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LETTER TO THE EDITOR

An unusual presentation of superficial siderosis with focal dystonia and 'Giant panda morphology' on MRI: atypical clinicoradiological amalgam

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Introduction

Superficial siderosis of the central nervous system is considered a rare condition, observed on gradient echo T2*-weighted magnetic resonance imaging (MRI) as a typical signal hypointensity outlining the brain surface.

'Classical' superficial siderosis of the CNS, first described in 1908 [1], primarily affects the infratentorial regions and spinal cord, and typically presents with progressive sensorineural hearing impairment, cerebellar ataxia and pyramidal signs, although this form of superficial siderosis is assumed to be caused by chronic intermittent or continuous bleeding. Another type of brain siderosis restricted to the supratentorial compartment and the convexities of the cerebral hemispheres, which has gained recent interest is referred to as 'cortical' superficial siderosis (cSS) [2]. cSS has a different range of potential causes and clinical presentation to classical siderosis, but in older individuals is emerging as a key feature of cerebral amyloid angiopathy (CAA) [3, 4]. cSS is associated with characteristic clinical symptoms, including transient focal neurological episodes, and might be a marker of future intracerebral haemorrhage (ICH) risk in CAA patient [5, 6]. In the population-based Rotterdam Scan Study, using a 1.5-Tesla (T) MRI, the overall incidence of SS was found to be 0.7%, all of whom had cortical microbleeds in their vicinity [7].

Case report

A 69-year-old male came with progressive dysarthria of speech with abnormal posturing of the right lower limb which aggravated on walking for the last 4 months. Abnormal posturing aggravated during walking and activity and subsided with rest. There was, however, no abnormal posturing seen in any other part of the body. There was no history of back pain, headache, hearing loss, numbness or weakness in any part of the body. No history of head trauma, stroke or any surgeries done in the past. No history of any chronic ailments in the past either. On examination the patient was normotensive; spastic dysarthria was noted. Mini-mental status examination score was 28/30 and no cognitive impairment was seen in lobar function assessment. Slit lamp examination did not reveal any Kayser-Fleisher (KF) ring. Cranial nerves were intact and there was no bradykinesia or cogwheel rigidity. Jaw jerk was normal; the patient had dystonic posturing of the right lower limb with dragging of the right foot and exaggerated eversion of the right foot with upgoing right toe noticed during walking. Interestingly, with backward walking, there was some relief in dystonic posturing. Motor and sensory examination were however normal and there was no limb incoordination. The patient had a normal based gait with impaired tandem walking. His routine blood parameters including serum calcium, parathormone levels, vitamin B_{12} levels, thyroid profile and kidney function tests were normal. Subsequently, MRI brain with whole spine screening was done which revealed T2* hypointensities

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seen circumferentially around the brainstem and superior cerebellar folia with vermian and cerebellar hemispheric atrophy seen. The findings suggestive of either calcification or paramagnetic substance deposition like hemosiderin (Fig. 1a–f) Therefore, we did a non-contrast CT head (Fig. 1h) but no calcification or haemorrhages were seen. Also, exaggerated hypointensity of the red nuclei and subtantia nigra and superior colliculus mimicking 'Face of giant panda sign' suggesting a 'Giant panda morphology' was visible on T2-weighted and FLAIR images.MR angiography of brain vessels was also normal (Fig. 1g). The patient was advised for lumbar puncture but the consent couldn't be obtained. In view of the short duration of his complaints, a detailed paraneoplastic workup was done which was non-contributory as well. Therefore, a diagnosis of superficial siderosis with dysarthria and focal limb dystonia was established and to start with, the patient was put on anticholinergics (trihexyphenidyl) and levodopa and carbidopa combination thrice daily.

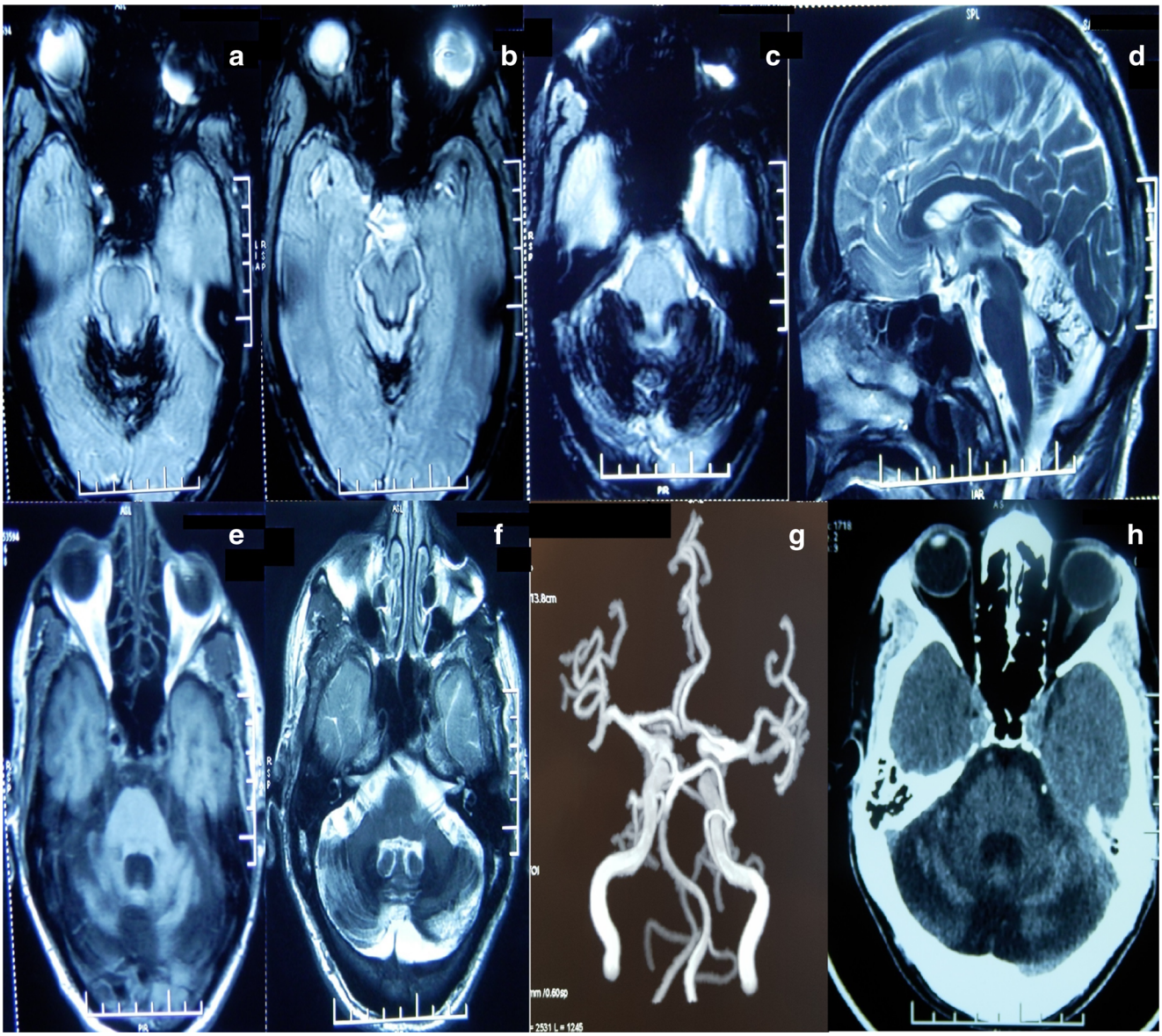

Fig. 1 **a**, **b** GRE T2* images suggestive of hypointensities seen at the level of superior cerebellar peduncle, circumferentially over brainstem and curvilinear hypointensities over temporal cortices suggestive of paramagnetic substance deposition. **c** GRE T2* images showing hypointensities over bilateral cerebellar hemispheres and atrophy of cerebellar folia. **d** T2W sagittal sections showing circumscribed hypointensity over belly of pons and cerebellar hemisphere with atrophy of cerebellar folia. **e** T1W images showing hypointensities over cerebellar hemispheres with cerebellar atrophy. **f** T2W axial sections showing hypointesities over bilateral cerebellar hemispheres with atrophy see. **g** Normal phase contrast MR angiography of brain. **h** Non-contrast CT head showing no hyperdense signals, but atrophy of cerebellar hemispheres and vermis could be seen

Discussion

Superficial siderosis of the CNS is a rare clinical entity that results from chronic hemosiderin deposition in the subpial layers of the brain and spinal cord that leads to gradual progressive neurologic deterioration. Siderosis—derived from the Greek word sideros meaning iron—refers to the deposition of iron-containing compounds in body tissues. Hemosiderin deposition in superficial siderosis creates a superficial brownish-yellowish pigmentation that has a predilection for the superior cerebellar vermis, crests of the cerebellar folia, basal frontal lobe, temporal cortex, brainstem, spinal cord, nerve roots, and cranial nerves I and VIII. Hemosiderin deposition along the cranial nerves and nerve roots extends peripherally up to the junction between the central glial segments of the nerves and peripheral Schwann cells.

The capacity of the brain to biosynthesize ferritin in response to prolonged contact with haemoglobin iron (iron-Hb) is important in the pathogenesis of superficial siderosis. Ferritin synthesis is thought to be neuroprotective by binding extracellular iron-Hb. Accelerated ferritin synthesis in the Bergmann glia of the cerebellum may account for the preferential cerebellar involvement seen in superficial siderosis. This along with chronic intrathecal bleeding overloads the capacity of the cerebellar microglia to biosynthesize ferritin [8]. Thereafter, subpial iron excess facilitates free radical damage, lipid peroxidation and neuronal injury with reactive gliosis, demyelination and neuronal loss [9]. The vulnerability of the eighth cranial nerve is explained by the greater length of hemosiderin deposition along its long glial segment. Hence, the commonest clinical scenario is slowly progressive gait ataxia and sensorineural hearing impairment wherein a clinical history of subarachnoid haemorrhage is often absent. For many years superficial siderosis could only be clearly identified at post-mortem. Common etiological factors associated with superficial siderosis were cerebral arteriovenous malformations, spinal teratoma, following posterior fossa surgery, bleeding pseudomeningocele, familial leptomeningeal amyloidosis and cavernous malformations [10]. Nowadays, with the advent of iron-sensitive MRI techniques, such as T2*-gradient recalled echo (T2*-GRE) or other susceptibility-weighted sequences, it can now be diagnosed in vivo as a characteristic low signal intensity or a dark rim around the outer surfaces of the brain or spinal cord. The role of MRI is not only confined to establish a diagnosis but simultaneously to look for any chronic haemorrhages accounting for deposition of hemosiderin.

The frequent clinical manifestations are ataxia, sensorineural hearing loss, pyramidal signs, anosmia, headache and dysarthria. Interestingly, our patient had a focal lower limb dystonia evident on action, with dysarthria [11]. On the other hand, there was significant involvement of cerebellar folia on MRI but clinically no significant cerebellar signs were evident. Other clinical and radiological signs suggesting an extrapyramidal system or basal ganglia involvement were not there either, so presumably, focal limb dystonia could be attributable to the differential involvement of brainstem and cerebral cortex. Another unusual finding which we term as 'Giant panda morphology' wherein exaggerated hypointensities in red nucleus and substantia nigra in contrast to tegmentum mimics 'Face of giant panda sign' [12], which on the contrary has normal signals in red nuclei and substantia nigra in contrast to hyperintense tegmentum. Our purpose to highlight this sign as a morphology rather; which should not make it clinically confined in context to Wilsons disease where it is frequently been mentioned (Fig. 2).

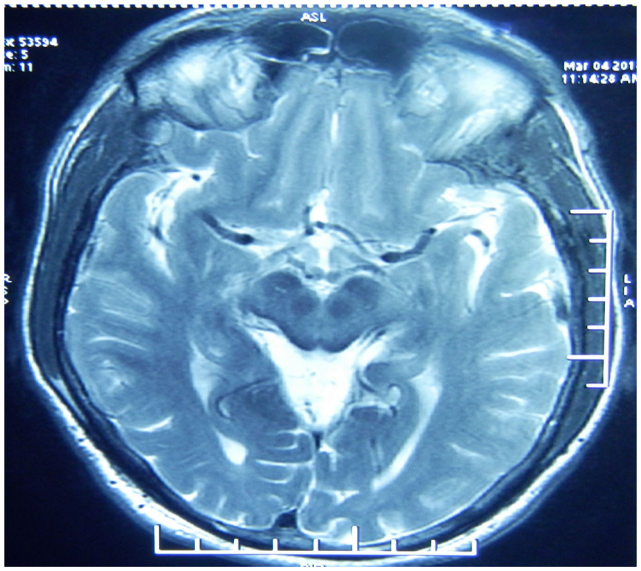

Fig. 2 T2W axial section of brain showing exaggerated hypointensities involving red nuclei, superior colliculus and substantia nigra mimicking 'giant panda' referred as 'Giant panda morphology'

Cerebrospinal fluid studies show the presence of xanthochromia, with high levels of CSF ferritin and presence of siderophages. But, our patient refused for the lumbar puncture [11].

Treatment of superficial siderosis is limited to removing the source of bleeding. Iron chelating agents have not shown any perceptible difference in the outcome of illness. Monoamine oxidase-B (MAO-B inhibitors) and vitamin C supplements have been tried without much benefit, in order to reduce the oxidative toxic effect of heme-iron complex [13].

Conclusion

Superficial siderosis of the central nervous system is a rare entity and an atypical clinical presentation can still unearth hidden clinical facts about the variable manifestations of this ailment. MRI of the neuraxis can help in determining the

cause of chronic bleeding and timely intervention can delay the progression of the disease. Furthermore, MRI changes with an only superficial resemblance to the face of giant panda sign may be termed as 'Face of giant panda morphology' and its presence should alarm us to actively search for neurometabolic conditions other than Wilson's disease.

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