Superficial Siderosis of the Central Nervous System Secondary to Chronic Bleeding From a Lumbar Paraganglioma

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Abstract

Superficial Siderosis (SS) is a rare neurological condition which results from hemosiderin deposition on the leptomeninges, subpial and the ependymal surfaces of the central nervous system (CNS). Patients commonly present with the classic triad of hearing loss, cerebellar ataxia and pyramidal signs. We report clinical, radiological and pathological findings in a patient with SS due to chronic haemorrhages from a paraganglioma of cauda equina.

ABBREVIATIONS

SS: Superficial Siderosis; CNS: Central Nervous System; CSF: Cerebro-Spinal Fluid; ROS: Reactive Oxygen Species; TNF: Tumor Necrosis Factor

INTRODUCTION

Superficial siderosis (SS) is a rare, chronic and progressive neurological condition due to deposition of hemosiderin on the leptomeningial, subpial and the ependymal surfaces of the CNS [1]. SS is associated with repetitive, low-grade hemorrhages in to the cerebro-spinal fluid (CSF). There have been approximately 270 cases of SS reported in the literature from 1908 to 2006 [2]. The most common causes of bleeding were CNS tumors (21%), head and neck trauma (13%), Arterio-venous malformations (AVM) and aneurysms (9%), neurosurgery (7%) and brachial plexus injury (6%), as well as amyloid angiopathy and chronic subdural hematomas (3%) [2]. The vast majority of SS cases present with sensorineural hearing loss (95%), cerebellar ataxia (88%) and pyramidal signs such as tremor, muscle weakness, loss of muscle control, and paralysis (76%) [1,3]. The reported cases show preponderance towards males versus females, and the most common age of manifestation is in the sixth and seventh decades of life [2].

We present a unique patient with the classic clinical symptoms of SS, subsequently confirmed by MRI findings. Extensive investigation revealed a paraganglioma of the cauda equina as source of chronic bleeding.

CLINICAL HISTORY

A 73-year-old Caucasian male presented to the Hamilton General Hospital Emergency Room with confusion, slurred speech, lower extremity weakness and gait ataxia. According to the patient’s family, his symptoms began five years prior to this episode, when they noticed behavioral changes. He became aloof and introverted. He also complained of ‘ringing’ in his ears. An auditory examination at that time demonstrated hearing loss, for which he started wearing hearing aids. Subsequently, there was a progressive decline in his functional mobility and other activities of daily living.

Upon physical examination, the patient was uncooperative. He had a short attention span with brief moments where he demonstrated mental competence. A Folstein mini mental status exam revealed baseline cognitive decline most likely due to his dementia (13/30). The cranial nerves examination demonstrated bilateral hearing loss. He had lower extremity weakness (more pronounced on the right than on the left), hyper-reflexia and Babinski sign bilaterally. No sensory deficits were noted. Disdiadokokinesia, finger-nose and heel-shin dysmetria were present.

The patient had a past medical history of hypertension, cerebellar strokes, left ventricular ejection fraction of 46%, dyslipidemia, prostatic hyperplasia, and gastroesophageal reflux disease. He was retired after 33 years of working as steel plant worker and a truck driver.

An MRI of the head showed a diffuse, superficial hypointense
coating of the cerebral hemispheres and the cerebellum, as well
as significant atrophic and cavitary changes in the cerebellum
(Figure 1A and 1B). The thick, hypointense layer extended from
the cerebellar hemispheres to the rest of the brainstem and the
spinal cord (Figure 2A); based on these findings a diagnosis of
SS was made. An MRI of the spine showed a well-delineated
intradural 12 x 14 mm space-occupying lesion at the level
of L3-L4, displacing the lumbosacral roots. There was trace
enhancement post-gadolinium injection (Figure 2B and 2C). A
spinal angiogram showed no evidence of vascular malformations.

Due to the high likelihood of further deterioration of the
patient’s mobility from increasing leg weakness, the decision was
made to resect the tumor and eliminate the source of the bleeding.
Intraoperatively, the lesion was round, firm, encapsulated and
tethered to the roots of the cauda equina and filum terminale
(Figure 3). Careful microsurgical dissection allowed complete
removal of the tumor.

Microscopic examination revealed a monomorphic tumor
composed of epithelioid neoplastic cells strongly positive
for synaptophysin and chromogranin (Figure 4A-4C). The
tumor contained many hyalinized vessels with hemosiderin-
impregnated walls. The accumulation of hemosiderin in
numerous macrophages and tumor cells was most pronounced
in the subcapsular area at the tumour periphery, and associated
with focal deposits of hematidin (Figure 5). Electron microscopy
revealed osmiophilic intracellular bodies consistent with
siderosome formation in the chief cells (Figure 6).

**DISCUSSION**

There have been 17 case reports of SS associated with spinal
tumors, most often myxopapillary ependymomas [1,4]. SS
attributable to a spinal paraganglioma has only been described
in two case reports [4,5]. Paragangliomas are rare, benign, highly
vascular tumors of neural crest origin [6]. The slow subclonal
growth and rich vascularity of these tumors may explain the
progression of clinically undetectable bleeding to full-blown
SS in some patients. Previous reports on paragangliomas
associated with SS offered only limited descriptions of the
pathological changes, namely calcifications and ossifications,
without documenting the source of bleeding [4,5]. The massive
accumulation of hemosiderin in the tumor cells, macrophages,
vessel walls and connective tissues of the capsule, as well as the
subcapsular deposits of hematidin, leave no doubt about the
cause of SS in our patient.

SS of the CNS develops in patients with chronic, low-grade
hemorrhaging into the CSF. Under normal circumstances, the
heme is degraded by hemeoxygenase, and the released iron is
phagocytized and converted to ferritin, preventing oxidative
stress [7]. However, repetitive low-grade hemorrhages in the CNS
may overwhelm the neurons ability to generate hemeoxygenase.
The labile iron from hemosiderin is cytotoxic and triggers the
production of mitochondrion-driven reactive oxygen species
(ROS) which leads to lipid peroxidation, membrane dysfunction
and cell death [8]. The resulting inflammation also promotes the
activation of tumor necrosis factor (TNF), which in turn generates
more ROS [7]. These multiple mechanisms acting in concert are
most likely responsible for the irreversible neurological damage,
resulting in symptoms of SS.

SS of the CNS has been associated with cognitive impairment.
Dementia has been noted in 24% of the patients with SS [9]. Six
patients with confirmed diagnoses of SS exhibited impairments
in speech production, visual recall, and executive function, as well
as inappropriate social interactions [10]. Our patient’s cognitive
decline is most likely attributable to SS. He scored a 13/30 on

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**Figure 1** Axial SWI MRI image of the head reveals a bilateral, diffuse,
hypointense coating of the cortex consistent with hemosiderin
deposition, including involvement of the interhemispheric and sylvian
fissures and the lateral ventricles (A). The coronal T2-weighted MRI sequence depicts atrophic changes and a
hypointense coat of hemosiderin deposition on the cerebellum (B).

**Figure 2** The sagittal T2-weighted MRI image of head and neck reveals
cerebellar cavitary changes along with hypointense coat on the
cerebellum, brainstem and the spinal cord (Fig. 2A). The sagittal T2-
weighted MRI images of the spine show a well-delineated intradural
lumbar mass at the L3-L4 levels of the spinal cord and heterogeneous
enhancement post-gadolinium injection in the T1-weighted MRI
sequence (Figure 2B and C).

**Figure 3** Intradural, extramedullary tumor (12 mm x 14 mm) in the
thecal sac tethered to the nerves of the cauda equina. There is subtle
yellow-tinged discoloration of the spinal nerves.
a Folstein mini mental status examination due to deficits in attention, concentration and recall as well as short-term memory loss. He was also easily irascible.

One of the classic symptoms in the triad of SS is sensorineural hearing loss. The cochlear nuclei and the organ of Corti are susceptible to damage in SS [11]. The Vestibulococchlear nerve is particularly vulnerable to hemosiderin deposition because of its long glial segment and exposure to the rapidly flowing pool of CSF in the cerebello-pontine angle [11,12]. Due to our patient’s dementia, it was difficult to determine whether he had conductive or sensorineural hearing loss. However, his hearing impairment could also be attributed to years of work as a steel plant worker and truck driver with SS as a detrimental cofactor.

Ataxia in SS is explained by damage to the cerebellum caused by hemosiderin deposition. However, our patient had a history of multiple cerebellar infarcts, which very likely also contributed to his ataxic gait. Although it has been demonstrated that hemosiderin deposition on the pia mater may result in sclerosis of the intracranial veins, leading to venous hypertension, it is not known whether hemosiderin deposition on arterial vasculature can account for our patient’s cerebellar infarcts. [13,14].

The main objective in the treatment of SS is to stop the chronic hemorrhaging and thus prevent further progression of the disease. Surgical treatment can not reverse the symptoms such as ataxia, hearing loss and pyramidal signs. In some patients presenting with hearing loss, cochlear implantation can be a viable option [15]. Grover et al. reported successful cochlear implantation in a patient with progressive hearing loss over a 25-year period due to SS. Although the short-term results of such a treatment seem promising, long-term data is lacking on the success of this therapy [15]. Iron chelation therapy is another mode of treatment currently under investigation. A pilot trial of Deferiprone, a lipid- soluble Iron chelator, resulted in a decrease in hemosiderin deposition in four out of ten study participants [16]. Four other participants reported improvement in neurological functioning, including better coordination and gait, better hearing, clearer thinking and reduced spasticity [16].

Our patient presented with classical, as well as some less-commonly reported, symptoms of SS such as dementia. He recovered well from the surgery however, due to the irreversible nature of the pathological process, his baseline mental function and other clinical manifestations remained unchanged three weeks postoperatively and he was subsequently transferred to a long-term health care facility.

REFERENCES


