Available online at www.sciencedirect.com
ScienceDirect
journal homepage: http://www.elsevier.com/locate/pjnns

Case Report and Review

Idiopathic infratentorial superficial siderosis of the central nervous system: Case report and review of literature

Andrea Stabile [a], Vincenzo Di Lazzaro [b], Cesare Colosimo [c], Fabrizio Piazza [d], Carlo Ferrarese [a,d], Jacopo C. DiFrancesco [a,d,*]

[a] Department of Neurology, ASST San Gerardo Hospital, Monza, Italy
[b] Unit of Neurology, Neurophysiology, Neurobiology, Department of Medicine, University Campus Bio-Medico, Rome, Italy
[c] Radiology and Neuroradiology Unit, Diagnostic Imaging Area, Fondazione Policlinico Universitario A. Gemelli, Institute of Radiology, School of Medicine, Catholic University, Rome, Italy
[d] Milan Center for Neuroscience, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy

ARTICLE INFO

Article history:
Received 11 September 2017
Accepted 18 October 2017
Available online xxx

Keywords:
Superficial siderosis
Cerebral amyloid angiopathy
Hemosiderin
Brain MRI
Susceptibility weighted imaging

ABSTRACT

The superficial siderosis (SS) of the central nervous system (CNS) is a rare condition characterized by a wide range of neurological manifestations directly linked to an acquired iron-mediated neurodegeneration. First described more than 100 years ago, only recently SS has been divided into two distinct entities, according to the distribution of iron deposition in the CNS: cortical superficial siderosis (cSS) and infratentorial superficial siderosis (iSS). Here we describe an adult case of iSS, with detailed clinical and radiological features. Moreover, we extensively review the literature of SS, particularly focusing on the pathogenesis, clinical-radiological classification, diagnostic algorithm and treatment options of this rare condition.

1. Case report

A 45-year-old Caucasian man presented with an 8-year history of slowly progressive gait difficulties, tinnitus and emotional liability. The patient also reported pharmacoresistant migraine since the age of 23, with gradual increase in intensity and number of attacks over the last few years. At the age of 27, he experienced a transient episode of acute headache and diplopia without papilledema, treated with oral corticosteroid therapy with gradual resolution of the symptoms. At that time, brain computed tomography (CT) scan and brain–spinal cord magnetic resonance imaging (MRI) were unremarkable.

* *Corresponding author at*: Department of Neurology, San Gerardo Hospital, School of Medicine and Surgery, University of Milano-Bicocca, Via Pergolesi, 33, 20052 Monza (MB), Italy.
E-mail addresses: jacopo.difrancesco@unimib.it, jacopo.difrancesco@gmail.com (J.C. DiFrancesco).
https://doi.org/10.1016/j.pjnns.2017.10.006
0028-3843/

Please cite this article in press as: Stabile A, et al. Idiopathic infratentorial superficial siderosis Q1of the central nervous system: Case report and review of literature. Neurol Neurochir Pol (2017), https://doi.org/10.1016/j.pjnns.2017.10.006

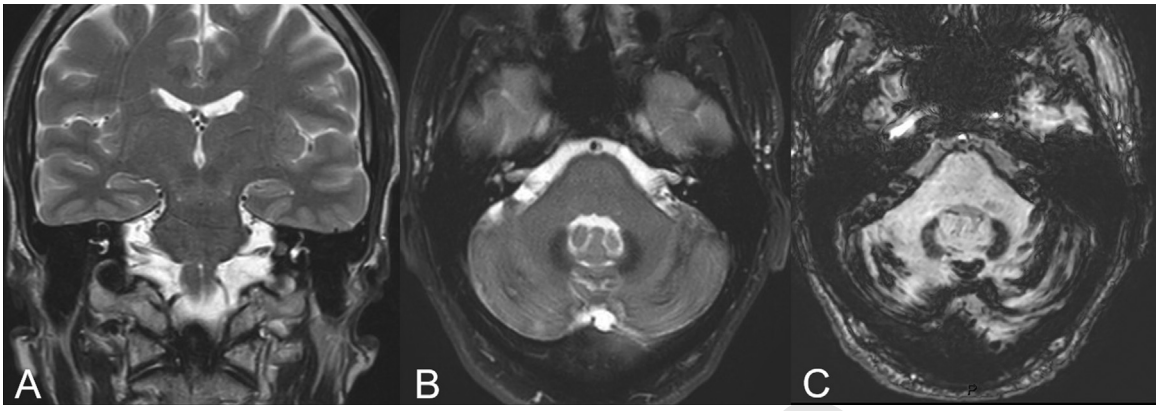

Fig. 1 – Brain MRI showing the principal neuroradiological features of iSS. (A) Coronal FSE T2-weighted image. (B) Axial fat-saturated FSE T2-weighted image. (C) Axial SWI T2*-weighted image. On FSE T2-WI (A and B) only a faint rim of hypointensity is seen on the brainstem and cerebellar surface. On T2*WI obtained by susceptibility weighted imaging sequence (SWI) there is a prominent evidence of paramagnetic deposition (hemosiderin) along the surface of the brainstem and cerebellum, as well as on the cisternal course of cranial nerves.

At the age of 44, a 1.5 T brain MRI, including T2* gradient echo (GRE) and susceptibility-weighted imaging (SWI) sequences, revealed a prominent hypointensity mainly along the surface of the infratentorial structures, particularly on the surface of the brainstem, the intracranial part of facial and vestibulocochlear nerves bilaterally and the cerebellum (paravermis cerebellar cortex and dentate nuclei), associated with atrophy of the cerebellar vermis (Fig. 1). No intraparenchymal hemorrhagic lesions, nor contrast enhancement were reported. No signs of intracranial hypertension nor *pseudotumor cerebri* were identified. Spinal cord MRI did not reveal any relevant disease, such as neoplasms, vascular malformations and dural abnormalities, in particular dural fistula or intraspinal fluid-filled collection.

The patient was then admitted to our Department for further diagnostic investigations. There was no evidence of arterial hypertension nor injury of the brain and spinal cord. Familiar history was unremarkable for neurological diseases. Neurological examination revealed horizontal bilateral nystagmus, minor increase in muscle tone at the lower limb bilaterally and hypoesthesia/dysesthesia at the left lower limb. Deep tendon reflexes were diffusely brisk and Babinski's sign was slightly positive bilaterally. Slight oscillations in Romberg were noted and gait was wide-based and unsteady, without marked ataxic features. The patient did not report neck stiffness or hearing loss. There was no abnormality in his coordination and no evidence of cognitive impairment. Routine laboratory tests were unremarkable. Cerebral and cervical digital subtraction angiography (DSA) resulted negative for aneurysms, other vascular malformations or any cause of hemosiderin deposition. The patients refused the execution of the lumbar puncture. The electromyography excluded the presence of polyneuropathy. Rectal mucosa biopsy excluded systemic amyloidosis.

Based on clinical features and neuroimaging findings, no major cause of occult bleeding in the CNS was identified and diagnosis of idiopathic iSS of the CNS was performed.

2. Review of literature

The SS of the CNS is an acquired neurological disorder resulting from hemosiderin deposition in the subpial layers of the brain, cranial nerves and spinal cord producing a progressive white matter and neuronal damage [1]. Hamill defined SS as ''melanosis of the brain, cord and meninges'' in the first report in literature [2]. Although previously defined as a rare condition, thanks to the development of specific MRI sequences for the detection of hemosiderin in the CNS, SS has been increasingly recognized in the recent past.

Even if the pathogenic mechanisms are not known yet, SS is supposed to result from a subtle, low-volume, enduring or repetitive, leakage of blood (''minor bleeding'') into the subarachnoid space [3]. Other important phases contribute to the clinico-radiological expression of SS: blood dissemination by the cerebrospinal fluid (CSF), hemolysis and entrance of heme into the exposed tissue, conversion of heme in free iron, ferritin and hemosiderin and, in the end, direct tissue damage. Only CNS tissues convert the heme in CSF to hemosiderin. In response to the exposure to the heme, Bergmann glia and microglia synthetize hemoxygenase-1 (HO-1) and ferritin. HO-1 breaks down the heme into free iron and biliverdin, while ferritin binds free iron to produce hemosiderin, the primary cause of the ''dark rim'', corresponding to the radiological hallmark of SS [4,5]. Chronic or intermittent red blood cells' extravasation in the subarachnoid space overwhelms toxic iron sequestering of glial cells, leading to iron accumulation with oxidative damage, membrane dysfunction and consequent neurodegeneration [1]. Usually, a period of many years is between the bleeding and the onset of the clinico-radiological signs of SS [5]. In the CNS, the posterior fossa seems to be mainly affected by the iron deposition because of the abundance of microglia and Bergmann glia, in particular in the cerebellum and vestibulocochlear nerves [6]. Furthermore, secondary atrophy of the cerebellar convexities and superior

Please cite this article in press as: Stabile A, et al. Idiopathic infratentorial superficial siderosis Q1of the central nervous system: Case report and review of literature. Neurol Neurochir Pol (2017), https://doi.org/10.1016/j.pjnns.2017.10.006