Superficial Siderosis of the CNS and Otoneurological Manifestations

Thota Ramadass · Nithya Narayanan ·
M. Dhanraj · N. Chidambarnathan

Received: 25 February 2009 / Accepted: 18 October 2009 / Published online: 18 March 2011
© Association of Otolaryngologists of India 2011

Abstract Superficial siderosis is an uncommon condition occurring in central nervous system (CNS) due to deposition of hemosiderin in the subpial meningeal layer causing progressive neurological dysfunction. The classical clinical manifestation is a triad of chronic ataxia, bipyramidal signs and progressive bilateral symmetrical sensorineural hearing loss (SNHL). It has rarely been reported in Indian literature. We report an unusual case of superficial siderosis in a 60-year-old farmer who presented with the *above triad along with involvement of olfactory nerve*. We present this case to highlight the fact that progressive SNHL can be an important sign for the early awareness of this rare disorder. The literature on superficial siderosis is reviewed and the pathogenesis is discussed.

Keywords Superficial siderosis · Sensorineural hearing loss · Subarachnoid haemorrhage · Hemosiderin · MRI · Iron-chelating agents

Introduction

Superficial siderosis of CNS occurs due to recurrent bleeding in the subarachnoid and subpial spaces [1]. It is an uncommon and potentially debilitating disorder. With the advent of magnetic resonance imaging (MRI), the radiologists have been able to diagnose this condition. The clinical otoneurological manifestations in this disorder are progressive SNHL, ataxia and smell disturbances. Superficial siderosis of CNS is a cause for progressive SNHL. Hemosiderin is deposited along the meninges, subpial tissues and subependymal layer of the ventricles due to chronic recurrent subarachnoid bleeding, which induces intracellular uptake of iron leading to damage of glial tissues [2]. Neoplasms, arteriovenous malformations and trauma also contribute to this condition [3].

We present a case report of a 60 year old patient presenting with progressive bilateral hearing loss, anosmia and gait ataxia whose MRI revealed diffuse CNS siderosis, which is probably one of the few case reports from India. We presume in this patient, recurrent bleeding into the subarachnoid space due to chronic trauma resulted in iron deposits in the CNS contributing to the involvement of the first and eighth cranial nerves.

Case Report

A 60 year old man was referred for ENT evaluation. The patient suffered from headache of 5 years duration, progressive hard of hearing and absolute loss of sense of smell. He could not appreciate any strong odours. He also had imbalance occasionally. He gave a history of repeated trauma to the head while entering his house, by a low wooden beam at the entrance. He never experienced any

T. Ramadass (✉) · N. Narayanan
Department of ENT and Head and Neck Surgery, Apollo
Hospital, 21 Greaves Lane, Off Greaves Road, Chennai,
Tamilnadu 600 006, India
e-mail: ramadasstota@yahoo.com

M. Dhanraj
Department of Neurology, Apollo Hospital, Chennai,
Tamilnadu, India

N. Chidambarnathan
Department of Radiology, Apollo Hospital, Chennai, Tamilnadu,
India

discomfort, unconsciousness or vomiting. He was a normotensive, euglycemic person and family history was not contributory. General examination was normal. Neurological examination revealed bilateral loss of smell, loss of hearing, gait ataxia and bipyramidal signs in both upper and lower limbs. Cranial nerve examination showed the involvement of the first and eighth cranial nerves on both sides, which were confirmed by audiological and smell tests. His vision was normal.

MRI of brain with contrast (Figs. 1, 2) showed bilateral diffuse symmetrical hypointensities in the subarachnoid and subpial space in location over the temporal and frontal

lobes on T-2 weighted images. There was obliteration of subarachnoid space at these levels. Rim of hypointensities were found in basal cisterns, ambient cisterns, quadrigeminal plate cistern, lateral sulcal and subarachnoid spaces over cerebellum on both sides. These lesions appeared dark in gradient echo imaging (GRE). There was gross reduction in volume of cerebellum on both sides with prominence of their folia.

MRI report was suggestive of hemosiderin pigment accumulation in brain. Cerebrospinal fluid (CSF) examination showed RBC, no xanthochromia, normal iron and ferritin levels. Audiogram showed bilateral symmetrical SNHL and electronystagmogram was normal.

Fig. 1 T-2 weighted images display symmetrical hypointensity in the subarachnoid space of temporal, frontal lobes and along the cerebellar foliae. Precontrast T-1 weighted images at the level of the brain stem show marked cerebellar degeneration; postcontrast T-1 weighted images reveal no contrast enhancement of these lesions

Fig. 2 Bilateral symmetrical dark signal intensity areas on T-2 weighted gradient echo images are seen over the cerebellar foliae, sylvian fissure and other basal cisternal spaces representing diffuse haemosiderin deposition

Discussion

Superficial siderosis of CNS is a relatively uncommon but under diagnosed cause of progressive, symmetrical, bilateral sensorineural hearing loss. It was first described in 1908 [4]. The largest review of literature to date, reported that patients presented with progressive bilateral SNHL (95%), ataxia (88%) and pyramidal tract signs (46%) [5]. Other manifestations may include dementia (cortical involvement), headache, bladder incontinence, anosmia and sensory deficits. The disorder has been identified in patients of all age groups. Men are affected more than women. CSF analysis intermittently may show xanthochromia and increase in RBC count and elevated iron and ferritin levels [6].

Superficial siderosis is a pathological condition in which hemosiderin—a product of breakdown of blood, is deposited in the subpial layer of CNS [1] leading to progressive and irreversible neurological deficits like sensorineural hearing loss, cerebellar ataxia and myelopathy. The hemosiderin deposition is seen in those parts of the CNS that are adjacent to CSF [7]. Only few cases have been reported in the literature before the advent of MRI, which is the only way to confirm the diagnosis without biopsy. It is accepted that superficial siderosis is caused by chronic bleeding into the subarachnoid space and deposition of blood breakdown products into the subpial layers of the brain and spinal cord. Highly vascular spinal tumours, CNS vascular abnormalities and posterior fossa surgical procedures are the most commonly identified sources of bleeding; other unusual causes are neurosurgical procedures, brachial plexus injury and chronic subdural haematomas [1]. Early case reports noted selective deposition of hemosiderin in the cerebellum, brainstem, ventricle and spinal cord, which explains the clinical presentation of cases. These areas are prone because of localization of special cells (Bergman cells), within the cerebellum, brainstem and spinal cord [8, 9], which attract deposition of hemosiderin. The ability of these special cells

to biosynthesize ferritin in response to prolonged contact with hemoglobin iron is important in the pathogenesis of superficial siderosis. Ferritin synthesis is thought to be neuroprotective by binding iron released by red cells [7]. Tissue damage occurs when this reserve is exhausted. It has been suggested that the excess free iron may then stimulate lipid peroxidation, leading to neuronal injury [10]. The distribution of deposition of siderosis is determined by the CSF exposure and presence of microglia thought necessary to produce apoferritin [11].

Superficial siderosis is a radiological diagnosis and not a clinical one, as there are no diagnostic symptoms. In the past, it was almost exclusively diagnosed by autopsy [12]. With the advent of MRI, siderosis is being identified in asymptomatic patients. In a large series of 8,843 consecutive MRI studies, 0.15% of patients had symptoms consistent with siderosis and 85% of these patients reported no symptoms [5], which only suggests that there may be many undiagnosed cases of siderosis in the population. MR imaging findings in siderosis are pathognomonic (Figs. 1, 2). T₂ weighted imaging reveals characteristic hypointensity along the pial surface and subarachnoid space of the brain.

This finding is detected along the surface of the brainstem and cerebellar vermis. Although a pathological examination revealed that cranial nerves are coated with hemosiderin, only 25% cases exhibited the disease in MR imaging [3]. Sometimes a hemosiderin deposit of VIII cranial nerve can be found. MRI using axial 3-D constructive interference in the steady state (CISS) images is a particularly useful technique for demonstrating this [4]. The extent or distribution of siderosis does not necessarily correlate with the severity of the clinical disease [13]. Some patients with diffuse deposits have minimal symptoms whereas others with less severe findings may be debilitated significantly. In patients with a longitudinal fluid-filled collection in the spinal canal visible on MRI scan; dynamic CT myelogram can sometimes help localize the site of the defect when angiography fails to localize the bleeding source [14].

Cranial nerves I and VIII are the most vulnerable because they remain within the cranium for relatively long distance outside the brain in comparison to other cranial nerves that exit from CNS within 1–2 mm of the brainstem. Cranial nerve VIII remains in the subarachnoid space until it enters the porous acoustics thus making it more vulnerable to damaging effects of subarachnoid haemorrhages. The optic nerve is less likely to be involved in the disease process, as it remains within the CNS and is devoid of the heme-absorbing glial cells along its tract [1]. The preferential involvement of VIII cranial nerve is because of its extensive lining with central myelin, which is also supported by siderosis susceptible microglia. In addition, its course through the pontine cistern exposes the nerve to

abundance of iron. Cranial nerve I is also affected for the same reasons and therefore it is speculated that anosmia is associated with siderosis, a symptom not documented frequently. It is speculated that this nerve comes into contact with significant CSF volumes for a short distance only in its course.

The management of *Superficial siderosis* is arrived at, by eliminating the cause of recurrent subarachnoid bleeding either by surgical or endovascular management. Iron chelators like desferrioxamine and antioxidants have been used as trial for idiopathic CNS siderosis [6]. However there is little evidence to support their effectiveness. Trientine, a copper and iron chelator, was reported to improve patient's symptoms and to lead to decreased CSF iron concentration [15]. In order to reduce the oxidative toxic effect of the heme iron complex, Selegiline (Monoamine oxidase B inhibitor) and Vitamin C have been administered [4]. Steroids were used successfully in one patient with autoimmune disease, but there are no other published studies of the use of steroids in treating non-inflammatory causes of superficial siderosis [16].

Conclusion

Superficial siderosis of the central nervous system is a very rare entity, diagnosed with the help of MRI. It is not a common cause of SNHL. Bilateral SNHL is commonly seen in presbycusis and other retrocochlear lesions. In the intra-axillary pathway of the VIII cranial nerve, SNHL may be due to ischemias, neoplasm, trauma or demyelinating disease. In this patient, we attribute the cause to recurrent subarachnoid haemorrhages from repeated head trauma. This case is interesting because the patient presented with chronic headache and had involvement of the olfactory nerve, both of which are not commonly seen in siderosis of CNS. Siderosis may be suspected in all patients presenting with ataxia, bipyramidal signs and bilateral progressive sensorineural deafness and the radiologist should be alerted so as to suspect this diagnosis. The radiologist is the one who usually picks up asymptomatic cases. This disease is clinically debilitating and potentially irreversible and as far as treatment is concerned, there is not much to offer except trying antioxidants and chelating agents, which might help in detoxicating the iron deposits.

Key Messages

- (1) Superficial siderosis is one of the rare causes of bilateral symmetrical sensorineural hearing loss, to be considered in its differential diagnosis.

- (2) This entity should be kept in mind in patients with history of repeated head trauma.
- (3) MRI has an incredible role in diagnosis of superficial siderosis of central nervous system and it is the radiologist who can diagnose it in asymptomatic patients.

Conflicts of interest None declared.

References

1. Levy M, Turtzo C, Llinas RH (2007) Superficial siderosis: a case report and review of the literature. *Nat Clin Pract Neurol* 3(1):54–58
2. Cammermeyer J (1947) Deposition of iron in paraventricular areas of the human brain in hemochromatosis. *J Neuropathol Exp Neurol* 6:111–127
3. Fearnley JM, Stevens JM, Rudge P (1995) Superficial siderosis of the central nervous system. *Brain* 118:1051–1066
4. Sahin S, Agilkaya S, Karsidag S (2006) SS of CNS: an unusual cause for headache and hearing loss. *Neurol Asia* 11:145–149
5. Hsu WC, Loevner LA, Forman MS, Thaler ER (1999) Superficial siderosis of the CNS associated with multiple cavernous malformations. *Am J Neuroradiol* 20:1245–1248
6. Bracchi M, Savoirdo M, Triulzi F et al (1993) Superficial siderosis of the CNS. MR diagnosis and clinical findings. *AJNR Am J Neuroradiol* 14:227–236
7. Kumar N et al (2007) Superficial siderosis—associations and therapeutic implications. *Arch Neurol* 64(4):491–496
8. Koeppen AH, Borke RC (1991) Experimental superficial siderosis of the central nervous system. I: morphological observations. *J Neuropathol Exp Neurol* 50:579–594
9. Koeppen AH et al (1992) Experimental superficial siderosis of the central nervous system: biochemical correlates. *J Neurol Sci* 112:38–45
10. Koeppen AH, Dickson AC, Chu RC, Thach RE (1993) The pathogenesis of superficial siderosis of the central nervous system. *Ann Neurol* 34:646–653
11. Fearnley J (2002) Superficial siderosis of the central nervous system. *Pract Neurol* 2:50–54
12. Koeppen AH, Dentinger MP (1988) Brain hemosiderin and superficial siderosis of the central nervous system. *J Neuropathol Exp Neurol* 47:249–270
13. Offenbacher H, Fazekas F, Schmidt R, Kapellar P, Fazekas G (1996) Superficial siderosis of the central nervous system. MRI findings and clinical significance. *Neuroradiology* 38:S51–S56
14. Kumar N et al (2006) Superficial siderosis. *Neurology* 66:1144–1152
15. River Y et al (1994) Superficial hemosiderosis of the central nervous system. *Mov Disord* 9:559–562
16. Angstwurm K et al (2002) Superficial siderosis of the central nervous system: response to steroid therapy. *J Neurol* 249:1223–1225