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CASE REPORT

Stroke at a Young Age: Could a Simple Folate Deficiency Be the Cause?

FAIZA[1]*, FATIMA GILANI[1], YASIR BILAL[2], MUHAMMAD SAROSH[1], BARIA ALI[1], MUHAMMAD NAUMAN SHAHID[3], SYED TALAL ALI[4]

[1]Shalamar Hospital, Lahore, Pakistan
[2]Children Hospital, Lahore, Pakistan
[3]Ghurki Trust Teaching Hospital, Lahore, Pakistan
[4]Central Park Medical College, Lahore, Pakistan
***Correspondence to:** Dr. Faiza , **E-mail:** faizanaeem500@gmail.com

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ABSTRACT

Background: Stroke is a leading cause of morbidity and mortality worldwide, yet its occurrence in young individuals without conventional risk factors presents diagnostic challenges. Emerging evidence suggests that folate deficiency, through hyperhomocysteinemia, may play a critical role in predisposing young adults to ischemic stroke.

Case Presentation: We report the case of an 18-year-old male who presented with acute right-sided weakness, slurred speech, and facial droop. He had no history of smoking, hypertension, diabetes, or cardiovascular disease. Laboratory investigations revealed low serum folate (0.7 ng/mL) and elevated serum homocysteine (18.81 µmol/L). Neuroimaging demonstrated ischemic changes in the posterior left basal ganglia. Thrombophilia screening, autoimmune markers, and cardiac evaluations were unremarkable. The patient received intravenous thrombolysis with tissue plasminogen activator (tPA), followed by folate and vitamin B12 supplementation, antiplatelet therapy, and statins. He showed marked neurological improvement with near-complete recovery within five days and further resolution at follow-up.

Discussion: This case underscores the role of folate deficiency-induced hyperhomocysteinemia as an independent risk factor for ischemic stroke in young patients. Elevated homocysteine promotes endothelial dysfunction, oxidative stress, and vascular smooth muscle proliferation, contributing to thrombotic and atherosclerotic events. In regions with high prevalence of nutritional deficiencies, early recognition and correction of folate deficiency may serve as a cost-effective preventive strategy.

Conclusion: Folate deficiency can present as a hidden but modifiable cause of ischemic stroke in young patients lacking conventional risk factors. Routine assessment of homocysteine and folate levels should be considered in cryptogenic stroke cases, with timely supplementation serving as both therapeutic and preventive intervention.

Keywords: Stroke, Folate deficiency, Hyperhomocysteinemia, Young adults, Ischemic stroke.

INTRODUCTION

Stroke is the second leading cause of death globally and a major contributor to long-term disability. It is commonly linked to modifiable risk factors (hypertension, diabetes, smoking, diet, and physical inactivity) and non-modifiable factors (age, sex, family history, and ethnicity)[1]. However, strokes can occur in individuals without these conventional risk factors, posing diagnostic and therapeutic challenges. The prevalence of stroke is higher in low- and middle-income countries, which account for 70% of strokes, 87% of stroke-related deaths, and most disability-adjusted life years lost[2]. Though rare, low folate levels have been identified as an independent risk factor

for cerebrovascular events. Studies in Pakistan found a significant association between hyperhomocysteinemia and ischemic stroke, with 68% of patients exhibiting elevated homocysteine levels above 13.0 µmol/L, and a mean level of 15.8 ±4.2 µmol/L [3].

Homocysteine (Hcy), a sulfur-containing amino acid, plays a crucial role in methionine and cysteine metabolism[4]. Elevated Hcy levels can result from genetic enzyme deficiencies, vitamin B6, B9 (folate), and B12 deficiencies, chronic renal or hepatic failure, and certain medications.

This report presents the case of an 18-year-old male who experienced a sudden ischemic stroke caused by folate deficiency-induced hyperhomocysteinemia.

CASE PRESENTATION

An 18-year-old male presented to the ER with sudden right-sided weakness, facial droop, and slurred speech, without seizures, vomiting, headache, blurred vision, or relevant medical/family history. He denied smoking, hypertension, diabetes, drug abuse, recent surgery, or heart disease. On examination, he was alert, oriented, and cognitively intact, with slurred speech, GCS 15/15, and preserved gag reflex. Cranial nerve exam revealed left facial deviation; other cranial nerves were normal. Muscle tone, bulk, and nutrition were unremarkable. Strength was 5/5 on the left and 1/5 on the right. Reflexes were brisk on the right with an extensor plantar response; left-side reflexes were normal. Sensation and coordination were intact. Respiratory, cardiovascular, and abdominal exams were normal. Random blood glucose was 137 mg/dL, and no edema or rashes were noted. Vitals included pulse 72 bpm, BP 110/75 mmHg, and SpO_2 97%. NIHSS score was 10, and TPA (0.9 mg/kg) was administered with close monitoring.

Laboratory tests (Supplemental Table 1) revealed normal coagulation, HbA1C, lipid profile, liver/renal function, CRP, serum electrolytes, and vitamin B12. Anti-HCV and HIV were non-reactive. Normal antithrombin III and protein C levels ruled out thrombophilia, and normal anticardiolipin antibodies and lupus anticoagulant excluded antiphospholipid syndrome. Hemoglobin electrophoresis was normal, excluding hemoglobinopathies. Low serum folate (0.7 ng/mL) and elevated homocysteine (18.81 µmol/L) indicated potential stroke risk from hyperhomocysteinemia. The patient had no signs of other hyperhomocysteinemia-related conditions, such as osteoporosis or renal failure[5]. Elevated homocysteine is an established independent risk factor for cardiovascular and cerebrovascular disease[6,7], and has also been linked to increased fracture risk[8].

A CT scan prior to TPA excluded intracranial hemorrhage, and a follow-up CT 24 hours later showed no abnormalities. Brain MRI with diffusion-weighted imaging (DWI) revealed ischemic changes in the posterior left basal ganglia (Supplemental Figure 1). Cardiac workup included an ECG showing left ventricular hypertrophy (Sokolow-Lyon criteria; Supplemental Figure 2) and transthoracic echocardiography with normal left ventricular function (ejection fraction 60%) and no significant valvular disease (Supplemental Figure 3). Holter monitoring (Supplemental Figure 4) and carotid Doppler studies were unremarkable. The patient was started on rosuvastatin 10 mg nightly, Disprin 300 mg daily (24 hours post-TPA), and Iberet Folic 500 mg daily for folate/iron deficiency anemia, along with Syrup Cremaffin for constipation. Limb physiotherapy was initiated, and the family was counseled on the diagnosis and treatment plan. By day 5, the patient showed near complete recovery (5/5) in the right limbs and minimal dysarthria, with an NIHSS score of 4 at discharge. At the three-week follow-up, Disprin was replaced with clopidogrel for secondary prevention, and rosuvastatin, Iberet Folic, and methylcobalamin therapy were continued. The patient was referred to gastroenterology for hepatitis B management.

Table 1: Laboratory Values of the Patient

Parameter	Reference Range	Result
Hemoglobin	14–18 g/dL	9.5 g/dL
Mean Corpuscular Volume (MCV)	77–93 fL	65.9 fL
Mean Corpuscular Hemoglobin (MCH)	29–32 pg	18.5 pg
Mean Corpuscular Hemoglobin Concentration (MCHC)	31–35 g/dL	28.1 g/dL
Platelet Count	150–450 $\times 10^3/\mu L$	608 $\times 10^3/\mu L$
Serum Folate	3.10–20.50 ng/mL	0.7 ng/mL
Serum Homocysteine	<15 µmol/L	18.81 µmol/L
Serum Ferritin (males)	21–274.66 ng/mL	4.01 ng/mL
Anti-Cardiolipin Antibody (IgG)	Negative <10 GPL U/mL; Borderline 10–20; Positive >20	<0.5 GPL U/mL
Anti-Cardiolipin Antibody (IgM)	Negative <10 MPL U/mL; Positive ≥10	3.5 MPL U/mL
Lupus Anticoagulant	31.00–44.00 seconds	34.4 seconds

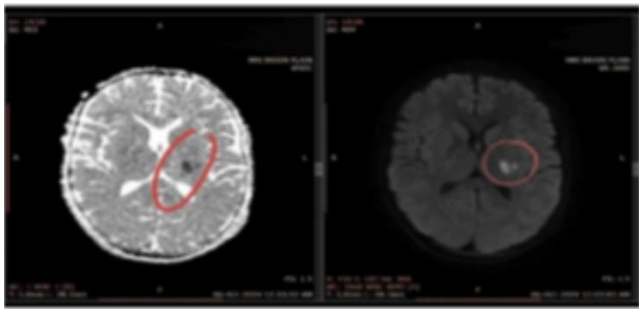

Figure 1: MRI brain shows areas of infarct in red markings. ADC image on right and DWI image of brain on left

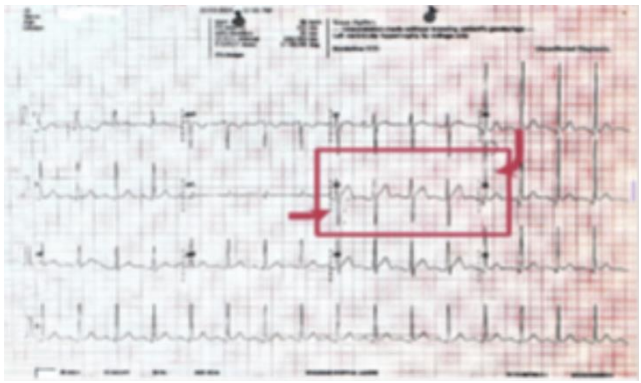

Figure 2: Shows LVH in lead V2 and V5

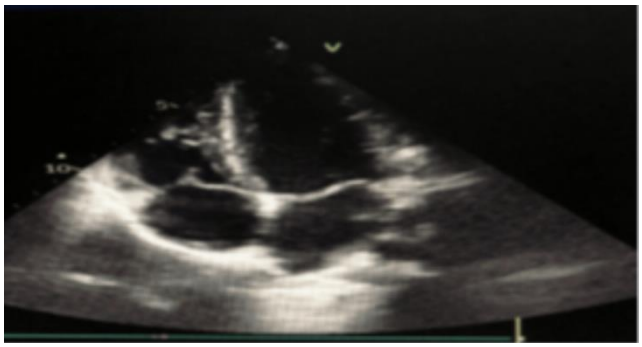

Figure 3: Shows Transthoracic echocardiograph

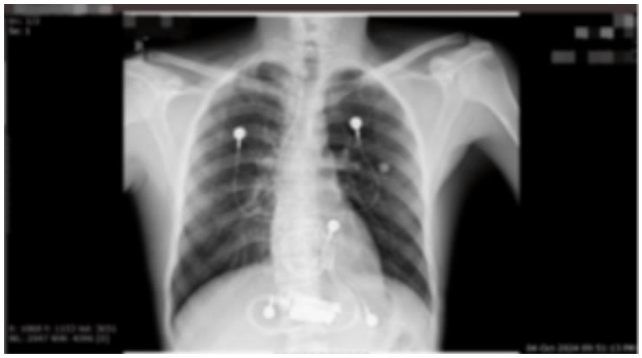

Figure 4: Shows Chest Xray with holter monitoring

DISCUSSION

Stroke is the leading cause of death and disability globally[6]. The number of new strokes has increased by twofold over the past three decades, with over 795,000 reported per year. On average, one person dies from a stroke every 3 min and 30 s[7]. Despite advancements in treatment, stroke survivors often experience high rates of disability, requiring long-term care and rehabilitation. Thus, primary prevention of stroke is crucial[6,7].

Among preventive strategies, homocysteine (Hcy)-lowering therapies have gained interest, as elevated Hcy levels are associated with increased stroke risk[8–10]. Folic acid, a key regulator in Hcy metabolism, is vital in preventing Hcy accumulation[11]. While the effectiveness of folic acid in stroke prevention has been debated, recent studies suggest that both dietary folate and supplements can reduce stroke risk[10,11]. However, the role of folic acid in primary stroke prevention remains unclear[9].

We present a case of a young male with no traditional stroke risk factors, such as smoking, hypertension, or diabetes, who experienced acute neurological deficits. His normal antithrombin III and protein C levels excluded thrombophilia, prompting exploration of other etiologies. Non-contrast CT initially showed no abnormalities, but MRI revealed ischemic changes in the MCA territory. Laboratory results indicated elevated homocysteine and iron deficiency anemia, suggesting a metabolic component to the stroke[3,5].

Although the patient's elevated homocysteine levels may have contributed to the stroke, he did not exhibit typical signs of folate deficiency, such as dietary inadequacies or gastrointestinal symptoms. Furthermore, he had no history of medications known to deplete folate, such as phenytoin or methotrexate[5,11]. This case underscores the importance of recognizing that elevated homocysteine can occur without obvious signs of folate deficiency, necessitating further investigation into potential underlying causes and appropriate management strategies[8–10].

CONLUSION

In conclusion, this case underscores the need for a comprehensive approach to young stroke patients, focusing on both immediate treatment and long-term prevention. Regular follow-up is essential for monitoring progress and adjusting treatment. Increasing dietary folate and supplementing with folic acid, vitamin B6, and B12 can lower homocysteine levels, potentially preventing atherosclerotic disease. This report highlights the importance of recognizing low folate as a risk factor for

elevated homocysteine and stroke in younger individuals, emphasizing the need for awareness and better prevention strategies.

DECLARATION

Ethics Statement

This study involves human participants and was conducted in accordance with the hospital's standard protocol for case reports. As a retrospective study, it was conducted without experimental interventions or deviations from standard medical care. According to the hospital's protocol, formal ethics review is not required for case reports of this nature. Informed consent was obtained from the patient, and all efforts were made to ensure patient anonymity and maintain confidentiality in strict compliance with ethical publishing standards. Due to the retrospective nature of the case report, no formal ethics committee approval letter was sought or provided, as it was not necessary under the hospital's protocol.

Competing Interest Statement

No competing interest

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Nil

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