Original Research Paper

Volume - 16 | Issue - 09 | September - 2026 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Medicine

TRANSIENT ISCHAEMIC ATTACK ASSOCIATED WITH SEVERE HYPERHOMOCYSTEINEMIA IN A TEENAGE BOY: A RARE CASE REPORT

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ABSTRACT **Background:** Hyperhomocysteinemia is a potentially modifiable vascular risk factor associated with arterial and venous thrombotic disease, including cerebrovascular events. Although its association with ischaemic stroke has been described in adults and paediatric stroke cohorts, clinically significant hyperhomocysteinemia presenting as a transient neurological event in an otherwise healthy adolescent is uncommon. **Case Presentation:** A 14-year-old boy with a remote history of febrile seizure presented with sudden-onset weakness involving all four limbs associated with slurring of speech. The episode lasted approximately 30 minutes and resolved completely before arrival at the hospital. Neurological examination following the event was normal. Routine laboratory investigations were unremarkable. Magnetic resonance imaging of the brain with diffusion-weighted imaging showed no acute infarction, while magnetic resonance angiography of the intracranial and extracranial vessels was normal. Electrocardiography and two-dimensional echocardiography did not reveal a cardiac source of embolism. Autoimmune and antiphospholipid antibody screening was negative, and protein C, protein S and fibrinogen were within normal limits. Serum homocysteine was markedly elevated at >50 µmol/L. The patient was treated with aspirin and vitamin supplementation with folic acid, vitamin B6 and vitamin B12. He remained neurologically intact during hospitalisation and was asymptomatic at 6-month follow-up, with improvement in plasma homocysteine levels. **Conclusion:** Severe hyperhomocysteinemia should be considered among the potentially treatable metabolic and vascular risk factors in adolescents presenting with unexplained transient neurological deficits. Early recognition and correction of associated vitamin deficiencies or inherited metabolic abnormalities may help reduce the risk of recurrent cerebrovascular events.

KEYWORDS : Hyperhomocysteinemia; transient ischaemic attack; adolescent; paediatric stroke; homocysteine; folic acid; vitamin B12

INTRODUCTION

Cerebrovascular disease is uncommon in children and adolescents, with an estimated combined incidence of approximately 2.7 per 100,000 children per year. The aetiological spectrum of paediatric stroke differs considerably from that of adults and includes arteriopathies, cardiac disorders, infections, thrombophilic conditions and inherited metabolic disorders. A substantial proportion of paediatric cerebrovascular events remain unexplained despite extensive investigation.

Homocysteine is a sulphur-containing amino acid formed during methionine metabolism and has been investigated as an independent vascular risk factor. Elevated homocysteine may contribute to endothelial dysfunction, oxidative stress, impaired nitric oxide activity and a prothrombotic state. Hyperhomocysteinemia may result from nutritional deficiencies of folate, vitamin B12 or vitamin B6, renal dysfunction, certain medications, or inherited abnormalities of homocysteine metabolism, including methylenetetrahydrofolate reductase (MTHFR) and cystathionine beta-synthase (CBS) abnormalities.

Paediatric studies have reported an association between elevated homocysteine and childhood ischaemic stroke. In a case-control study of children with ischaemic stroke, plasma homocysteine levels were higher in affected children than controls, and elevated levels were associated with increased odds of ischaemic stroke.[1] Other paediatric studies have also reported increased homocysteine concentrations in children with stroke, although the relationship between MTHFR polymorphisms and cerebrovascular events has been inconsistent.[2]

We report a 14-year-old boy who presented with a transient episode of bilateral limb weakness and dysarthria and was found to have severe hyperhomocysteinemia after an extensive evaluation for alternative vascular, cardiac, autoimmune and thrombophilic causes.

Case Presentation

A 14-year-old boy presented to the emergency department with sudden-onset weakness involving both upper and lower limbs, associated with slurring of speech. The neurological symptoms lasted approximately 30 minutes and resolved completely before arrival at the hospital.

The patient had a remote history of a febrile seizure during early childhood. There was no history of trauma, headache, loss of consciousness, fever, similar previous episodes or known chronic medical illness.

On arrival, the patient was conscious, alert and oriented. His vital signs were stable. General physical examination was unremarkable. Neurological examination revealed no residual motor, sensory, cranial nerve or cerebellar deficit. Cardiovascular and respiratory examinations were normal.

Initial laboratory investigations, including complete blood count, blood glucose, renal function, liver function and serum electrolytes, were within normal limits. Serum calcium and magnesium were also normal.

Magnetic resonance imaging of the brain, including diffusion-weighted sequences, showed no evidence of acute cerebral infarction. Magnetic resonance angiography of the intracranial and extracranial vessels was normal, with no evidence of significant stenosis, occlusion or arterial dissection.

Cardiac evaluation, including electrocardiography and two-dimensional echocardiography, did not identify a potential cardioembolic source. Autoimmune screening and antiphospholipid antibody testing were negative. Protein C, protein S and fibrinogen levels were within normal limits.

Further metabolic evaluation revealed a markedly elevated serum/plasma homocysteine concentration of >50 µmol/L, compared with the laboratory reference range of approximately 5–15 µmol/L.

Based on the transient neurological presentation, absence of acute infarction on diffusion-weighted MRI and extensive exclusion of alternative vascular, cardiac, autoimmune and thrombophilic causes, the episode was considered clinically consistent with a transient ischaemic event in the setting of severe hyperhomocysteinemia.

Table 1. Summary of Clinical Presentation, Investigations, Treatment and Outcome

Parameter	Finding
Age/Sex	14-year-old male
Presenting complaint	Sudden-onset weakness of both upper and lower limbs with slurring of speech
Duration	Approximately 30 minutes
Outcome of episode	Complete spontaneous resolution before hospital arrival
Past history	Febrile seizure in early childhood

Associated features	No trauma, headache or loss of consciousness
Neurological examination	Normal after resolution of episode; no residual deficit
Routine investigations	Within normal limits
Serum homocysteine	>50 µmol/L (markedly elevated)
MRI brain with DWI	No acute infarction
MRA intracranial /extracranial vessels	Normal
Cardiac evaluation	ECG and 2D echocardiography normal
Autoimmune/thrombophilia evaluation	Autoimmune and antiphospholipid screens negative; protein C, protein S and fibrinogen normal
Serum calcium/magnesium	Within normal limits
Treatment	Aspirin 75 mg once daily; folic acid 5 mg once daily; vitamin B6 and vitamin B12 supplementation
Hospital course	Neurologically intact; discharged stable
6-month follow-up	Asymptomatic; repeat homocysteine improved

Differential Diagnosis

The transient and completely reversible neurological deficit in this adolescent required consideration of several differential diagnoses, including transient ischaemic attack, focal seizure with postictal paresis, hemiplegic migraine, cardioembolic disease, thrombophilia, cerebral vasculitis, arterial dissection and metabolic or toxic disorders. Focal seizure with postictal paresis was considered because of the patient's remote history of febrile seizure; however, there was no witnessed seizure, loss of consciousness or other definite ictal manifestation during the current episode. Hemiplegic migraine was also considered, although there was no associated headache or migrainous history. MRI with diffusion-weighted imaging did not demonstrate acute infarction, while intracranial and extracranial MRA did not show significant vascular stenosis, occlusion or dissection. Cardiac evaluation was unrevealing. Autoimmune and antiphospholipid testing was negative, and protein C, protein S and fibrinogen were normal. These findings, together with the marked elevation of homocysteine, supported hyperhomocysteinemia-associated transient cerebral ischaemia as the most likely diagnosis.

Treatment and Outcome

The patient received aspirin 75 mg once daily and vitamin supplementation with folic acid 5 mg once daily, vitamin B6 and vitamin B12. He remained neurologically intact throughout the hospital stay and was discharged in stable condition.

At 6-month follow-up, there was no recurrence of weakness, dysarthria or other neurological symptoms. Repeat plasma homocysteine demonstrated improvement compared with the initial level.

DISCUSSION

This case highlights severe hyperhomocysteinemia as a potentially treatable vascular risk factor in an adolescent presenting with a transient neurological event.

The association between elevated homocysteine and cerebrovascular disease has been described in both adult and paediatric populations. In children with ischaemic stroke, Sirachainan et al. found higher plasma homocysteine levels compared with controls and reported increased odds of ischaemic stroke among children with elevated homocysteine.[1] Cardo et al. similarly reported increased homocysteine concentrations in children with stroke and demonstrated relationships between homocysteine and folate and vitamin B12 concentrations.[2] These observations suggest that disturbances in homocysteine metabolism may contribute to cerebrovascular risk during childhood and adolescence.

A previously published case report described a 13-year-old girl with recurrent episodes of hemiplegia associated with hyperhomo cysteinemia, with improvement following folic acid, vitamin B12 and vitamin B6 supplementation.[3] The present case differs in that the patient was a teenage boy who presented with transient bilateral upper- and lower-limb weakness and dysarthria, with complete resolution and no acute infarction on diffusion-weighted MRI.

The bilateral distribution of symptoms is noteworthy. A conventional TIA caused by a single arterial territory would more commonly produce unilateral or focal deficits. Bilateral limb involvement may indicate involvement of multiple vascular territories or a mechanism that cannot be demonstrated on conventional angiography. It also raises the possibility of a seizure-related or migraine-related mimic. Therefore, the diagnosis should be interpreted in the context of the clinical presentation and extensive negative investigations rather than being considered definitive proof of a direct causal relationship between hyperhomocysteinemia and the episode.

The patient's homocysteine concentration of >50 µmol/L represents marked elevation and warrants evaluation for potentially reversible and inherited causes. Nutritional deficiency of folate, vitamin B12 or vitamin B6 should be assessed. In a young patient with substantial elevation, inherited disorders of homocysteine metabolism should also be considered. Severe hyperhomocysteinemia may occur in CBS deficiency, which has been associated with premature cerebrovascular disease and arterial thrombosis.4

MTHFR variants have also been investigated in relation to paediatric cerebrovascular disease. Cardo et al. reported increased prevalence of hyperhomocysteinemia and MTHFR C677T polymorphism among children with stroke, although the relationship between genotype and homocysteine elevation has not been consistent.[2] These observations support consideration of metabolic and genetic evaluation in selected young patients with unexplained cerebrovascular events.

In the present case, correction of hyperhomocysteinemia with folate and vitamin supplementation was followed by biochemical improvement and absence of recurrent neurological symptoms over 6 months. However, the clinical improvement cannot by itself establish causality because antiplatelet therapy and spontaneous resolution of the initial event may also have contributed.

The case therefore emphasises two important clinical points. First, hyperhomocysteinemia is a potentially modifiable abnormality that may be overlooked during evaluation of cerebrovascular events in young individuals. Second, a markedly elevated homocysteine level in an adolescent should prompt investigation for nutritional deficiencies and, when clinically appropriate, inherited disorders of homocysteine metabolism.

CONCLUSION

Severe hyperhomocysteinemia should be considered in the evaluation of adolescents presenting with unexplained transient neurological deficits, particularly when conventional vascular, cardiac, autoimmune and thrombophilic investigations are unrevealing. Measurement of plasma homocysteine may identify a potentially treatable metabolic abnormality. Early correction of nutritional deficiencies and appropriate evaluation for inherited disorders may help reduce future cerebrovascular risk.

Abbreviations

TIA – Transient ischaemic attack; MRI – Magnetic resonance imaging; DWI – Diffusion-weighted imaging; MRA – Magnetic resonance angiography; ECG – Electrocardiography; MTHFR – Methylenetetrahydrofolate reductase; CBS – Cystathionine beta-synthase.

Declarations

Patient Consent

Written informed consent for publication of the case report and associated clinical information was obtained from the patient's parent/guardian. Assent from the adolescent patient was obtained where applicable. Documentation of consent is available and will be provided to the journal if required.

Ethics Approval: Case reports at the authors' institution are handled per institutional policy.
Conflict of Interest: The authors declare that they have no conflict of interest.
Funding: No external funding was received for this case report.

Authors' Contributions: Karuna Tayade: Conceptualisation, clinical data collection, literature review and manuscript preparation. Chinmay Gadhave: Clinical data interpretation, literature review and critical revision of the manuscript. Both authors approved the final version of the manuscript.

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