



Ten years of iron chelation in a patient with superficial siderosis

Michael Levy¹

Received: 15 February 2019 / Accepted: 25 February 2019 / Published online: 4 March 2019
© Fondazione Società Italiana di Neurologia 2019

Keywords Superficial siderosis of the central nervous system · Deferiprone · Iron chelation · MRI brain · Hemosiderosis

Dear Dr. Federico,

Superficial siderosis (SS) is a rare neurodegenerative condition in which chronic bleeding into the cerebrospinal fluid leads to hemosiderosis around the brain and spinal cord [1]. Although it takes 10–30 years to become symptomatic depending on the degree of hemosiderosis and the individual sensitivity to the free iron damage, the typical course of disease is an insidious progressive hearing loss, ataxia, and myelopathy associated with hemosiderosis on the eighth cranial nerve, cerebellum, and spinal cord respectively [2].

In 2011, we published the first case of superficial siderosis that was treated with deferiprone, an iron chelator that easily crosses the blood-brain barrier, which demonstrated a reduction in hemosiderin deposition by MRI [3]. In two subsequent trials of 10 and 38 superficial siderosis patients using deferiprone for up to 2 years, we found that reduction in MRI hemosiderosis correlated with modest clinical benefit defined as a slowing of disease progression or improvement in a few cases [4, 5].

Our experience with deferiprone in superficial siderosis thus far had been limited by the availability of the drug in the USA as it was approved only 5 years ago. However, we recently had the opportunity to study a case of superficial siderosis in Belgium where the patient had been treated with deferiprone for 10 years. His history dated back 35 years when he suffered severe spinal cord trauma from a motorcycle accident that included a brachial plexus avulsion of the right arm with

subsequent denervation and atrophy. To treat the pain in his right arm, he underwent a dorsal root rhizotomy of the cervical ganglion 26 years later with good results. When this gentleman presented to the clinic at age 54, he complained of difficulty with hearing and walking that began 2 years prior. Neurological exam was notable for only mild ataxia on finger-to-nose testing but moderate sway on walking. He could not perform a tandem walk. A hearing test at the time confirmed hearing loss of approximately 10 dB in each ear. MRI showed extensive hemosiderosis of the brain and spinal cord consistent with superficial siderosis.

The patient started on deferiprone at a dose of 3 g per day divided into two daily doses. He continued on this regimen for 10 years. At year 4, he was told his MRI of the brain showed no change from baseline and he did not notice any clinical change at the time. Over the course of the next 6 years, he states that he has continued to slowly decline in function although the rate of decline may have been less more recently compared to prior. Audiometry testing between 2012 and 2017 showed essentially no change (Fig. 1). An MRI of his brain repeated after 10 years of deferiprone demonstrates markedly reduced hemosiderosis over nearly the entire brain including the cortex, brainstem, and cerebellum (Fig. 2).

This case provides a unique insight into using deferiprone for 10 years to effectively reduce hemosiderosis in a case of long-standing superficial siderosis.

✉ Michael Levy
mlevy11@mgh.harvard.edu

¹ Department of Neurology, Massachusetts General Hospital and Harvard Medical School, 15 Parkman St., Boston, MA 02114, USA

Fig. 1 Audiometry testing at four intervals between 2012 and 2017 shows essentially no change over this time period

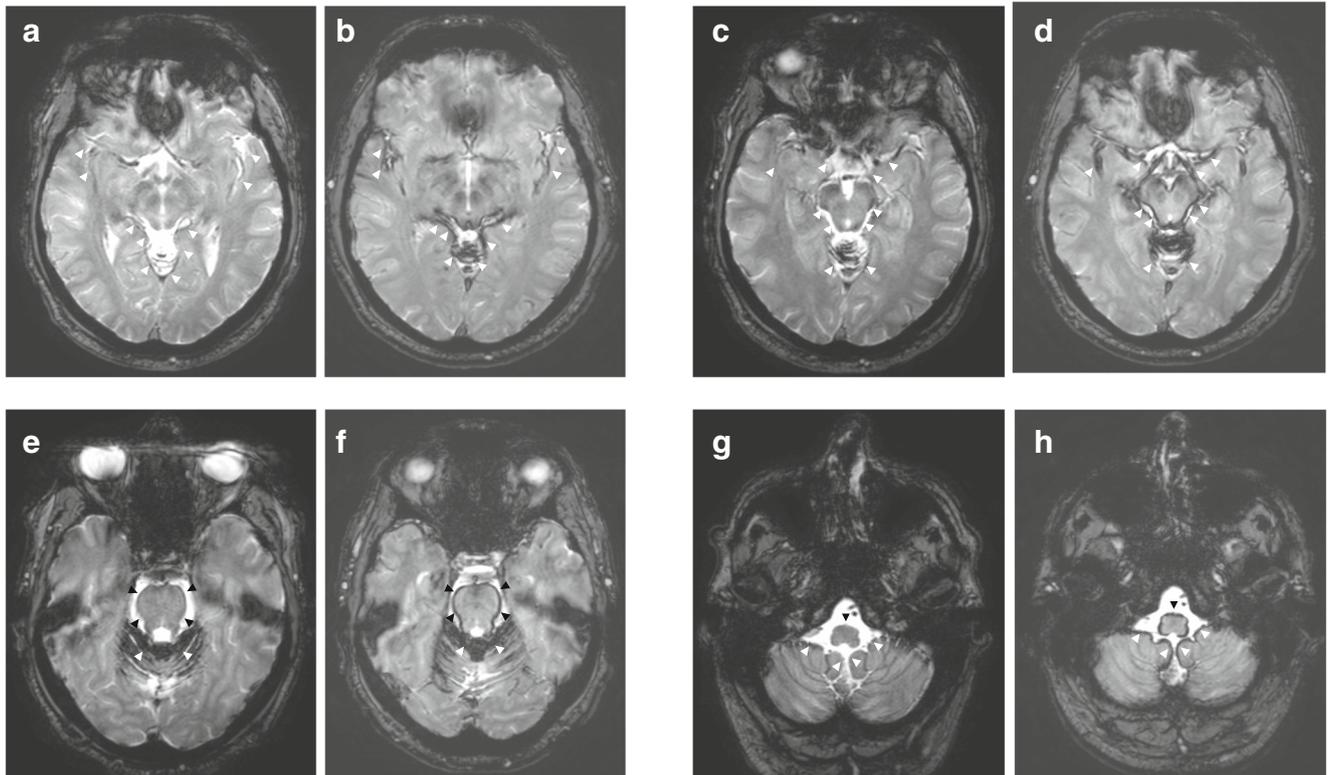
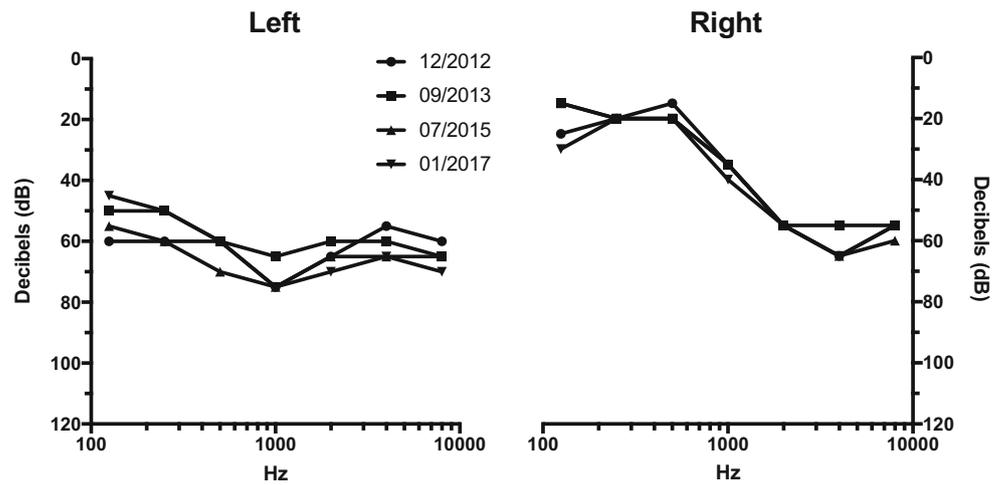


Fig. 2 **a–h** Susceptibility-weighted MRI comparing axial sections from 2009 to 2018. In each pair of images, the 2009 scan is on the right and the 2018 scan is on the left. Small white/black triangles point to the hemosiderosis deposition which shows up as black lines. In each pair of

figures, there is less hemosiderosis in the scan on the left (2018). In panels **e** and **f**, while there is reduced hemosiderosis around the brainstem (black triangles), there is no change in the hemosiderosis in the folia of the cerebellum (white triangles)

Compliance with ethical standards

Ethical considerations The patient provided informed consent to publish the details of his case.

Conflict of interest Dr. Levy previously received a research award from the manufacturer of Ferriprox (deferiprone), Apopharma Inc., to conduct a trial of deferiprone in superficial siderosis between 2014 and 2016.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Wilson D, Chatterjee F, Farmer SF, Rudge P, McCarron MO, Cowley P, Werring DJ (2017) Infratentorial superficial siderosis: classification, diagnostic criteria, and rational investigation pathway. *Ann Neurol* 81(3):333–343
2. Levy M, Turtzo C, Llinas RH (2007) Superficial siderosis: a case report and review of the literature. *Nat Clin Pract Neurol* 3(1):54–58 quiz 59
3. Levy M, Llinas RH (2011) Deferiprone reduces hemosiderin deposits in the brain of a patient with superficial siderosis. *AJNR Am J Neuroradiol* 32(1):E1–E2
4. Kessler RA, Li X, Schwartz K, Huang H, Mealy MA, Levy M (2018) Two-year observational study of deferiprone in superficial siderosis. *CNS Neurosci Ther* 24(3):187–192
5. Levy M, Llinas R (2012) Pilot safety trial of deferiprone in 10 subjects with superficial siderosis. *Stroke* 43(1):120–124