Research Square

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Superficial siderosis of the central nervous system mimicking degenerative cerebellar ataxia

Quan-Fu Li
The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine)
Qing Zhang
The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine)
Juan Zhang
The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine)
Guan-shu Qi
qgs7779@163.com

The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Chinese Medicine)

Research Article

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Abstract

Background

Superficial siderosis of the central nervous system (SSCNS) is a rare neurological disorder characterized by hemosiderin deposits on the surface of the brain, spinal cord, and cranial nerves. SSCNS is easily misdiagnosed and the etiology is unknown in some patients.

Case presentation:

We reported a 64-year-old Chinese male patient of SSCNS, who was diagnosed as neurodegenerative cerebellar ataxia for ten years. Susceptibility-weighted imaging (SWI) showed extensive hemosiderin deposits on brain surfaces. Spinal magnetic resonance hydrography revealed a dural defect and cerebrospinal fluid leak at the third thoracic vertebrae level. He received iron chelator (deferoxamine mesylate) and the neurological symptoms improved.

Conclusions

SSCNS is easily misdiagnosed at the early disease stage and SWI is sensitive to detect superficial siderosis. Iron chelator is a worthwhile drug treatment option for SSCNS.

Introduction

Superficial siderosis of the central nervous system (SSCNS) is a rare neurodegenerative disease characterized by hemosiderin deposits on the surface of the brain, spinal cord, and cranial nerves, caused by chronic recurrent bleeding into the cerebrospinal fluid[1]. The typical clinical features of SSCNS include progressive hearing loss, cerebellar ataxia, and myelopathy[2]. The diagnosis of SSCNS is mainly based on clinical manifestations, cerebrospinal fluid test and brain magnetic resonance (MR) imaging examination, especially susceptibility-weighted imaging (SWI)[3]. However, some of the early SSCNS patients are easily misdiagnosed for the atypical symptoms and lack of brain SWI. So far, effective treatments with evidence-based medicine of SSCNS have rarely been reported.

We report a case of SSCNS with an initial symptom of dizziness and gait ataxia. He was diagnosed as degenerative cerebellar ataxia for ten years. The etiology of SSCNS in this patient was spontaneous intracranial hypotension due to cerebrospinal fluid leakage. After treatment with an iron chelator, the symptoms improved. The case is helpful to the diagnosis and treatment of SSCNS.

Case report

A 64-year-old Chinese male patient was admitted to hospital suffering from progressive unsteady gait for several years. He presented severe dizziness initially in his fifth decades of life. Then he couldn't walk steadily and appeared dysphagia and hearing impairment. He went to many hospitals to seek medical examination and treatment. Brain MR imaging showed severe cerebellar atrophy. Metabolic and hereditary factors were excluded. His clinical features were attributed to degenerative cerebellar ataxia disease, but the etiology was unknown. Although he had tried mecobalamine, idebenone and coenzyme Q10, the treatment was noneffective. He appeared memory decline and complete hearing loss at his 60 years old.

His past medical history was negative. He had no history of receiving anticoagulant drugs, alcohol abuse, brain injury or accident. A neurologic examination revealed slurred speech, severe hearing impairment, unstable finger-nose test, positive Romberg's sign and unsteady gait. General medical examination results were normal.

Serum ferritin was significantly higher than normal level (735.7ng/ml vs normal 16.4-293.9 ng/ml). A lumbar puncture was performed and cerebrospinal fluid (CSF) protein was slightly elevated to 77mg/dL (normal, < 42) with red cell count 628/μL. The intracranial pressure was low to 70mm H2O. Other blood tests showed that tumor markers, thyroid function, syphilis antibodies, autoimmune serum markers were all negative. Electric audiometry revealed binaural sensorineural deafness.

Cranial sagittal T1 weighted MR imaging showed significant cerebellar atrophy (Fig. 1A). Axial SWI showed extensive hemosiderin deposits on bilateral cerebral cortex, brainstem, auditory nerves, and cerebellum surfaces (Fig. 1D-E). In contrast, axial T2 and flair MR imaging revealed this abnormal signal not obviously (Fig. 1B-C). Sagittal T2-weighted gradient-echo imaging of cervical spine showed hemosiderin deposition along and around the entire cord surface (Fig. 1F). To find the etiology of the chronic bleeding, we performed brain magnetic resonance artery (MRA) and carotid artery of computer tomography angiography (CTA), but no aneurysms or vascular malformations was found. Fortunately, epidural CSF collection was showed in the sagittal T2-weighted MR imaging of thoracic spine (Fig. 1G) and spinal MR hydrography (Fig. 1H), which suggested a dural defect and CSF leak at the third thoracic vertebrae level.

Finally, SSCNS and spontaneous intracranial hypotension with CSF leak were diagnosed, but the patient refused surgery. He received deferoxamine mesylate (an iron chelator) infusions 3000mg (50mg/Kg) and 2000 milliliter intravenous fluids per day for 5 consecutive days a week. Four weeks later, his dizziness was significantly relieved and walking instability symptoms improved, but the hearing impairment was the same. There were no serious adverse events during the whole treatment.

Discussion

SSCNS is a rare neurological disorder. We report a case of SSCNS diagnosed as degenerative cerebellar ataxia for ten years, which was responsive to the treatment with iron chelator. The symptoms of SSCNS are particularly numerous. The most common clinical manifestations are ataxia, hearing loss, and

pyramidal tract sign. Other clinical symptoms include headache, dizziness, cognitive decline, vision loss, tinnitus, epilepsy, tremor, olfactory dysfunction, back pain, constipation disorder, sexual dysfunction and so on[4–6]. The early symptoms are atypical and confusing. If the clinician has insufficient understanding of SSCNS disease, it's easy to be misdiagnosed.

In addition to autopsy, the detection of superficial siderosis require imaging support. Brain MR imaging is an important imaging method for the diagnosis of SSCNS. The appearance of SSCNS on MR imaging is derived from hemosiderin-based paramagnetic blood breakdown products, which cause uneven magnetic field distribution and appear as linear low signals along the surface of the cerebral sulci on T2*-GRE and SWI sequences[7]. The detection of superficial siderosis depends on the sequence type and parameters, including spatial resolution, echo time, layer thickness, and magnetic field strength[4]. Several recent studies have shown that SWI is more sensitive to superficial siderosis detection than T2*-GRE, showing low signal around the cerebral, brain stem, cerebellum, spinal cord, and cranial nerves[8, 9]. Most superficial siderosis cannot be detected on T1WI, but can occasionally be displayed on T2WI. In our case, superficial siderosis was not demonstrated obviously on T1WI and T2WI, so the patient was misdiagnosed for several years until he did the SWI sequence. Therefore, SWI should be performed early especially for the patients with unexplained dizziness and cerebellar ataxia.

A biomarker for early diagnosis of SSCNS is urgently needed at a preclinical phase without symptoms or imaging signs. SWI is sensitive to superficial siderosis detection. However, the imaging findings of SSCNS might represent a late stage of disease[10]. The iron-sensitive imaging technology needs to be further developed, thus contributing to the early diagnosis of SSCNS. There is also a lack of body fluid biomarkers. Hani et al reported that CSF ferritin was elevated in patients with spontaneous intracranial hypotension, who were potentially at risk of developing superficial siderosis[11]. The present case showed that serum ferritin was significantly higher than normal level. Serum and CSF ferritin may be a potential biomarker for the early diagnosis and evaluation of therapeutic effect of SSCNS, which need more research to confirm.

Chronic recurrent subarachnoid hemorrhage leads to free iron in the cerebrospinal fluid, resulting in neuronal death, glial cell proliferation and hemosiderosis[12]. The essential treatment of SSCNS is to identify the source of chronic subarachnoid hemorrhage. According to the location of hemosiderin deposition, SSCNS was classified as cortical superficial siderosis and infratentorial superficial siderosis by Wilson et al[3]. Typical SSCNS is thought to be caused by repeated subarachnoid hemorrhage due to trauma, brain tumor, cerebral amyloid angiopathy or vascular malformation[1][1]. Some etiologies may be treated by surgery to remove the cause[13, 14]. The present patient was diagnosed with a spontaneous CSF leak, and the bleeding source was attributed to a ventral dural defect. Two theories have been proposed to explain the pathogenesis: bleeding from intracranial veins caused by brain sagging due to intracranial hypotension or bleeding from fragile vessels associated with dural defect[15, 16].

The main treatment for SSCNS is to remove the etiology of the bleeding. The choices of treatment for cases with CSF leak are epidural blood patch and neurosurgical dural repair[17]. However, currently there is a lack of effective drug treatment for hemosiderosis. Previous studies have shown that SSCNS may be treated by iron chelator[18, 19], which is still controversial[20]. Our patient refused epidural blood patch and neurosurgery. Fortunately, his symptoms were improved with the use of plenty of intravenous fluids and deferoxamine mesylate, which is widely used to reduce iron accumulation and deposition in tissues[21]. It suggests that iron chelator is a worthwhile drug treatment option for SSCNS.

In conclusion, SSCNS with spontaneous intracranial hypotension due to CSF leakage is extremely rare and easily misdiagnosed. SWI is sensitive to detect superficial siderosis. In addition to surgery, the drug iron chelator is a worthwhile treatment for SSCNS. Our results contribute to the diagnosis and treatment of SSCNS.

Declarations

Ethics approval and consent to participate

This case report was approved by the Ethics Committee for Clinical Medical Research of the First Affiliated Hospital of Zhejiang Chinese Medical University.

Consent for publication

The written informed consent has been obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

Data are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

QF-L, QZ, JZ evaluated and managed the patient. QFL wrote the manuscript and prepared the figures. GS-Q revised the manuscript for important intellectual content and finalized the manuscript. All authors read and approved the final manuscript.

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Figures

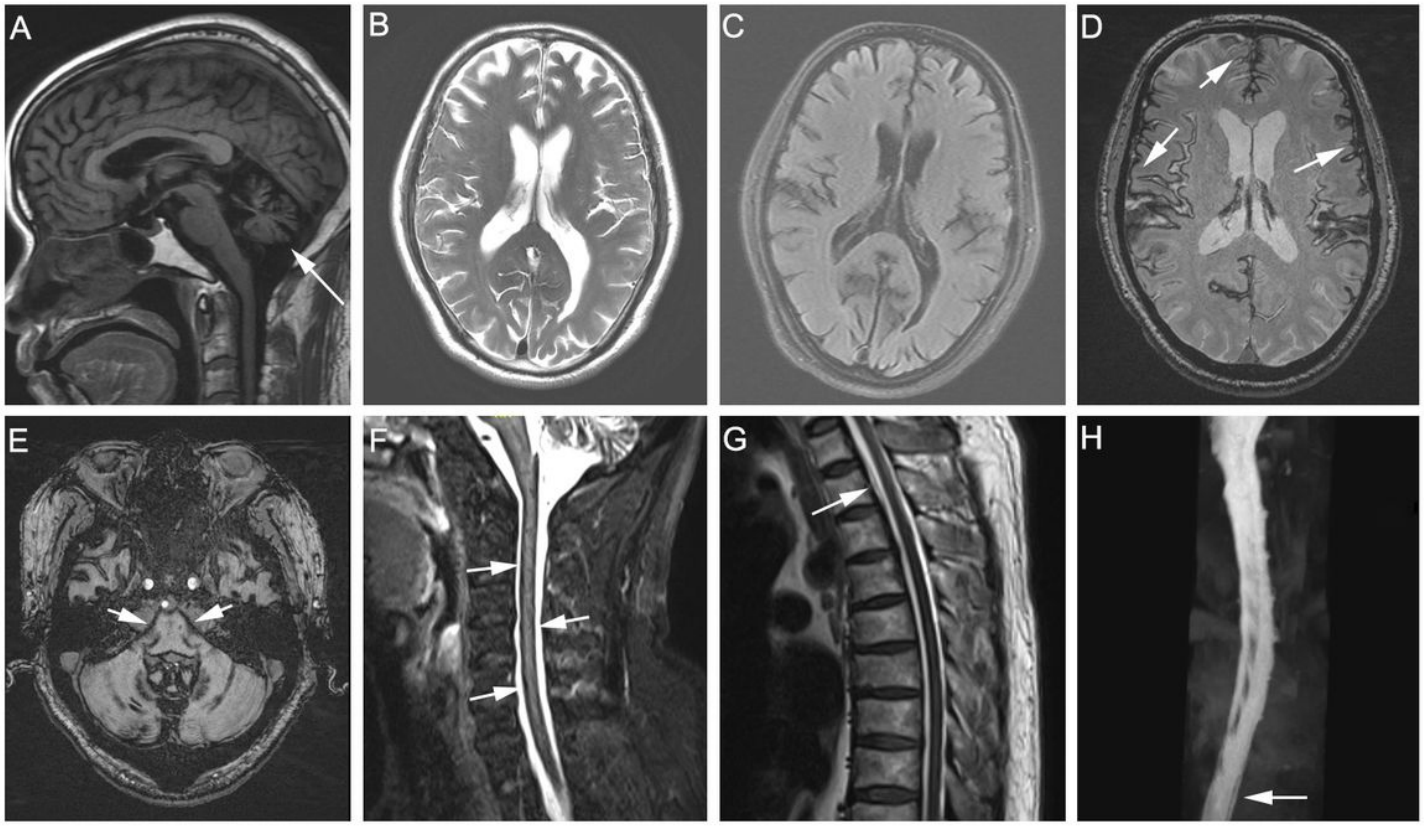

Figure 1

MR imaging of the present patient with superficial siderosis of the central nervous system. Sagittal brain T1 weighted MR imaging (A) showing significant cerebellar atrophy. T2 weighted MR and Flair imaging (B, C) were normal. Axial susceptibility-weighted images (D, E) demonstrating extensive cortical and infratentorial superficial siderosis (arrows). Sagittal T2-weighted tirm imaging of cervical spine (F)

showing hemosiderin deposition along and around the entire cord surface. Sagittal T2-weighted MR imaging of thoracic spine (G) and spinal MR hydrography (H) showing epidural CSF collection (arrows) at the T3 level.