The Effects of Deferiprone in Superficial Siderosis: a case report

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Background

Superficial Siderosis (SS) is a rare neurodegenerative disease characterized by hemosiderin deposition on the pial surface of the brain and spinal cord. This condition is caused by recurrent hemorrhage in the subarachnoid space. The most common causes of the hemorrhage include trauma, vascular lesions, neurosurgical procedures, dural defect or tumor.
Ataxia, myelopathy and sensorineural hearing loss are the typical triad of the SS.
No real effective treatment for this condition have been reported. Surgical correction of the bleeding source should stop the progressive neural injury, although the source of hemorrhage is not detected in 50% of patients.
Deferiprone is the only iron chelator that can penetrate the blood brain barrier, actually approved for treatment of thalassemia major. However, some pilot trials of Deferiprone in patients with SS have been conducted, with positive results.

Methods

We report the case of a 51-old man with Superficial Siderosis, treated with Deferiprone. The patient had a 10-years history of progressive ataxo-spastic syndrome, bilateral sensorineural hearing loss with pulsatile tinnitus, hyposmia and urinary incontinence. He had history of severe traumatic brain injury about thirty years before symptoms.
MRI of the brain showed hemosiderin deposition (hypointensity on T2-weighted sequences) along the leptomeningeal surface, most markedly in posterior cranial fossa and along cranial nerves. MRI of the spinal cord showed superficial siderosis along all the spine surface and a cerebrospinal fluid collection detaching dura made along cervical spine. This dural defect was identified with the probable source of the bleeding. An attempt to surgically correct the defect had been made two years before starting Deferiprone, without clinical and MRI improvement.
The patient was treated with oral Deferiprone off-label for 6 months at 30 mg/kg/day, divided into 2 daily doses.
We followed him with periodic complete blood count, assessment of ferritin and liver enzymes levels to monitor side effects. We performed clinical examination, Ashworth Scale, International Co-Operative Ataxia Rating Scale and audiometry before and after six months of treatment.
MRI of the brain and spinal cord was also performed before and after therapy to evaluate changes in iron deposition.

Results

Six months later, the patient showed improvement in spasticity, coordination and Kinetic functions, in accordance with scale scores (table 1-2). Hyposmia decreased but urinary incontinence got worse.
The audiometry was unchanged (bilateral neurosensorial hearing loss, more severe on the right) although a subjective improvement in hearing.
Despite some clinical improvements, no considerable changes in haemosiderin deposition were observed at MRI performed after chelation therapy (Figure 1).
The patient didn't show side effects: the ferritin level, liver function and neutrophil counts remained in the normal range throughout the course of treatment.

Conclusions

Superficial siderosis is a neurodegenerative disease that progresses due to the irreversible neural damage caused by haemosiderin deposition. The progressive neurological decline is associated with an increase of haemosiderin deposition along the surface of the central nervous system,
Actually, surgery is the only possible treatment of the superficial siderosis, but the disease often progresses because the source of the bleeding isn't' identified or can't been corrected.
Deferiprone is the only iron chelator that can penetrate the blood brain barrier and it could be an effective medical treatment for SS.
In our case and in other trials, patients showed improvement in symptoms, without severe side effects. It could potentially slow the haemosiderin deposition and the course of the disease, although further studies are required to evaluate Deferiprone efficacy.
In the future, Deferiprone could be used as a therapeutic attempt for other neurodegenerative conditions secondary to iron deposition on the brain.

Table 1. Ashworth Scale

	Upper limbs	*Lower limbs*
Before drug	2/24	7/24
After drug	0/24	5/24

Table 1 showes the Ashworth Scale Score for spasticity before and after six months of treatment. The score pre-Deferiprone was 2/24 for upper limbs and 7/24 for lower limbs; the score post-Deferiprone was 0/24 for upper limbs and 5/24 for lower limbs. So, an improvement in spasticity was reported after therapy.

Table 2. International Ataxia Rating Scale

	Posture and Gait Score	**Kinetic Score (limb coordination)**	**Dysarthria Score**	***Oculomotor Movement Score***	***Total Ataxia Score***
Before drug	16/34	11/52	2/3	4/6	**33/100**
After Drug	17/34	8/52	1/3	3/6	**29/100**

The International Ataxia Rating Scale Scores before and after six months of treatment are compared in Table 2. The patient improved his posture, kinetic functions, dysartria and oculomotor movement. Total Ataxia Score showed a 4-point decrease after six months of tratment.

Before treatment **After treatment**

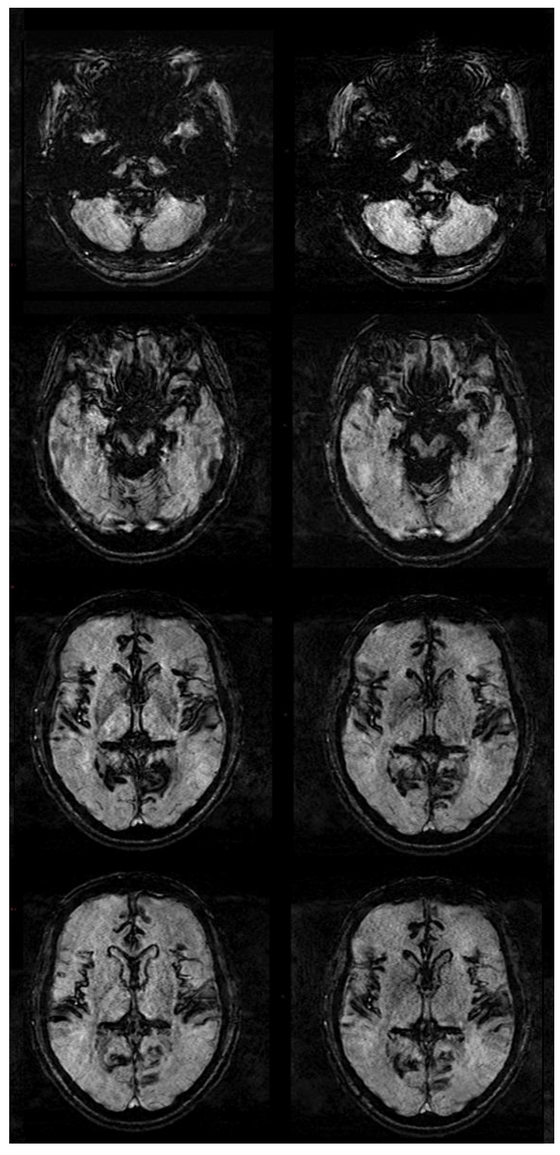

Figure 1. *At MR imaging, serial non consecutive susceptibility weighted imeges performed before (left column) and after Deferiprone (right column) didn't show significant changes.*

References

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