LETTER TO THE EDITOR

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Deferiprone Reduces Hemosiderin Deposition in Superficial Siderosis

Keywords: Superficial siderosis, ataxia, deferiprone

We reported with great interest a case of superficial siderosis treated with oral deferiprone for six months. A 59-year-old woman developed progressive ataxic gait for six years, along with tinnitus, hearing impairment, and scanning speech. She did not have a history of subarachnoid hemorrhage, traumatic brain injury, or spinal surgery. Her neurological examination showed

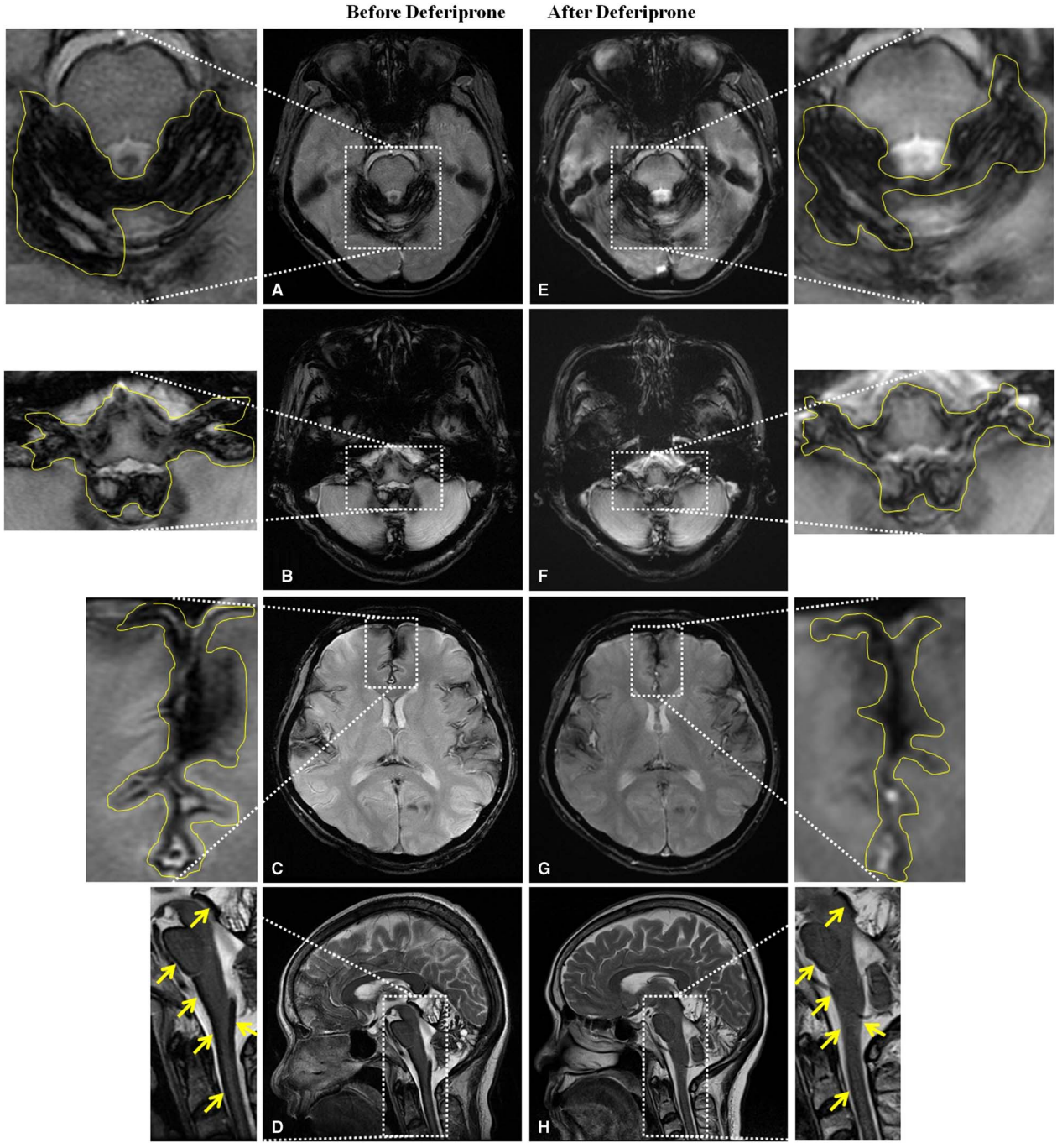

Figure 1: *The brain MRI showed hypointensity covering the brain surface on T2*GRE (A-C, E-G, axial view) and T2-wieghted (D, H, sagittal view) sequances before (A-D) and after (E-H) deferiprone treatment. Yellow outlines and arrows indicate the areas of iron deposition.*

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generalized hyper-reflexia, wide-based gait, and dysmetria and dysdiadochokinesia in four limbs. The eye movement examination showed smooth pursuit and normal saccade without nystagmus. The pure tone audiometry revealed sensorineural hearing impairment. The magnetic resonance imaging (MRI) showed widespread hypointensity on T2-wieghted and T2*GRE sequences, covering the surface of brainstem, cerebellum, sylvian fissure, and spinal cord (Figures 1A-D), without microbleeds in the brain parenchyma, consistent with a diagnosis of superficial siderosis. Serial MRI over the past 6 years revealed gradual increase of hemosiderin deposition on the brain surface.

She was treated with oral deferiprone 15mg/kg/day for six months. The Scale for the Assessment and Rating of Ataxia (SARA) was chosen to measure disease severity, with a total score ranging from 0 to 40; higher SARA scores reflected poor motor performance.[1] Her SARA improved from 13 to 10.5, especially in the domains of limb coordination (nose-finger test and heel-shin slide) and speech, which improved 1.5 and 1 point, respectively. Her deep tendon reflex remained generalized hyper-reflexia, and her hearing loss did not improve. No adverse effect was reported for deferiprone. The follow-up MRI revealed slight though visible reduction in hemosiderin deposition on the surface of the brainstem, cerebellum, and cortex on T2-wieghted and T2*GRE sequences (Figures 1E-H).

The toxicity from the iron breakdown products in superficial siderosis may induce glial cell and neuronal death, but no effective medical treatment has been established. Among three approved iron chelators for thalassemia, deferiprone has low molecular weight and lipophilicity to cross blood-brain barrier. Levy et al. reported a case of superficial siderosis whose follow-up MRI showed reduction of hemosiderin deposition on the brain surface, together with noticeable improvement in ataxia and hearing after 3 years of oral deferiprone (15 mg/kg/day),[2] suggesting that hemosiderin deposition and its neurotoxicity in the central nervous system may be reversible. The clinical improvement (2.5 points in SARA score) in our case indicated that even six-month, low dose, oral deferiprone could bring a noticeable benefit.

In an open pilot safety study conducted by Levy et al., the reduction of hemosiderin deposition was revealed in the follow-up MRI in four out of ten cases that received oral deferiprone 30 mg/kg/day for 90 days.[3] In our case, on the other hand, the hemosiderin reduction in MRI was visible after 180 days of treatment, suggesting that T2*GRE sequences of MRI is a sensitive marker to track therapeutic effects of deferiprone in about six months. A more quantitative measure of MRI of iron deposition might be required for future clinical trials.

Deferiprone has also been tested in neurodegeneration with brain iron accumulation at a dose of 30mg/kg/day in six patients, who reported no serious adverse events within four years.[4] In a six-month clinical trial of deferiprone for Friedreich ataxia, only one out of 72 patients experienced neutropenia at a dose of 20 mg/kg/day, which resolved soon after discontinuation of deferiprone.[5] The regular dosage of deferiprone in the treatment of thalassemia is 75 mg/kg/day, and common adverse effects include gastrointestinal discomfort, agranulocytosis, arthralgia, and abnormal liver enzymes. Thus the side effects of deferiprone may be dose-dependent, and oral deferiprone at a dose of 15 mg/kg/day is considered both safe and effective. Longer observation and clinical trials are warranted to confirm the therapeutic effects of deferiprone for superficial siderosis.

Disclosures

Pei-Hsin Kuo, Sheng-Han Kuo, and Raymond Lo do not have anything to disclose.

Statement of Authorship

Pei-Hsin Kuo: primary patient care, literature search, drafting the manuscript. Sheng-Han Kuo: critical revision of the manuscript. Raymond Y. Lo: study concept, critical revision of the manuscript.

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