A Rare Cause of Cerebellar Ataxia Syndrome: Superficial Siderosis of Central Nervous System

Simon Kang Seng Ting, MRCP, Kumar M Prakash, FRCP

Abstract-

Purpose: To describe and emphasize importance of recognizing superficial siderosis (SS) of the central nervous system (CNS) when assessing cerebellar ataxia syndrome

Case Report: Superficial siderosis (SS) of the central nervous system (CNS) is a rare disorder that results from chronic hemosiderin deposition in the subpial layers of the brain and the spinal cord. Although recurrent bleeding in the subarachnoid space is the most likely explanation, a definite history of subarachnoid hemorrhage (SAH) is often lacking. Among the clinical presentations described in the literature include sensorineural deafness, dementia, anosmia, pyramidal tract signs and cerebellar ataxia. However, due to its rarity, SS remains one of the least considered differential diagnosis in patients with sporadic ataxia syndrome. We describe a case of progressive gait imbalance that was initially misdiagnosed for several years until a brain MRI study showed evidence of diffuse hemosiderin deposition suggestive of SS of CNS.

Conclusion: MR brain with gradient-echo T2-weightd images should be included in all MR studies carried out to investigate the etiology of cerebellar ataxia to allow early diagnosis and prompt intervention for SS.

Key Words: cerebellar ataxia, superficial siderosis

Acta Neurol Taiwan 2011;20:257-261

INTRODUCTION

Superficial siderosis (SS) of the central nervous system (CNS) is a rare neurological condition and the etiology is still not clear. It results from chronic deposition of hemosiderin in parts of the CNS that are adjacent to the cerebrospinal fluid (CSF). This in turn causes the brownish discoloration of the leptomeninges and the adjacent brain parenchyma. The pigmentation has a predilection for the superior vermis, crests of the cerebellar folia, basal frontal lobe, temporal lobe cortex, brainstem, cranial nerves I and VIII as well as the spinal cord and nerve roots. It is postulated that SS is secondary to recurrent subarachnoid hemorrhage (SAH) which induce intracellular uptake of iron and ultimately leading to destruction of the neural tissues. SS can also

From the Department of Neurology, National Neuroscience Institute Singapore General Hospital campus, Outram Road, Singapore 169608.
Received May 13, 2011. Revised June 21, 2011.
Accepted December 5, 2011.
Correspondence to: Simon Kang-Seng Ting, MD. Department of Neurology, National Neuroscience Institute Singapore General Hospital campus, Outram Road, Singapore 169608.
E-mail: simon.ting.k.s@sgh.com.sg

occur as a late complication of neurosurgical procedures, or as a genetic disease caused by primary ceruloplasmin deficiency. The most common clinical presentation is slowly progressive bilateral hearing impairment, which is often associated with gait imbalance. Less commonly it has also been reported to cause anosmia, cognitive impairment, seizures, pyramidal tract signs, as well as sensory and autonomic symptoms[1].

We report a 60-year-old man who had gradual onset of severe sensorineural deafness and gait ataxia for 6 years who was eventually diagnosed with SS of CNS.

CASE REPORT

A 60-year-old Indonesian gentleman presented with a 6-year history of gradual progressive bilateral deafness. One year after the onset of hearing loss, he started experiencing unsteadiness of gait. These symptoms progressed over the years and resulted in frequent falls. He denied history of loss of smell, chronic recurrent headaches, head trauma, head surgery or excessive alcohol consumption. He had no positive family history of similar hearing or gait disturbances. He had sought medical opinion in many hospitals in different parts of the world and series of neuroimaging as well as laboratory studies were conducted. He was told to have a significant amount of cerebellar atrophy but no definite cause was found.

Neurological examination showed evidence of dysarthria with scanning speech, bilateral sensorineural deafness, dysmetria, abnormal heel shin test and broad-based ataxic gait. The extraocular eye movements were normal and there was no clinical involvement of the pyramidal tracts, extrapyramidal or autonomic system. Routine laboratory investigations as well as serum ceruloplasmin (232mg/l) were within normal limits.

The T2 weighted (figure 1) and susceptibility weighted (figure 2) MR images of the brain showed areas of linear hypointensity along the sylvian fissures, cortical sulci, surfaces of the brainstem and cerebellum. There was also evidence of significant cerebellar atrophy. In addition, the T2-weighted MR images of the spinal cord showed similar findings along the cord surface as well (figure 3). These MRI findings were suggestive of extensive hemosiderin deposition on the surface of both hemispheres of the brain (supra and infra-tentorial regions) as well as the spinal cord in keeping with the diagnosis of SS of CNS.

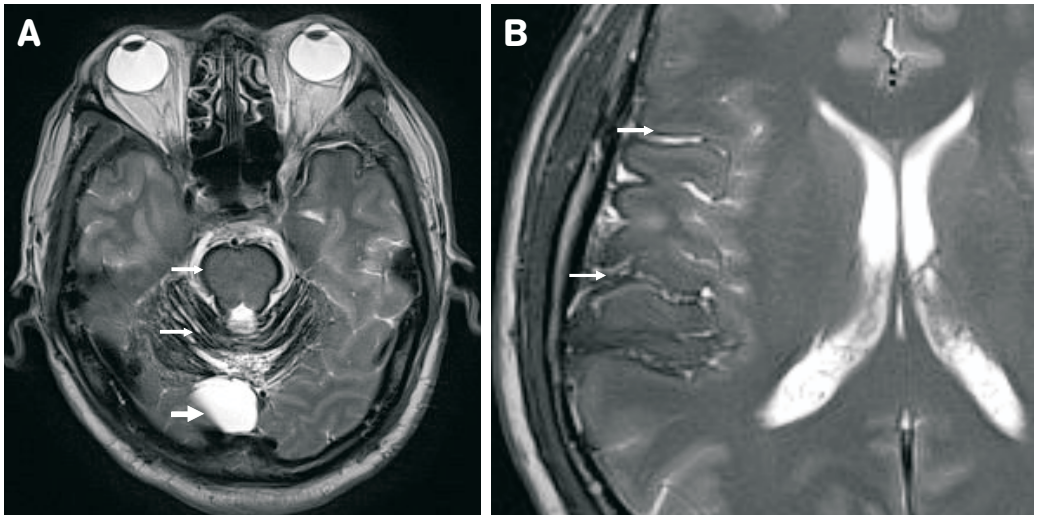

Figure 1. (A): T2-weighted MRI image showing linear hypointensities along the surfaces of the brainstem and cerebellum (thin arrows) as well as cerebellar atrophy. There is a retro-vermian cerebellar arachnoid cyst (thick arrow). (B): T2-weighted MRI image showing linear hypointensities along the surfaces cortical sulci (thin arrows).

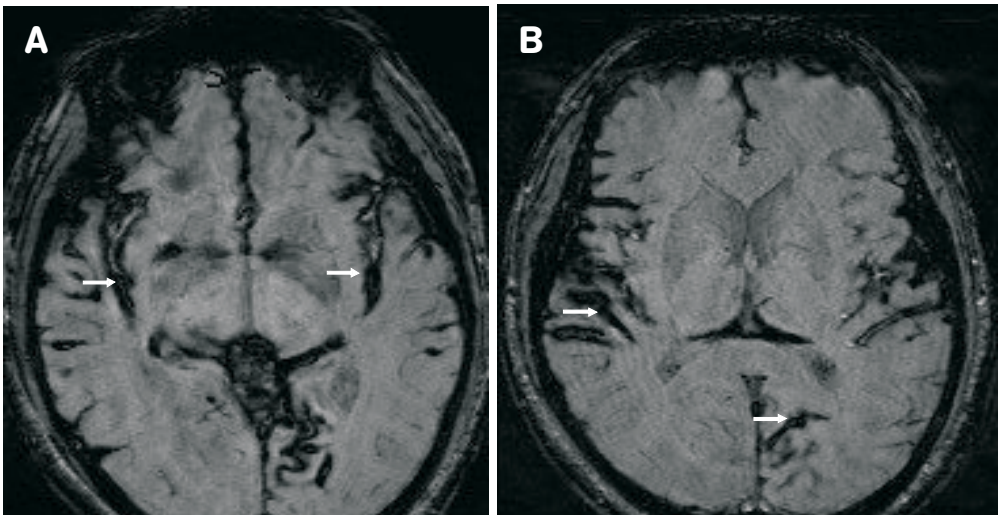

Figure 2. (A): Susceptibility-weighted MRI image showing linear hypointensities along the sylvian fissures (thin arrows). (B): Susceptibility-weighted MRI image showing linear hypointensities along the cortical sulci (thin arrows).

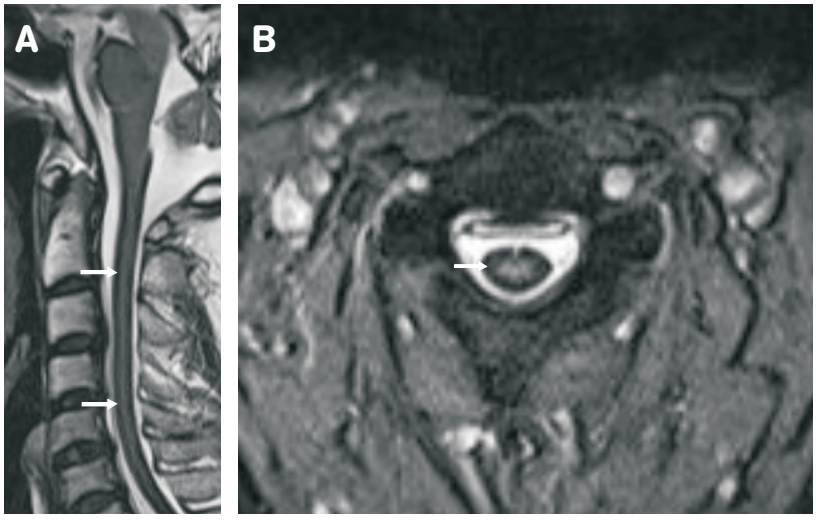

Figure 3. (A), (B): T2-weighted MRI images showing linear hypointensity on surface of cervical cord due to extensive hemosiderin coating (thin arrows).

DISCUSSION

The etiology of sporadic adult-onset ataxia in the majority of cases is unexplained. In a case series published by Abele et al, it was shown that only in 42% of patients the cause was known[2]. Among the differential diagnosis of ataxia published in various reports as well as review articles, SS of CNS is not included as one of the common causes of gait imbalance. This is not surprising, as the prevalence of this condition, although not accurately known, is likely to be relatively low. Therefore SS remains as an under-recognized condition and is more likely to be misdiagnosed, like in our patient, particularly in the early stages.

The hall mark of SS is hemosiderin deposition along the pial and subpial structures of the brain and spinal

cord, as a result of recurrent bleeding in the subarachnoid space, resulting in damage to the cerebellar cortex, cochlear nerves, cerebral cortex, and spinal cord. The clinical presentation of SS closely mimics a degenerative cerebellar disorder and usually is associated with bilateral sensorineural hearing loss. Other manifestations may include and pyramidal tract signs, dementia, bladder incontinence, anosmia, anisocoria, and sensory deficits. Our patient also complained of progressive deafness and gait ataxia for 6 years. However, despite extensive investigations including neuroimaging studies in multiple medical institutions, no etiological cause was established until recently.

MR imaging (particularly T2-weighted imaging) is the investigation of choice for the diagnosis of SS. The characteristic linear hypointensity seen on T2-weighted in vivo MR imaging correlated with the hemosiderin deposition around the surface of the central nervous system seen at postmortem. However, in the early stages of SS, the findings may be subtle and the T2 hypointensity following the contours of the brain and spinal cord may be easily missed. Gradient-echo T2-weighted images have a higher sensitivity for hemosiderin deposition. The magnetic susceptibility effects of blood-degradation products such as ferritin and hemosiderin are also more pronounced at higher field strengths.

T2-weighted MR imaging typically shows a rim of hypointensity around the cerebellum and brain stem. The superior vermis, quadrigeminal plate, and basal cerebral surface are preferentially affected. Cerebellar atrophy is often present, and the superior vermis and anterior cerebellar hemispheres may be preferentially involved by the atrophy. 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[4]. The linear marginal T2 hypointensity may also involve the Sylvian fissure, interhemispheric fissure, and cortical sulci[3]. These MR changes were seen in our patient.

The pathologic changes of SS are characterized well[4]. Macroscopically, there is dark brown discoloration of the leptomeninges and superficial CNS parenchyma as well as the subependymal lining throughout the neuroaxis. Microscopically, there is extensive hemosiderin deposition in the leptomeninges, subpial and subependymal regions. The leptomeninges are thickened, and there are varying degrees of neuronal loss, reactive gliosis, and demyelination. The superficial folia of the cerebellum almost always are involved with loss of Purkinje cells and Bergmann gliosis. In addition, cranial nerve VIII and, to a lesser extent, cranial nerves I exhibit dense accumulation of hemosiderin, that is often associated with demyelination and atrophy. The exact reason for the differential cranial nerve involvement is not known. However Fearnley et al has suggested that the differential surface contact of the cranial nerves with the CSF hemosiderin may account for this[5].

An important follow on step, after diagnosing SS, would be to identify and correct the potential source of recurrent subarachnoid hemorrhage in order to arrest the clinical deterioration. In the absence of an intracranial abnormality, further evaluation should include MR imaging of the spine. If no source is identified, further investigation with catheter angiography may be warranted to find the potential bleeders. However, in some cases, the source of bleeding remains obscure even with extensive investigations.

SS is known to be associated with a spectrum of lesions, including CSF cavity lesions (meningoceles, pseudomeningoceles, pseudoencephaloceles, cavity remaining after a hemispherectomy), trauma (such as cervical nerve root avulsions), neoplasms (ependymomas, oligodendrogliomas, and astrocytomas), and vascular abnormalities (arteriovenous malformations, aneurysms, and fragile capillary regrowth after brain surgery)[5,6]. In our patient a relatively large retrovermian arachnoid cyst was detected on MR causing mild mass effect on the adjacent right cerebellar hemisphere. Surgical excision of the cyst may result in symptom improvement, as highlighted in several case reports[7,8].

In conclusion, it is important to be aware of SS of CNS in the evaluation for cerebellar ataxia. MR brain remains the investigation of choice although in the early stages the findings may be subtle and thus easily over-

looked. Gradient-echo T2-weightd images should be included in all MR studies carried out to investigate the etiology of cerebellar ataxia. This may spare patients incurring other expensive investigations and allow early diagnosis and prompt intervention.

REFERENCE

1. Kumar N. Superficial siderosis: associations and therapeutic implications. Arch Neurol 2007;64:491-496.
2. Abele M, Burk K et al. The aetiology of sporadic adult-onset ataxia. Brain 2002;125:961-968.
3. Kumar N. Neuroimaging in superficial siderosis: an in-depth look. Am J Neuroradiol 2010;31:5-14.
4. Koeppen AH, Dentinger MP. Brain hemosiderin and superficial siderosis of the central nervous system. J Neuropathol Exp Neurol 1988;47:249-270.
5. Fearnley JM, Stevens JM, Rudge P. Superficial siderosis of the central nervous system. Brain 1995;118:1051-1066.
6. Bürk K, Skaley M, Dichgans J. High prevalence of CSF-containing cysts in superficial hemosiderosis of the central nervous system. J Neurol 2001;248:1005-1007.
7. Kumar N, Cohen-Gadol AA, Wright RA, et al. Superficial siderosis. Neurology 2006;66:1144-1152.
8. Kumar N, Bledsoe JM, Davis DH. Intracranial fluid filled collection and superficial siderosis. J Neurol Neurosurg Psychiatry 2007;78:652-653.