Objective: To report new manifestations of cerebral folate deficiency, a rare metabolic autoimmune syndrome, in an adult.

Design: Case report.

Setting: University teaching hospital.

Patient: A 58-year-old woman with progressive memory loss and myoclonus presented for medical attention. Results of cerebral spinal fluid analysis showed low levels of tetrahydrobiopterin and 5-methyltetrahydrofolate. The patient’s serum folate level was normal. Serum contained folate receptor 1 blocking and binding antibodies.

Results: The patient was treated successfully with folinic acid supplementation, and after 6 months of treatment, clinical symptoms had resolved.

Conclusions: To our knowledge, we report the first case of adult-onset cerebral folate deficiency. Furthermore, this condition could represent a treatable form of early-onset dementia.


Typical autoimmune cerebral folate deficiency is characterized by normal early development followed by abrupt neurological regression. At approximately 4 months, affected children develop marked irritability, decelerated head growth, psychomotor retardation, ataxia, spasticity, dyskinesia (choreoathetosis and ballismus), visual loss, hearing loss, and myoclonic epilepsy.

REPORT OF A CASE

A 58-year-old woman presented to the neurology clinic at The University of Texas at Houston, with progressive memory loss and myoclonus. The myoclonus consisted of brief jerks to the arms and legs that did not result in disability. She had a history of rheumatoid arthritis and migraine headaches. On physical examination, no neurological deficits other than mild myoclonus and impairment of short-term recall (formal neurocognitive testing was not performed) were noted. Results of cerebrospinal fluid (CSF) analysis showed low levels of tetrahydrobiopterin (8 nmol/L; reference, 10-30 nmol/L) and 5-methyltetrahydrofolate (29 nmol/L; reference, 40-120 nmol/L). The patient’s serum folate level was normal (20.4 ng/mL; reference, >5.4 ng/mL [to convert to nanomoles per liter, multiply by 2.266]). Serum contained a folate receptor 1–blocking antibody titer of 0.41 pmol/mL (reference, <0.2 mL/mL) and an folate receptor 1–binding antibody titer of 0.81 ML IgG/mL (reference, <0.5 ML IgG/mL).

Our patient was treated successfully with folinic acid (25 mg/d), a stable form of metabolically active reduced folate that can access the CSF by the alternate folate carrier.1 After 6 months of treatment, a second CSF 5-methyltetrahydrofolate level was 68 nmol/L (reference, 40-120 nmol/L), and clinical symptoms had resolved.

COMMENT

Folate is essential for the formation of biogenic amines and pterins in the central nervous system. Folate deficiency produces a variety of neurologic symptoms, including neuropsychiatric disturbances and movement disorders. In healthy adults, CSF folate levels do not decline with age,1 but CSF folate levels have been found to be lower in patients with late-onset Alzheimer disease than in age-matched control subjects.1
Folate is absorbed into the bloodstream via the gastrointestinal tract. In the bloodstream, folate binds to the folate receptor 1 on the basolateral endothelial surface of the choroid plexus. Through receptor-mediated endocytosis, folate is then transported across the blood-brain barrier into the CSF. Binding of the folate receptor 1 autoantibody to this receptor blocks the ability of the receptor to bind and transport folate.2

Classic autoimmune cerebral folate deficiency is characterized by normal early development followed by abrupt neurological regression. At approximately 4 months, children develop marked irritability, decelerated head growth, psychomotor retardation, ataxia, spasticity, dyskinesia (choreoathetosis and ballismus), visual loss, hearing loss, and myoclonic epilepsy.3,4 Treatment is with reduced folate in the form of folinic acid. Dose is titrated to maintain normal CSF 5-methyltetrahydrofolate levels. The optimal length of treatment is unknown.

A recent case report described a 15-year-old girl with cerebral folate deficiency and rheumatoid arthritis and no history of developmental abnormalities.5 The current case reported herein further defines the syndrome of autoimmune cerebral folate deficiency to include adult onset presenting with symptoms of dementia and myoclonus. This case highlights the importance for clinicians to consider CSF analysis, including 5-methyltetrahydrofolate levels, in all patients with a history of autoimmune disease and dementia.

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REFERENCES