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Case Reports & Case Series

Superficial siderosis of central nervous system in a patient with hemophilia

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ABSTRACT

Superficial siderosis of central nervous system is a rare disease that consists in the continuous subarachnoid leakage of red blood cells into subarachnoid space, leading to progressive neurological deficits. We present the first clinical description of a patient with superficial siderosis and hemophilia as the trigger of bleedings. Brain MRI was crucial for diagnosis.

1. Introduction

Superficial siderosis of central nervous system is a rare disease that consist in the continuous subarachnoid leakage of red blood cells into subarachnoid space [1,2]. Small repeated bleedings leads to the neurotoxic heme converts to hemosiderin deposits in the subpial layers of the brain, cranial nerves and spinal cord. Two variants have been described according to central nervous system (CNS) distribution: cortical superficial siderosis and infratentorial siderosis (with or without supratentorial involvement). Main clinical features are persistent focal neurological deficits in cortical superficial siderosis, and progressive spastic paresis, neurosensorial hypoacusis and ataxia when location is infratentorial [3]. Subarachnoid hemorrhage from intracranial aneurysms, arteriovenous malformations, tumors, cerebral amyloid angiopathy, and spinal epidural cerebrospinal fluid collections are described as the most frequent etiologies [3,4].

2. Case report

We present a 48-year-old patient with mild hemophilia A, that presented slowly progressive spastic paraparesis of lower limbs since he was 39-year-old. His medical history revealed chronic Hepatitis C (HCV), without HIV infection. History of important smoking habit was present, but no inhibitor was known. He was operated from spontaneous subdural hemorrhage between levels D7-D11 at age of 40. After the surgery, patient remained with spastic paraparesis in lower limbs and neurogenic bladder but he could be able to walk autonomously with crutches. However, these symptoms slowly progressed and conditioned several falls, provoking several soft tissues and joint hemorrhages along one year before the admission in our hospital. In addition, he noticed progressive mild paresis in upper limbs, bilateral neurosensorial hypoacusis and progressive gait difficulties in last two years before consultation. Four years after the surgery, a spinal magnetic resonance imaging (MRI) performed in other medical center, described a chronic spinal cyst in D9 but images were not available. We show in Fig. 1 the spine MRI performed in our medical center at the time of consultation (nine years after symptomatology started).

Spine MRI and Brain MRI are shown in Figs. 1 and 2.

3. Discussion

To the best of our knowledge, this is the first case report of superficial siderosis of central nervous system in a patient with hemophilia. Repeated unadvised central nervous system mild bleedings are supposed to condition the development of siderosis in this patient. However, several reflections should be remarked.

Initially, the damage of the spinal subdural hemorrhage was supposed to explain neurological impairment in lower limbs and was the main factor of delay in diagnosis in this patient. However, this disease is often underdiagnosed [2]. Second, the presence of spinal cysts has been described in cases of superficial siderosis and possibly have influence on blood leakage to subarachnoid space [3]. Also, spinal trauma or prior surgery have been identified as mechanism of cerebrospinal fluid (CSF) leakage that lead to CSF hypotension and intradural vascular engorgement favouring increased CSF erythrocytes in superficial siderosis [5]. This way, in our patient, the history spinal hemorrhage surgery and epidural spinal cyst should warn us to include superficial siderosis in differential diagnosis. Third, the magnetic resonance imaging (MRI)

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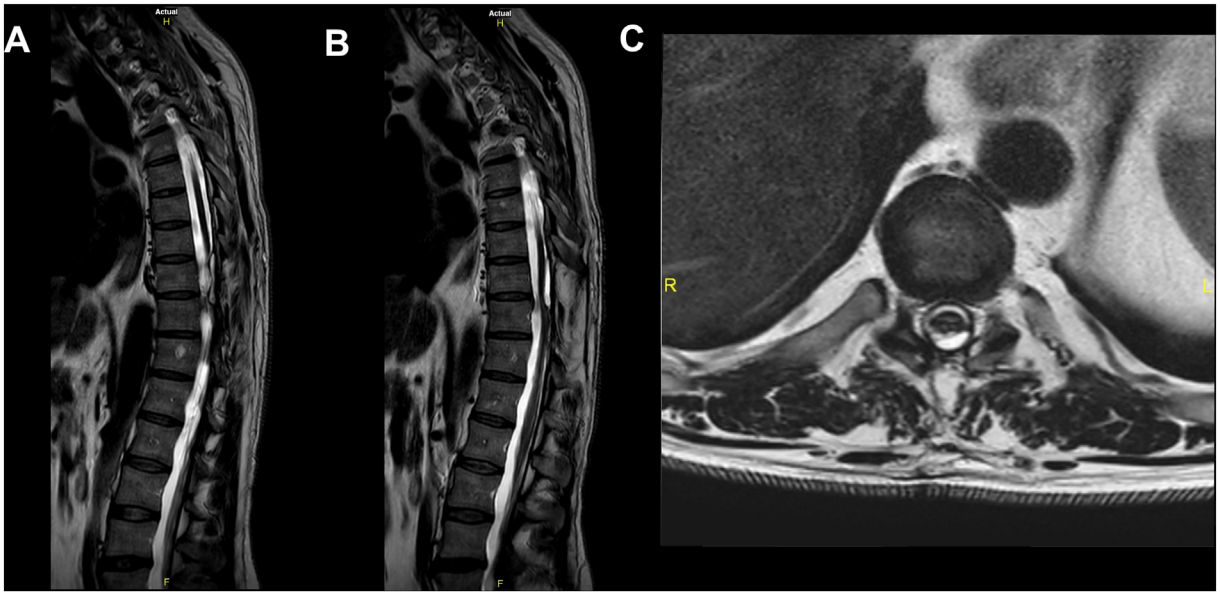

Fig. 1. Dorso-lumbar spine MRI on sagital axis T2-weigthed (A,B) and D9 transversal slice (C). A and B shows spinal atrophy and epidural cyst between D9-D10.

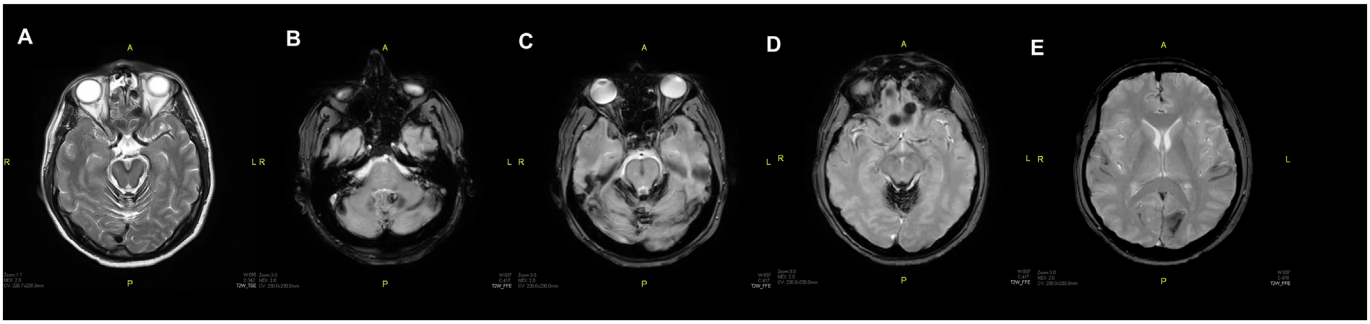

Fig. 2. Brain MRI on transversal slices, T2-weighted (A) and echo-gradient (B-E). Hemosiderin hypointensity is evidenced peripherally in midbrain (A). Also hemosiderin is found in the surfaces of cerebellum, pons, midbrain and temporal and occipital sulcus (B-E).

with magnetic susceptibility sequences was crucial in the diagnosis of this patient and it is the most important tool to detect it [3]. Last, despite the fact that hemophilia tends to produce whole body-parts bleeding after minor traumatisms, there are absence of previous central nervous system siderosis descriptions in hemophilic patients. Only, cerebral microbleeds (CMB) have been described commonly in patients with hemophilia. The older age, HCV infection, cardiovascular risk factors, and the presence of inhibitors were associated with CMB [6]. Thus, isolated hemophilia may not be enough condition to produce superficial siderosis of CNS. Hence, we suggest that impairment in hemosiderin clearance on CNS may be important in superficial siderosis development in hemophilic patients with this comorbidity.

Therefore, early diagnosis is important in these patients to try new therapies. Iron chelators, such as deferiprone, have shown potential benefits in central nervous system iron load. In one two-year observational study was shown a reduction detected by MRI in half of patients [7]. However, further clinical trials should be performed to confirm these findings. Our patient was proposed as compassionate use and is pending to receive deferiprone.

4. Conclusion

Hemophilia can be a triggering factor to develop repeated central nervous system mild hemorrhages leading to superficial siderosis in patients with HCV, cardiovascular risk factors, spinal surgery and spinal cysts.

Declaration of Competing Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

All authors agree with journal terms, and state this is an original unpublished work, and is not being submitted for publication elsewhere.

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We are grateful to the patient for consenting this publication.

Ethical standards

Patient permission was obtained.

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