Superficial Siderosis
Associations and Therapeutic Implications

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Superficial siderosis of the central nervous system results from hemosiderin deposition in the subpial layers of the brain and spinal cord. A clinical history of subarachnoid hemorrhage is often absent. Patients present with slowly progressive gait ataxia and sensorineural hearing impairment. A history of prior intradural surgery or trauma is common. With widespread use of magnetic resonance imaging, presymptomatic cases are being diagnosed and it is difficult to be certain about the true incidence of this disorder. Despite extensive investigations, the cause of bleeding is often not apparent. An intraspinal fluid-filled collection is a common accompaniment and may be the likely bleeding source. An early diagnosis and prompt intervention directed at removal of the bleeding source may prevent progression. This review discusses the role of multimodality imaging in evaluation of superficial siderosis and the therapeutic implications of identified associations.

In superficial siderosis of the central nervous system, hemosiderin deposition is seen in those parts of the central nervous system that are adjacent to cerebrospinal fluid (CSF). There is a brownish discoloration of the leptomeninges and adjacent parenchyma. The pigmentation has a predilection for the superior vermis, crests of the cerebellar folia, basal frontal lobe, temporal cortex, brainstem, spinal cord, nerve roots, and cranial nerves I and VIII. There is a sharp cutoff in the spinal roots and cranial nerves at the junction between the peripheral Schwann cell and central glial segments. The vulnerability of the eighth cranial nerve may be explained by the greater length of hemosiderin deposition (due to its long glial segment). In vivo magnetic resonance imaging (MRI) and autopsy correlation has shown that the hemosiderin deposition around the brain, brainstem, and spinal cord results in the characteristic hypointensity seen on T2-weighted MRI.1

ETIOLOGY AND PATHOGENESIS

At times, patients have an obvious intracranial source of chronic subarachnoid bleeding. In a 1995 survey of the reported superficial siderosis cases in the literature, an underlying cause was identified in 34 of 63 cases.2 A dural pathology was found in 47% of cases. This included CSF cavity lesions (eg, meningoceles, pseudomeningoceles, pseudoencephaloceles, cavity remaining after a hemispherectomy, and chronic suboccipital hematomas) or root pathology (eg, root avulsions or epidural cysts). Tumors, such as ependymomas, meningiomas, oligodendrogliomas, pineocytomas, and paragangliomas, were seen in 35% of cases, and vascular abnormalities (eg, arteriovenous malformations or aneurysms) were seen in 18%. In a recently reported single-institution series of 30 patients, fluid-filled collections were seen on MRI in 14 patients.3 In 4 of these patients, the collection was fairly localized and suggested the possibility of a meningocoele or pseudomeningocoele.

A commonly identified risk factor in patients with superficial siderosis is a prior...
Branial plexus injury with associated nerve root avulsion is a commonly reported association. Brachial plexus injury may be associated with injury of nerve root sleeves, and this may lead to the formation of a pseudomeningocele.

A history of intradural cranial surgery as a risk factor for later development of superficial siderosis is being increasingly recognized. Spinal surgical procedures may be complicated by a dural tear with subsequent development of a pseudomeningocele and superficial siderosis. Surgical procedures may provide CSF access to a bleeding source within the brain. The cavity left after a surgical procedure is the likely source of bleeding. The dura of the cavity following a hemispherectomy may have multiple bleeding points that have direct access to the ventricular system. Telangiectasia and cavernous angiomas may be found in the brain and spinal cord after radiotherapy.

The ability of the brain to biosynthesize ferritin in response to prolonged contact with hemoglobin iron is important in the pathogenesis of superficial siderosis. Accelerated ferritin synthesis in the Bergmann glia of the cerebellum may account for the preferential cerebellar involvement. Ferritin synthesis is thought to be neuroprotective by binding iron released by red cells. Tissue damage occurs when this reserve is exhausted. It has been suggested that the excess intrathecal iron may overload the ferritin biosynthesis capacity of the microglial cells; subsequent free radical damage and lipid peroxidation may cause neuronal injury.

### Clinical Features

Even in the absence of an inciting event, years of chronic bleeding can precede clinical manifestations. Patients often present after they are 40 years old. The most common clinical presentation is slowly progressive cerebellar ataxia, which is often associated with hearing impairment. Sensorineural hearing loss (at times with vestibular failure) may be the first symptom, which may be accompanied by tinnitus. Cerebellar dysarthria is common and nystagmus may be present. A myelopathic presentation is also recognized. Pyramidal and sensory signs, and bladder dysfunction are common and may relate to brainstem or spinal cord involvement. Sensory symptoms of a sensory level are rarely present. Anosmia or hyposmia are commonly reported. Also reported are optic and trigeminal neuropathy. A distinct pattern of cognitive and social impairment in superficial siderosis has been recognized. Affected areas include speech production, executive functions, and visual recall memory. Clinical or electrophysiologic evidence of lower motor neuron involvement is rare but has been described and may be caused by radiculopathy. Severe headache indicative of symptomatic subarachnoid hemorrhage was noted in approximately one third of cases in an earlier literature review but was relatively infrequent in a recent large series.

### Investigations

Magnetic resonance imaging is the investigation modality of choice, though (particularly in the early stages) the findings are subtle and a high index of suspicion is necessary to permit an early diagnosis. The hypointensity follows the contours of the brain and spinal cord and may be easily missed. Imaging of the entire neuraxis is indicated to localize a potential bleeding source. The bleeding source may not be detected despite MRI of the brain and spine, computed tomography (CT) myelography, magnetic resonance angiography, and cerebral and spinal angiography. Radiolabeled red blood cell scanning with technetium has been employed but has not been found to be useful.

### Magnetic Resonance Imaging

Gradient-echo T2-weighted images have higher sensitivity for hemosiderin deposition. The magnetic susceptibility effects of blood degradation products, such as ferritin and hemosiderin, are also more pronounced at high-field strength. Abnormal MRI results may be present in the absence of secondary symptoms of superficial siderosis.

Gradient-echo T2-weighted MRI shows a rim of hypointensity around the cerebellum (Figure 1A and B) and brainstem (Figure 1C-E). The marginal T2 hypointensity is due to hemosiderin deposition and may also involve the cortical sulci (Figure 1F), sylvian fissure (Figure 1G), and interhemispheric fissure (Figure 1H). The superior vermis, quadrigeminal plate, and basal cerebrospinal fluid are preferentially involved by the T2 hypointensity. Hemosiderin deposition may also be seen along cranial nerve VIII. Cerebellar atrophy is often present and the superior vermis and anterior cerebellar hemispheres may be preferentially involved by the atrophy (Figure 1K). Gliosis may result in a high signal from the adjacent cerebellar tissue. Alternatively, it may be only an apparent increase due to the overlying hypointensity. A hyperintense rim is rarely seen. This may be due to methemoglobin and represents a recent episode of subarachnoid hemorrhage. Hydrocephalus has generally been seen in association with a history of hemispherectomy.

Hemosiderin deposition is commonly seen around the spinal cord (Figure 1J, L). There may be clumping (CT myelogram on Figure 3C) or peripheralization (Figure 1M) of the nerve roots due to arachnoiditis. Spinal cord atrophy is common (Figure 1I). Blood accumulation with reactive changes in the cul-de-sac may give the mistaken impression of a tumor (Figure 2E and F). Prominent vessels may be seen on the surface of the spinal cord in the absence of a vascular malformation (Figure 2C). It has been suggested that pial siderosis may result in sclerosis of the veins, with venous hypertension and prominent vasculature. An interruption in the circumferential hypointensity may indicate root avulsion and is possibly caused by absence of the pia mater at the avulsion site (Figure 3B).

Indirect clues explaining the cause of superficial siderosis may include a neoplasm, vascular malformation, or fluid-filled cavity of variable dimension and may be visible on MRI (Figure 4). Magnetic resonance imaging may also show T2 hyperintensity due to myelomalacia (Figure 2D) or encephalomalacia secondary to
prior injury. There may also be evidence of prior bony injury (Figure 2G). Enhancement of the pial surface of the cord is rarely seen.

**Computed Tomography**

Though head CT results are generally unremarkable, cerebellar atrophy or a clue to the potential cause of superficial siderosis may be evident. Evidence of bony injury due to prior trauma, if present, may be better seen on CT than MRI. Rarely, a rim of hyperdensity may be seen around the brainstem on CT (Figure 2H).\(^1^4\)

**CT Myelography**

Dural diverticula, pseudomeningoceles, and associated dural defects are best characterized on myelography and CT myelography (Figure 3D and E). Computed tomography myelography may show these even when MRI may not.\(^3\) At times, a transdural leak may be seen on the CT myelogram.\(^3\) The rim of hypointensity around the cord may be interrupted at the site of root avulsion (Figure 3A).\(^8\) The exact site of dural defect in longitudinally extensive intraspinal collections may be accurately localized by dynamic CT myelography.\(^3,18\) This technique was first introduced for localizing high-flow CSF leaks.\(^1^9\)

**Angiography**

Cerebral and spinal angiography are often undertaken but are generally unrewarding, possibly because of the slow and often intermittent nature of the bleeding. Small slow-flow pial arteriovenous malformations may be detected only by angiography.

**Cerebrospinal Fluid**

Cerebrospinal fluid analysis may show xanthochromia and an increased number of red blood cells. It is pos-
sible that the red cell count will be significantly higher if the CSF is taken from the cavity responsible for the bleeding, such as a pseudomeningocele or hemispherectomy cavity. A slight elevation in the white blood cell count may be present. Cerebrospinal fluid protein may be elevated, and significant elevation may be accompanied by discoloration due to hemorrhage that may mimic the xanthochromia seen. Protein elevation may be caused by arachnoiditis. Other reported CSF findings in superficial siderosis include the presence of erythrophages, siderophages, and elevated iron and ferritin levels. Because of the intermittent nature of the bleeding, these findings may be absent.

**TREATMENT**

The surgical treatment of superficial siderosis depends on early identification of the bleeding source. Excision of the offending neoplasm, vascular malformation, or pseudomeningocele and repair of dural defects is a logical therapeutic strategy. Exploration and repair of a pseudomeningocele or a meningeal diverticulum caused by root avulsion has been done in some cases. Exploration of dural pseudomeningoceles may reveal clotted blood within the pseudomeningocele, chronic ooze of blood from a defect in the pseudomeningocele, or hyperemic scar tissue with...
Friable vessels. Spider angioma in an arachnoid scar has been described in a patient with root avulsion. Cauterization of abnormal vessels in the pseudomeningocele may be undertaken. With a longitudinally extensive intraspinal fluid-filled collection, the focus of therapy is localization and repair of the dural defect. Repair of pseudomeningoceles or longitudinally extensive collections often required a piece of muscle. Gel foam and fibrin glue have also been employed. Postoperative follow-up has often been associated with a lack of further progression and, in an isolated case, some improvement. A repeat CSF study completed months after the surgical procedure may show resolution or decrease of the xanthochromia and CSF red blood cells. In some of these cases, absence of red blood cells on CSF examination after the surgical procedure has been documented. Patients who have had surgical intervention for superficial siderosis have had brief reported follow-up duration, as compared with the natural history of the disorder. Given the slowly pro-
gressive nature of the disorder, a long follow-up is required to be certain about halting progression by surgical intervention.

CONCLUSIONS

Magnetic resonance imaging in superficial siderosis shows the characteristic marginal T2 hypointensity around the brainstem, cerebellum, and spinal cord, and may also provide a clue to its possible cause. Fluid-filled collections of variable dimensions are often seen on spinal MRI or CT myelography in patients with or without a prior history of injury or a surgical procedure. Angiography is generally unrewarding. With a longitudinally extensive collection, a dynamic CT myelography may help localize the defect and direct physicians to the site of laminectomy. Despite these investigations, a cause for the bleeding may not be evident. Cerebrospinal fluid examination commonly shows the presence of red blood cells or xanthochromia. An accurate diagnosis can spare the patient an expensive search for the many other causes of ataxia. An early diagnosis and prompt intervention are necessary to prevent severe deficits. Surgical correction of the cause of bleeding is a logical therapeutic strategy and holds hope for arresting disease progression. Postsurgical CSF examination and neuroimaging should be done. Longer follow-up in patients who have undergone a surgical procedure is required to confirm that elimination of the source of bleeding halts clinical progression. Owing to widespread use of MRI, superficial siderosis is being increasingly recognized. The diagnosis may be made even in the absence of symptoms.

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REFERENCES