. Laboratory parameters

Lab test	Value	Range
Hemoglobin	4.8	13-16.5(gm/dl)
Hct/PCV	11.9%	40-48%
RBC count	0.71	4.5-7.5(million/cumm)
Reticulocyte count	40.48	0.2-2%
Reticulocyte production index	4.3	
TLC	17250(N 71, L 23, E 1.5, M 3.7)	4000-11000 cells/cumm
Platelets	2.41	1.5-4.5 lakhs/cumm
ESR	100	0-10 mm/hr
Peripheral smear	Normocytic normochromic anemia with reticulocytosis and neutrophilic leukocytosis with hemolytic anemia	
Bone marrow aspiration & biopsy	Hypercellular marrow with erythroid and megakaryocytic hyperplasia	
CRP	9.82	0-5 mg/L
ANA profile	SSA+, CENP 3+, AMA M2+	
Urea	15 mg/dl	12.6-42.6 mg/dl
Creatinine	0.77 mg/dl	0.7-1.3 mg/dl
Uric acid	9.8 mg/dl	3.4-7 mg/dl
RBS	97 mg/dl	70-140 mg/dl
Total Protein	7	6-8.3 gm/dl
Serum Albumin	3.6	3.2-5.2 mg/dl
Total bilirubin/direct bilirubin	3.99/0.92	0-1.2/0-0.2 mg/dl
A/G	1.1	1.2-1.5
AST/ALT	42/18	0-41/40-129 U/L
Direct coombs test	positive	
Indirect Coombs test	positive	
Urine routine	normal	
C3	65.9	75-135 mg/dl
C4	7.8	9-36 mg/dl
APLA Panel	Negative	

selective exposure to specific regions for calcium deposition [10].

The differential diagnosis includes bilateral striopallidodentate calcinosis (Fahr disease), hyperparathyroidism, (pseudo)hypoparathyroidism, lead intoxication, AIDS, radiation therapy, etc. [11]. We reviewed literature with search terms SLE, Fahr's disease and Intracranial calcification, and autoimmune hemolytic anemia. Around 12 cases were reported in the literature. Nordstrom et al. reported two cases of SLE which had seizures and CT showed basal ganglia calcification. These cases were managed with antiepileptics and steroids with resolution of symptoms. Ten out of 12 cases reported so far had bilateral basal ganglia calcification. The outcome of Fahr's disease is these case reports is variable. The median age of disease duration was 12 years. However, in our case, Fahr's disease was diagnosed at the initial presentation.Raymond et al. studied CT scan of 27 SLE patients and found calcification in 8 patients. Their study also found no relationship between the presence or extent of calcification and the patient's age, course of disease, or neurological presentation [8]. Systemic lupus erythematosus is frequently accompanied by hematological abnormalities (SLE). In particular, people with SLE may experience autoimmune hemolytic anemia (AHA) at the time of diagnosis or during the first year of the illness [12]. Our case report has a similar finding, which is corroborative to previous data. Table 2 shows the clinical and imaging data of similarly reported cases in the literature.

Table 2. The clinical and imaging data of cases reviewed and our case – provides a concise overview of the various case presentations, including various clinical manifestations, disease duration, neurological manifestations, CT findings, therapeutic approaches, and clinical outcomes.

CONCLUSION

Intracranial calcification is rarely reported in SLE and may not correlate with the severity of neuropsychiatric symptoms. Fahr's disease, also known as idiopathic basal ganglia calcification, is a rare condition, and SLE is one of the secondary causes of Fahr's. Around 12 cases have been reported in the literature. The mechanism may be immune damage in SLE and requires further studies. CT is the most effective way to determine the size and degree of calcium deposits, even if MRI is the most sensitive and useful technique in the management of CNS lupus.

TABLE 2. The clinical and imaging data of cases reviewed and our case

Case (Year)	Sex/ Age	Disease duration	SLE disease activity	Neurological examination	CT Brain	Treatment	Outcome
2022 [13]	F/43	23 years	Yes	Transient loss of consciousness with seizures	Calcification in bilateral basal ganglia,frontal and parietal cotex,pons	methylprednisolone human immunoglobulin and mycophenolate mofetil	Improved
2019 [14]	F/53	13 Years	Yes	Dysarthria, bradykinesia, increased DTRs of the upper extremities, abnormal tandem gait	Symmetric calcification in basal ganglia and radiating lesions along the periventricular region	Steroids	Improved
2015 [15]	F/54	–	–	Parkinsonism	Calcification in basal ganglia, centrum semiovale, and cerebellum with atrophy of the brain	–	–
2013 [16]	F/65	17 Years	Yes	Decreased sleep, Parkinsonism, Pyramidal signs	B/L symmetric calcifications in the cerebrum, basal ganglia, periventricular white matter, and cerebellum	Zolpidem	Improved
2010 [17]	F/56	13 Years	Yes	Cognitive decline, Parkinsonism, Pyramidal signs	calcifications in paraventricular area, BG cortex, cerebral WM Cerebellum, cerebral atrophy	–	–
2008 [18]	F/18	5 Years	–	Recurrent seizures depression, cerebellar signals, general spasticity, neurogenic bladder, and difficulty in walking.	Calcification in BG, centrum semiovale, cerebellar hemispheres, brainstem. Secondary hydrocephalus	Anti-seizure drugs azathioprine, cyclophosphamide, rituximab Plasmapheresis intravenous immunoglobulin	No improvement
2008 [19]	F/53	20 Years	Yes	sychosis, progressive depression, insomnia, cognitive decline, impaired gait, tremors	calcification of the basal ganglia, centrum semiovale, cerebellar hemispheres, and brainstem	High-dose immunosuppressive therapy	No improvement
1998 [20]	F/22	10 Years	No	Left hemiparesis. Impaired consciousness	asymmetric calcification in BG, internal capsule, and subcortical and periventricular WM, atrophy in perisulcus	methylprednisolone	Death
1994 [21]	F/38	14 Years	–	Transient loss of consciousness, and sphincter relaxation	Bilateral calcifications in DN, cerebellar WM, pons, BG, corona radiata, and subcortical WM	–	–
1988 [22] (Case 1)	F/26	1 Year	–	Right hemiparesis	Calcification in right BG, right paraventricular area, and the frontal cortex of both hemispheres	–	–
1988 [22] (Case 2)	F/21	6 Years	Yes	Right hemiparesis	Left paraventricular calcification, hypodense area in the fight frontoparietal region, and diffuse cerebral atrophy	–	–
1985 [23] (Case 1)	F/20	7 Years	Yes	Cognitive decline, choreiform movements in arms, and paraplegia of the legs	Calcifications in BG and peri sulcal atrophy	Steroids Anti-seizure medications	Resolution of symptoms
1985 [23] (Case 2)	F/19	5 Years	–	Seizures	Calcifications in BG and peri sulcal atrophy	Steroids Anti-seizure medications	Resolution of symptoms
In our case	M/40	–	Yes	AIHA	Bilateral symmetrical dense radial and punctate calcifications involving bilateral cerebral and cerebellar hemispheres suggestive of Fahr's Syndrome	Steroids	

**BG-Basal Ganglia, DN-Dentate Nucleus, WM- White Matter*

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