LEUKOENCEPHALOPATHY RELATED TO PHENYTOIN IN A PATIENT WITH METHYLENETETRAHYDROFOLATE REDUCTASE C6777T POLYMORPHISM

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We report a patient with a heterozyous CT variant of MTHFR who developed leukoencephalopathy after phenytoin medication. A 36-year-old man was admitted to our hospital for progressive worsening of mental status over one week after phenytoin medication. The patient had been diagnosed with juvenile rheumatic arthritis and ankylosing spondylitis in his preteens and suffered recurrent convulsive seizures from the age of thirties. The patient had recurrent convulsive seizures after he stopped taking the medication and eventually had received treatment as an inpatient for status epilepticus and aspiration pneumonia three weeks before this admission. Phenytoin had been prescribed to control the seizures and the patient had been improved and discharged. The patient was stuporous on this admission and routine serum chemistry and complete blood counts were normal. MRI of the brain demonstrated new onset of extensive leukoencephalopathy which was prominent on FLAIR images. Sequence analysis of the MTHFR revealed compound heterozygous mutation for 677CT. Serum homocysteine level was within normal limits and serum folate level was decreased (4.21 ng/mL). The neurological status of the patient did not improved after discontinuing phenytoin. In individuals heterozygous for MTHFR C677T polymorphism, the enzyme activity is decreased to 60% of wild type activity of MTHFR. The patient developed subacute onset of mental deterioration and diffuse white matter lesions on MRI. It is probable that impaired folate metabolism and enhanced vulnerability of the CNS to the effect of phenytoin in our patient are related to the development of the leukoencephalopathy.