

Superficial siderosis of the central nervous system: magnetic resonance imaging and pathological correlation

Case report

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✓ The authors report a 32-year-old woman who had undergone repair of an occipital encephalocele in infancy and who experienced a 20-year history of progressive hearing loss and intermittent vertigo. After parturition, she developed a rapidly progressive quadriparesis and brain-stem dysfunction associated with persistent intraventricular and subarachnoid hemorrhage. Serial magnetic resonance (MR) images showed progressive deposition of hemosiderin along the surface of the brain, brain stem, and spinal cord, and enhanced thickened membranes at the site of the original encephalocele repair. Posterior fossa exploration disclosed hemorrhagic membranes, which were resected; despite removal of this tissue, the patient deteriorated and died. Postmortem examination confirmed iron-containing pigment along the meninges, cerebral hemispheres, brain stem, spinal cord, and cranial nerves accompanied by atrophy of the superficial cerebellar cortex.

It is concluded that superficial siderosis may accompany encephalocele repair. This is believed to be the first report in the literature of superficial siderosis of the central nervous system to correlate *in vivo* MR images with autopsy results.

KEY WORDS • superficial siderosis • hemosiderin • magnetic resonance imaging • subarachnoid hemorrhage

SUPERFICIAL siderosis of the central nervous system results from recurrent extravasation of blood into the subarachnoid space. The entity was first reported by Noetzel¹⁰ in 1940 and is characterized by progressive sensorineural hearing loss, cerebellar ataxia, myelopathy, dementia, and persistent xanthochromic cerebrospinal fluid (CSF).^{13,15} Less common features include headache, tremor, ageusia, anosmia, and motor, sensory, or sphincter dysfunction.^{6-9,13-15} Many patients have no clear ictus and symptoms may appear insidiously.⁷⁻⁹ The time course of disease progression ranges from months^{6,7} to as much as 37 years,^{13,15} and may involve a subacute deterioration resulting in death.^{6,7,14}

Identification and removal of the source of bleeding is the focus of clinical management. The most common pathology associated with superficial siderosis is brain tumor (ependymomas,^{1,6,13,15} carcinomatosis of the leptomeninges due to gastric or breast cancer,^{10,13-15} oligodendroglioma,^{5,13,15} pinealoma,^{13,15} and hemangioblastic meningioma,^{12,13,15}) followed by hemispherectomy,³ aneurysms,³ and arteriovenous malformations.^{7,11,13-15} Subdural hematomas^{3,13,15} and neonatal ventricular

bleeding² have also been reported in patients with superficial siderosis. Remarkably, many authors have been unable to identify a source of bleeding despite extensive diagnostic and postmortem studies.^{3,13,15}

The pathological changes observed with superficial siderosis have been well characterized.^{3,6,7,14} Deposition of hemosiderin results in a yellowish-brown discoloration on gross inspection, which extends from the pial surface 2 to 3 mm into the tissue along the entire neuraxis. Microscopic examination reveals fine granules of hemosiderin in macrophages, astrocytes, microglia, and neurons. Varying degrees of atrophy are seen in the cerebellum with folial shearing, loss of Purkinje cells, and Bergmann gliosis. The first, second, third, and eighth cranial nerves exhibit dense accumulation of hemosiderin with demyelination and atrophy. Hemosiderin-laden astrocytes are also found intraparenchymally around the cochlear nucleus.^{7,14}

We report the case of a 32-year-old woman born with an occipital encephalocele who developed superficial siderosis diagnosed by characteristic clinical, CSF, and radiographic features.

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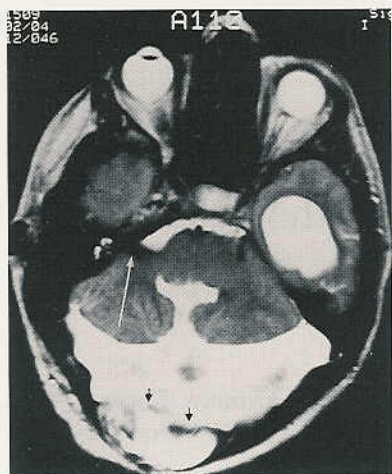


FIG. 1. Magnetic resonance T₂-weighted axial image (TR 3000 msec, TE 90 msec) demonstrating marked hypointensity along the right eighth cranial nerve (white arrow). The pseudomeningocele and bone ridge (black arrows) from the previous surgery are seen in the posterior fossa along with the dilated cisterna magna and temporal horn.

Case Report

This 32-year-old right-handed woman presented with worsening headaches and gait instability in the 8th month of her pregnancy. She had been born with an occipital encephalocele that was repaired 2 days after her birth. She was macrocephalic due to asymptomatic compensated hydrocephalus. At 14 years of age she was evaluated for complaints of tinnitus, light-headedness, and vertigo and was found to be neurologically normal except for bilateral hearing loss. Computerized tomography (CT) of the brain at 20 years of age documented hydrocephalus and a cystic cavity at the site of the encephalocele repair. Despite progressive hearing loss, she completed 2 years of college and maintained full-time employment. In August, 1991, during the 8th month of her first pregnancy, she developed bifrontal headaches, worsening vertigo, and nausea. An elective Caesarean section was performed.

Admissions. In October, 1991, the patient was hospitalized with continued headaches, nausea, and vertigo. Her neurological examination was remarkable for macrocephaly, a blunted affect, bilateral hearing loss, and mild gait instability. Her serum electrolytes, coagulation studies, and hematological profile were normal. A CT scan of the head revealed hydrocephalus, and a right ventriculoperitoneal shunt was placed without complication. In spite of an atraumatic ventricular cannulation, CSF collected intraoperatively was grossly bloody. Postoperative magnetic resonance (MR) imaging of the brain revealed marked persistent dilation of the third and lateral ventricles; the cystic dilation of the posterior fossa contained fluid with a slightly higher signal intensity than that of CSF, and loculation was suspected. Hemosiderin deposits were seen around the brain stem and extending along the seventh and eighth cranial nerves (Fig. 1). No tumor or aneurysm was

TABLE 1
Cerebrospinal fluid profile in a patient with superficial siderosis of the central nervous system

Collection Date	Collection Site	Glucose (mg/dl)	Protein (mg/dl)	Cells (/cu mm)*	
				RBC	WBC
11/19/91	post. fossa cyst & rt lat ventricle	87	638	29,460	18
12/10/91	post. fossa cyst & rt lat ventricle	77	879	46,000	50
01/7/92	post. fossa cyst	69	863	52,679	2
01/12/92	rt lat ventricle			27,750	6
	post. fossa cyst			51,000	2
01/16/92	lumbar puncture			2,973	1
01/19/92	rt lat ventricle	68	882	9,100	3
	post. fossa cyst	108	1197	21,750	44
01/21/92	rt lat ventricle	60	801	2,970	3
	post. fossa cyst	93	1167	28,961	1
02/7/92	post. fossa cyst & rt lat ventricle			150,000	200
02/11/92	post. fossa cyst & rt lat ventricle			4,480	1
02/18/92	post. fossa cyst & rt lat ventricle	90	717	11,235	10

* RBC = red blood cells; WBC = white blood cells.

identified. Thereafter, CSF collected from the shunt during several outpatient visits was found to be hemorrhagic, but intracranial pressure was normal (120 to 150 mm H₂O).

In November, 1991, the patient was admitted to the hospital for evaluation of persistent symptoms. A second shunt catheter was placed into the posterior fossa cyst and connected to the ventriculoperitoneal shunt, but her symptoms did not improve. The shunt was then revised to adjust the drainage pressure; the CSF was found to be under normal pressure, but continued to show the presence of red blood cells (Table 1). The patient's symptoms continued to progress and, independent of surgical manipulations, she developed lethargy and urinary retention. Neurological examination was remarkable for psychomotor retardation, up-gaze paresis, eyelid retraction, pupillary light-near dissociation, intermittent downbeat nystagmus, convergence-retraction nystagmus, bilateral dysmetria, diffuse hyperreflexia, and a right extensor plantar reflex. Magnetic resonance imaging of the cervical spine revealed a prominent central canal with low signal in the canal and around the cord surface, consistent with siderosis (Fig. 2). There was no enhancement following injection of gadolinium. During this hospitalization, the patient attempted suicide and was transferred to the psychiatric unit.

In January, 1992, a four-vessel angiogram did not identify a source of bleeding. The ventricular shunts were externalized to better evaluate the source of intraventricular hemorrhage and the relationship between symptoms and intraventricular pressure; symptoms were independent of external drainage pressure. The gradient of red blood cells between the two compartments suggested that the source of CSF bleeding was in the posterior fossa (Table 1). Repeat MR imaging of

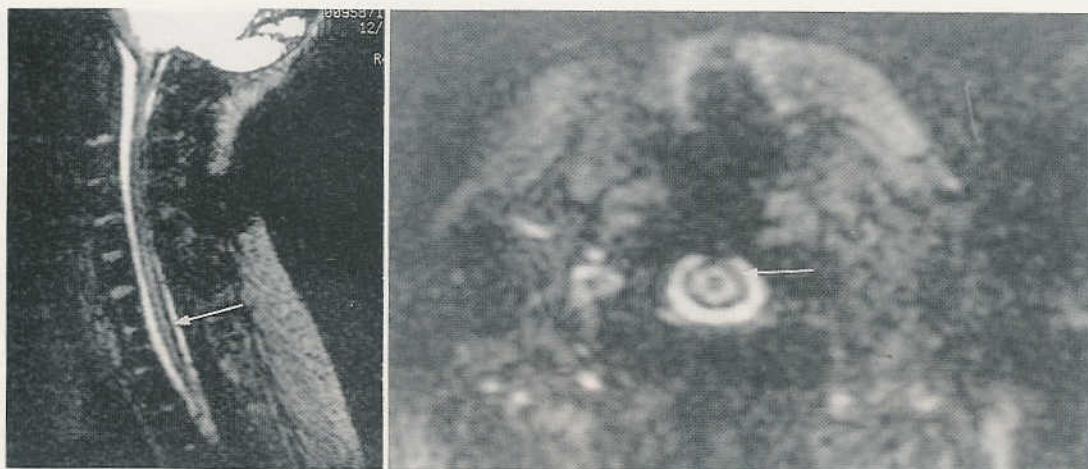


FIG. 2. Gradient-echo magnetic resonance images (TR 750 msec, TE 40 msec, flip angle 10°). *Left:* Sagittal image demonstrating an area of hypointensity (representing hemosiderin) surrounding the surface of the cervical spinal cord (arrow). *Right:* Axial image demonstrating the area of hypointensity (representing hemosiderin) in the central canal as well as along the surface (arrow) of the cervical spinal cord.

the head and entire spine revealed deposition of hemosiderin in the meninges and ependyma and along the surface of the spinal cord. A small amount of intraventricular blood was seen in the occipital horns. No intraparenchymal abnormalities were seen.

Operation. Since clinical and radiographic evidence indicated that the posterior fossa cyst was a potential source of intracranial bleeding, the ventricular shunts were internalized and the posterior fossa was explored. The previous midline incision was reopened and a pseudomeningocele containing yellow blood-tinged fluid was entered. At the superior aspect of the pseudomeningocele, a shelf of thinly ossified, dark red membrane was observed arising from the occipital bone near the superior extent of the posterior fossa, as had

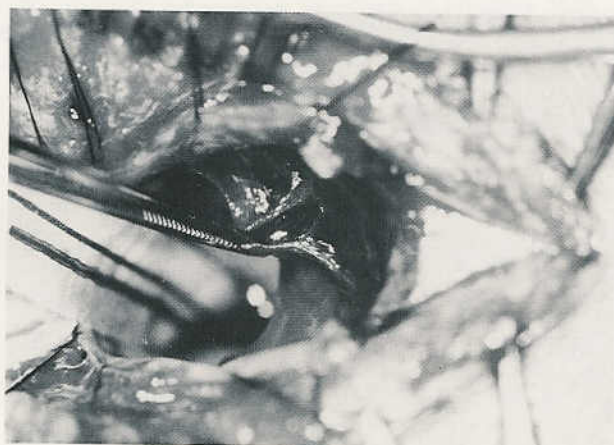


FIG. 3. Operative photograph showing the thickened hemorrhagic subdural membrane (in forceps), which spanned the superior portion of the patient's encephalocele defect. A pseudomeningocele was present posteriorly.

been demonstrated by MR imaging (Fig. 1). This membrane, which partially bridged the circular defect left by the original encephalocele, was covered by old clot and blood which appeared to be at various stages of resolution (Fig. 3). Free communication could be demonstrated between CSF in the pseudomeningocele, the subarachnoid space, and the fourth ventricle. The membrane and underlying shelf of bone were resected until more normal-appearing dural tissue was encountered; this step involved re-exposing the original circular dural defect. The defect was repaired with a lyophilized dural patch and the occipital bone defect was reconstructed with methyl methacrylate.

Postoperative Course. Immediately after surgery, the patient showed mild improvement in her headache, but her weakness progressed. Neurological examination showed lethargy, up-gaze paresis, facial diparesis, hypotonia with only antigravity strength in all four extremities, diffuse hyperreflexia, and bilateral extensor plantar reflexes. She remained bedridden and, on February 7, 1992, developed an aspiration pneumonia. She required intubation for airway protection, suffered from recurrent fevers and, despite broad antibiotic coverage, died 2 weeks later.

Postmortem Examination. General autopsy findings included organizing pneumonia, but no abnormal systemic collections of iron. On gross inspection of the brain, blood clot was seen in the posterior fossa and the anterior horns of the lateral ventricles. There was evidence of hydrocephalus and compression of the cerebellum without herniation or ventricular obstruction. The surfaces of the cerebral hemispheres, cerebellum, brain stem, cranial nerves, spinal cord, leptomeninges, and ependyma were colored orange-brown to orange-tan. All of the discolored areas were positive when exposed to Prussian blue stain for iron (Fig. 4). Microscopically, the meninges were thickened. Numerous

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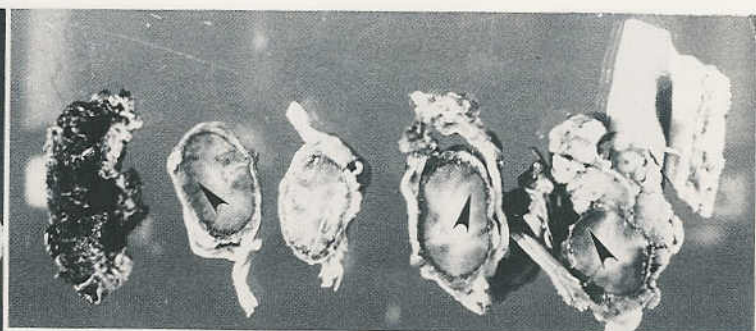
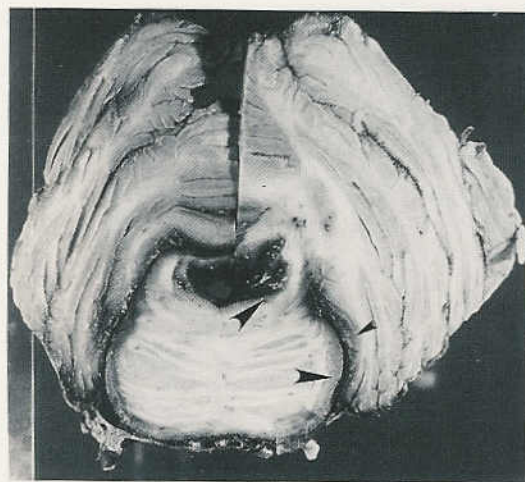


FIG. 4. Gross pathological specimens stained by the Prussian blue method. *Left:* cross section of the brain stem at the level of the pons showing the marked iron deposit present in the subpial and subependymal neuropil (*large arrows*) and on the surface of the cerebellar hemispheres (*small arrow*). *Right:* Section of the spinal cord showing marked deposition of iron in the superficial aspect of the spinal cord (*arrows*). The structure to the far left of the photograph is the choroid plexus, which exhibits intense iron staining.

hemosiderin-laden macrophages and extracellular iron granules were identified in the subpial brain parenchyma, spinal cord, and cerebellum. The most intense staining of iron was seen in the Purkinje cell layer of the cerebellum (Fig. 5 *left*). The rostral portion of the cervical spinal cord and caudal medulla showed central necrosis with macrophage infiltration (Fig. 5 *right*). Rosenthal fiber formation and superficial hemosiderin deposition was prominent in the region of the posterior commissure. No additional bleeding site was identified.

Discussion

Our report demonstrates the clinical and pathological features of superficial siderosis, and emphasizes the importance of MR imaging in confirming the diagnosis prior to death. Bleeding in the posterior fossa most likely began years before this patient's illness became manifest and was probably responsible for her progressive deafness and other insidious symptoms. The diag-

nosis of superficial siderosis was considered when exacerbation of her headaches, vertigo, and ataxia during pregnancy was not relieved by shunting and the CSF remained hemorrhagic. Surgical exploration revealed an abnormal membrane between the subarachnoid space and the pseudomeningocele. Chronic small-volume hemorrhage in our patient could have been the result of disruption of the membrane due to compression and traction of the overlying scalp and fluid in the pseudomeningocele whenever there were changes in head position or pressure on the back of the head.

The clinical and pathological features of superficial siderosis have been reproduced experimentally by repeated intrathecal injection of autologous blood or an iron-dextran complex (Imferon).⁴ This suggests that iron is the toxic agent responsible for the syndrome. Unfortunately, attempts to treat superficial siderosis by

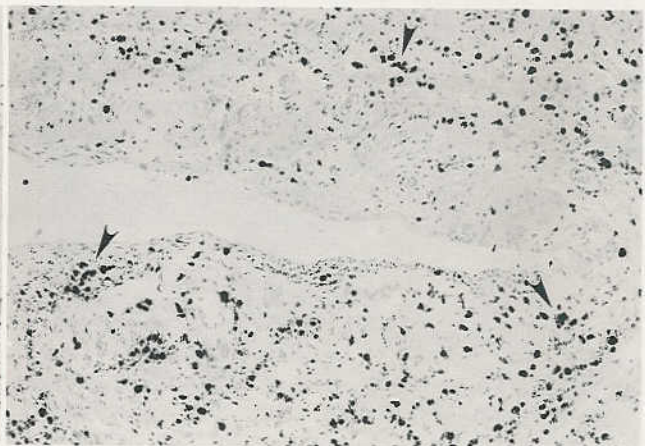


FIG. 5. Photomicrographs of brain and spinal cord sections. *Left:* The superficial cerebellum showing thinning of the molecular layer (*small arrows*), Purkinje cell loss with iron deposition (*large arrows*), and marked depletion of the granule cells. H & E, $\times 50$. *Right:* Marked iron deposition (*arrows*) and tissue fragmentation surrounding a dilated central canal of the rostral cervical spinal cord. Gomori iron stain, $\times 40$.

systemic administration of iron-chelating agents such as trientine dihydrochloride have been ineffective.^{13,15}

The rapid development of cranial neuropathy, dementia, and ataxia in superficial siderosis has precedent. Kott, *et al.*,⁶ reported the case of a 29-year-old woman whose features of superficial siderosis developed over 1 month following her second pregnancy. She was found post mortem to have an intraventricular ependymoma and the typical pathological findings of superficial siderosis. There is no known association between pregnancy and superficial siderosis, but it is conceivable that altered intravascular volume or endocrinological or hematological factors might trigger bleeding in patients predisposed to leakage of blood into the subarachnoid space.

Magnetic resonance imaging and occasionally CT scanning may be used to confirm the diagnosis of superficial siderosis.^{1,2,11} High-field T₂-weighted spin-echo MR imaging detects hemosiderin deposits in patients with superficial siderosis by documenting a hypointense signal along the gyri, the ependymal surface of the ventricles, the surface of the brain stem, and the spinal cord.^{1,2,13,15} Gradient-echo MR imaging is more sensitive for detecting iron deposition, although it produces a poorer-quality image.^{2,13} When the diagnosis of superficial siderosis is suspected, routine spin-echo MR imaging should be supplemented by gradient-echo MR studies.

The absence of satisfactory pharmacological therapy in this potentially lethal disorder mandates an aggressive search for the source of bleeding. In our patient, MR imaging was more useful than angiography in localizing the potential source of hemorrhage. Superficial siderosis should be considered as a cause of insidious neurological deterioration in patients with persistently hemorrhagic or xanthochromic CSF. Magnetic resonance imaging was diagnostic in our patient and the distribution of hemosiderin deposits correlated well with the clinical and postmortem findings.

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