Superficial Siderosis Revealed by Isolated Cognitive Impairment

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Superficial siderosis (SS) is a rare disorder due to chronic bleeding into the subarachnoid or intraventricular space. The most common clinical presentation is progressive ataxia and hearing loss. The authors report two patients who presented with dementia as the primary manifestation of SS. The cognitive impairment marked by cortical frontotemporoparietal dysfunction was consistent with the pattern of signal abnormalities seen on brain magnetic resonance imaging (MRI). Diagnosis of SS must be considered when T2*-weighted MRI shows typical signal hypointensity outlining the brain and spinal cord surfaces. Performing such MRI sequences appears to be of particular interest in the context of dementia etiological diagnosis.

Key Words: Dementia—Diagnosis—Superficial siderosis.

Brief Report

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Superficial siderosis (SS) is an uncommon disorder due to chronic or repeated bleeding into the subarachnoid or intraventricular space. The bleeding, for which source remains unidentified in half the cases (1), leads to hemosiderin deposits in the central nervous system (CNS) and the spinal cord subpial layers parenchymal damage.

The most common clinical presentation is progressive cerebellar ataxia and sensorineural hearing loss (2). We report here two cases of SS revealed by a subacute dementia and discuss this atypical clinical presentation.

CASE REPORTS

Case 1

A 71-year-old man treated for hypercholesterolemia and chronic obstructive bronchitis had been referred to the department of geriatrics because of a cognitive impairment and neuropsychiatric disorders. He had been presenting for 1 year with progressive cognitive and behavioral changes including fluctuating disorientation to time and space, slow ideation, apathy, and anxiety. His relatives noted hygiene deficiency, oralalimentary, and dressing troubles. Antidepressant treatment had not improved his behavior. Bilateral hearing loss had been observed for 2 years.

On initial medical examination, the patient appeared cooperative but perplexed. He showed poor attention and perseverations, but he was well oriented to time and space. He could not recall the three words of the Mini-Mental State Examination (MMSE), for which the total score was 22/30. Lexical fluencies were poor, the patient providing only seven animal names and six names beginning by the letter “p” in 2 minutes. Visuoconstructive abilities were impaired. Gait was normal and ocular movements were full. No cerebellar, pyramidal, or parkinsonian syndrome was observed. Remaining clinical examination was normal.

Standardized neuropsychological testing confirmed an impairment of attention, and executive and visuoconstructive functioning. Brain magnetic resonance imaging (MRI) showed a clear marginal signal hypointensity of the cortex, especially in left frontal and parietal areas on T2*-weighted scans (Figure 1). No coagulation deficit or metabolic disorder was detected. Cerebrospinal fluid (CSF) was normal. Intracranial and spinal magnetic resonance angiography (MRA) did not detect any vascular lesion.

These features led to the diagnosis of brain SS.

Case 2

A 73-year-old Spanish man affected by chronic respiratory insufficiency was referred to the neurology department by his family because of cognitive and behavioral disorders progressing for 1 year. Neurosurgery had been performed 20 years earlier to cure a posterior brain benign cyst. The patient developed cognitive and behavioral disorders shortly after a fall responsible for a lumbar vertebra fracture. His wife described progressive apathy and indifference to domestic activities and to his relatives. He showed marked memory loss for recent events with no confabulation. Acetylcholine esterase inhibitors prescribed 4 months before our examination had not modified the symptoms.

On neuropsychological examination, the patient was well oriented to time and space. He was able to recall only one of three MMSE words, for which the total score was 24/30.

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Verbal memory retrieval as assessed by the RI-RL16 test, working memory, lexical fluencies, and mental flexibility was impaired suggesting an executive dysfunction. Language comprehension and naming were spared. Mental calculation and visuoconstructive abilities were dramatically reduced, as well as attention and speed of processing. On clinical examination, the patient presented with slowness of gait, but no Parkinsonian or cerebellar sign.

The xanthochromic CSF revealed 1,870 red blood cells/mm$^3$, protein elevation (0.63 g/L), and the presence of siderophages and erythrophages. Brain and spinal MRI revealed typical aspects of SS (Figure 1). Cranial and spinal artery MRA and conventional angiography were normal. The chronic intracranial bleeding was related to the neurosurgical history.

**DISCUSSION**

These two patients presented a rapid progressive cognitive impairment initially related to neurodegenerative dementia. The diagnosis of SS was suggested by neuroimaging as clinical presentation was atypical. To our knowledge, these are the first reported cases of SS revealed by a cognitive decline.

Indeed, the most common clinical presentation of SS is marked by a slow progressive gait ataxia, associated to hearing loss and anosmia (2). These cardinal features related to cerebellar and cranial nerve dysfunction occur in approximately 90% of cases (3). Fearnley and colleagues noted that 95% of the 63 cases of SS of the central nervous system they reviewed had sensorineural deafness, 88% a cerebellar ataxia, and 76% pyramid signs (3). In the ataxia cases, limb and gait ataxia was observed in 56% and predominant gait ataxia in 44%. Nystagmus was present in 22%. Other cranial nerve may be involved like oculomotor (3), optic, and trigeminal nerves (4). Moreover, pyramidal and somesthesic signs, as well as vesicosphincterian disorders suggestive of a neurogenic bladder, are not exceptional (1), suggesting sometimes a spinal cord syndrome (5). Our patients presented with unusual clinical symptoms because the first

Figure 1. Axial T2*-weighted brain magnetic resonance imaging showing typical signal hypointensity reflecting hemosiderin deposition in brain surfaces—upper row (Case 1): in left frontal (upper left) and parietal (upper right) areas; lower row (Case 2): in the midbrain (lower left), Sylvian, and interhemispheric fissures (lower right).
case did have hearing loss but no cerebellar sign and the second had none of these last features.

Few reports formally described a cognitive impairment in SS (3, 6–9), but 24% of the patients may develop dementia during the course of the disease (3). However, revelation of SS by cognitive disorders as reported in our study is original. Dementia occurring lately in SS is usually severe, causing major disability in 16% (3). Cognitive impairment and dementia observed in this disease may be related to cortical lesions and functional impairment. Autopsy studies show that no superficial area of the cerebral cortex is spared, although maximal damage, including atrophy and gliosis underly the iron deposition (8), is always in the hindbrain structures and frontal lobes. Clinical signs reflecting a cortical dysfunction may be related to the regional cortical location of predominant SS lesions. As depicted by our cases, a dysexecutive syndrome may be associated to iron deposition in frontal lobes and visuoconstructive impairment to lesions in parietal areas.

Moreover, no correlation seems to be observed between the duration of disease and the severity of the dementia (3). To date, in all published cases, dementia occurred later than other neurological symptoms, mainly gait and hearing disorders. In the literature, the patients developed a cognitive impairment from 1 (8) to 32 years (7) after clinical onset. Interestingly, a distinct cognitive pattern related to SS, marked by an impairment of speech production, executive functions, and visual memory, has been suggested (10). In our patients, the good anatomofunctional correlation between the neuropsychological impairment and the location of SS on brain MRI suggests that the main symptoms are directly related to the siderosis, which often affects heterogeneously the cortex. Indeed, in case 1, the impairment of executive and visuoconstructive functions may be related to frontal and parietal cortex involvement that is mostly concerned by siderosis as assessed by brain MRI. SS involves all subpial structures in the CNS, but some are more severely affected. Typically, the pigmentation has a predilection for the hindbrain structures, especially the cerebellum. The cranial nerves I and VIII, temporal cortex, basal frontal lobe, and brainstem are often damaged (1). The deep nuclei are classically not involved.

The history and clinical examination of the two presented cases initially suggested a neurodegenerative disorder. Only T2*–weighted MRI corrected the diagnosis by showing the typical signal hypointensity outlining the brain and spinal cord surfaces (4). These MRI sequences are crucial to detect these hemosiderin deposits. As illustrated by case 1, CSF analysis may be normal because of the intermittent nature of the bleeding (2). The origin of the chronic bleeding may be detected by conventional angiography or MRA of the brain and the spinal cord. Negative MRA should lead to conventional angiography. Despite these investigations, the cause of bleeding is often not detected. A history of intradural cranial surgery or injury is a well-recognized risk factor for later development of SS. Owing the widespread use of MRI, SS may be increasingly recognized.

The treatment of SS depending on identification of the bleeding source is neurosurgical or neuroradiological. Post-treatment follow-up has often been associated with a lack of further progression, even some improvement in an isolated case. Posttreatment CSF examination can show resolution or decrease of the xanthochromia and CSF red blood cells. Given the slow progression of SS, a long follow-up is required after treatment.

CONCLUSIONS

In conclusion, dementia can reveal SS, which diagnosis can be performed easily by T2*–weighted MRI with a high sensitivity and specificity. As a history of trauma or prior intradural surgery of the CNS is not enhanced in all cases and treatments can be sometimes considered, performing such MRI sequences appears to be of particular interest in etiological diagnosis of dementia.

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