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Original Research Paper

General Medicine

REVERSIBLE ENCEPHALOPATHY CAUSING DIAGNOSTIC DILEMMA :A CASE REPORT

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ABSTRACT Encephalopathy is a presentation of various disorders ranging from infections , intoxications ,nutrient deficiencies ,metabolic derangements and other causes .Folate deficiency presents with both haematologic and non haematologic manifestations .Unlike Vitamin B12 deficiency which occurs in vegetarians ,folate deficiency may occur in both vegetarians and persons on mixed diet as folate is found in green leafy vegetables ,unlike vitamin B12. Folate deficiency may present with megaloblastic anaemia and is often associated with anti folate medications .It may rarely present with encephalopathy as the predominant clinical feature .The case presented here is an elderly patient,79 years of age ,who presented with altered sensorium for 14 days without any history of fever .After ruling out other causes of encephalopathy ,work up of mild anaemia led to detection of low levels of serum and RBC folate with normal Vitamin B12 levels .The patient responded to oral Folate therapy with improvement of neurological manifestations within 2 weeks and encephalopathy on EEG also resolved with folate therapy ,thus establishing the diagnosis. The importance of this case lies in the fact that folate deficiency may rarely cause encephalopathy with reversal of manifestations following folate therapy ,thus avoiding unnecessary investigations and treatment.

KEYWORDS : Folate deficiency, Encephalopathy, RBC folate, reversible

CASE REPORT

A 79 years old non diabetic ,non hypertensive,non addict male presented with altered sensorium for 14 days without any definite history of fever ,vomiting ,loose motions or involuntary movements .The patient was on a vegetarian diet with history of poor food intake for about 2 months. The patient had restricted mobility due to old age without any history of trauma .There was no history of any medications ,no contact with pulmonary tuberculosis, nor was there any weakness of any side of the body.

On examination, the patient was conscious, but non cooperative with intermittent episodes of psychosis .He was haemodynamically stable with normal body temperature ,respiratory rate .There was mild pallor without any oedema or icterus.

On examination of the Neurological system ,neck was supple with no signs of meningeal irritation .Plantar response was bilaterally extensor .Examination of other systems were unremarkable with no organomegaly.

A provisional diagnosis of metabolic encephalopathy was made and blood was sent for CBC(Complete Blood Count),Random Blood Sugar(RBS), urea,creatinine, electrolytes, LFT, Ft4, TSH.Chest X Ray was done with ECG,2D Echocardiography with colour doppler and IVC collapsibility .CT Brain plain was done with EEG (Electroencephalogram). CBC revealed mild pallor with serum sodium of 131 m eq /l(mild hyponatremia). Urea ,creatinine ,potassium, magnesium ,LFT reports were unremarkable .Chest X ray ,ECG was normal with echocardiography showing mild concentric LVH with normal ejection fraction .CT Brain revealed age related cerebral atrophy with microangiopathic changes .EEG revealed encephalopathy .Serum Ammonia level was normal.

Patient was put on intravenous 0.9% Normal saline with injectable PPI , ondansetron ,Ceftriaxone with catheterisation and patient was put on air mattress .Patient was taking liquid diet orally and Ryle's tube sos was adviced with preventive measures being taken to avoid aspiration pneumonia .USG WA revealed cholelithiasis with grade 1 prostratomegaly .Procalcitonin was normal with unremarkable results of blood culture aerobic single hand and urine RE/CS .Thyroid profile was normal with reduced vitamin D3 levels and CRP was normal .Patient was given Vitamin D3 supplementation ,patient was not improving with the current treatment .Iron profile revealed mild iron deficiency with raised RDW ,reduced serum iron, increased TIBC and decreased transferrin saturation with low normal serum ferritin as patient had history of haemorrhoids .Vitamin B12,serum and RBC folate were sent and patient was given haloperidol drops sos for psychosis .Vitamin B12 level was normal with reduced serum folate of 4.51 ng/ml (5.9-24.8)and markedly reduced RBC folate of 82.2 ng/ml(366-1356).Urine spot sodium ,urine osmolality ,serum cortisol assay at 8 am were normal with normal levels of serum total and free PSA .Eye examination did not reveal papilledema and after normal INR blood reports CSF study revealed mildly elevated protein with 60 cells/mm3 and 90% lymphocytes .CSF ADA,CBNAAT,HSV 1 and 2 DNA PCR ,Indian ink preparation were negative .NCV of all 4 limbs was refused by patient party .MRI Brain revealed bilateral basal ganglia calcification with chronic lacunar infarct in bilateral ganglio capsular region with cerebral atrophy and chronic small vessel white matter ischaemic changes.(**Figure1**)

The patient started to improve with oral folate 5 mg once daily therapy and within 12 days of starting therapy ,the episodes of psychosis resolved and EEG was normal which was initially showing encephalopathy (**Figure 2,3**).The case was diagnosed as folate deficiency encephalopathy with normal serum homocysteine and methyl malonic acid levels .Intravenous fluid was stopped and patient was discharged on day 19 of hospital admission and was adviced follow up in

Haematology and Neurology department.

DISCUSSION

Folate is an important water soluble vitamin which is present in natural food like fruits ,green leafy vegetables and liver.[1,2]The synthesised form of folate is folic acid having a higher bio availability than natural folate .It is needed for forming several coenzymes in metabolic system for synthesis of purine ,pyrimidine and nucleotides and erythropoesis maintenance .[1]Tetrahydrofolate is the potent form of folic acid. Folic acid deficiency may be caused by inadequate intake ,heating during cooking and jejunal malabsorption. Achlorhydria causes poor folate absorption and medications like phenytoin, methotrexate ,sulfasalazine ,trimethoprim may cause deficiency .Folic acid deficiency may be due to vitamin B12 deficiency due to methionine synthase impairment causing trapping of folate and urinary excretion of folate .Alcoholism ,pregnancy ,haemolytic anaemia and dialysis also causes folate deficiency.

Loss of appetite is an important manifestation which was present in the case presented here .Folate deficiency presents with red beefy tongue and anaemia with macrocytosis on peripheral blood smear .About 25% of patients with folate responsive neuropsychiatric features do not have macrocytosis and anaemia(Bottiglieri et al.,1995)[3].The neurological features of folate deficiency are dementia ,depression, cognitive impairment ,peripheral neuropathy and subacute combined degeneration of the spinal cord .Dissociation is present between neurologic and haematological manifestations of folate deficiency .Improper folate administration in vitamin B12 deficiency may lead to neurological followed by haematological relapse .Decreased maternal folate intake leads to neural tube defects in offsprings.

Cerebral folate deficiency may cause encephalopathy with unknown aetiology ,but a decrease in folate receptor autoantibodies by adopting milk free diet was seen.[4]Folate deficiency may cause acute or subacute encephalopathy directly or indirectly by reducing thiamine malabsorption.[5,6] Neuropathy due to folate deficiency alone is axonal with sensory involvement of lower limbs and a slower progression than thiamine deficiency neuropathy.[7]Clinical responses are slow over weeks to months due to efficient blood brain barrier.[3] The case presented here had marked reduction of RBC folate with reversal of neurological manifestations following folate therapy.

CONCLUSION

Folate deficiency may cause haematological , neurological and other manifestations .There is often a dissociation of haematological and neurological manifestations with diagnostic challenge .Clinicians must consider folate deficiency as an uncommon cause of encephalopathy ,even in non alcoholics as folate supplementation leads to reversal of symptoms.

Conflicts Of Interest-None
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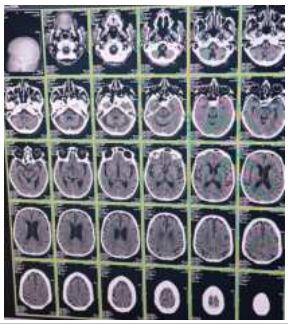

Figure1: MRI Brain Showing Chronic Lacunar Infarct With Cerebral Atrophy And Microangiopathy

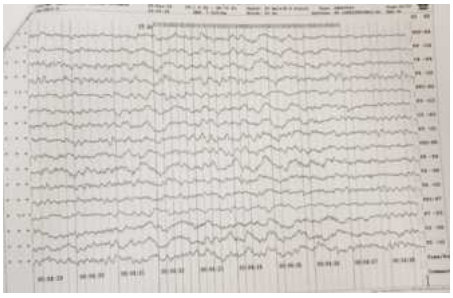

Figure 2: Abnormal EEG Showing Encephalopathy

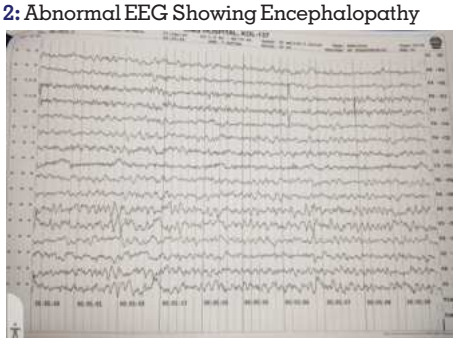

Figure 3: Normal EEG Following Folate Therapy

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