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Lesions in the splenium of the corpus callosum: Clinical and radiological implications

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Abstract

Background: Brain MRI may unexpectedly display abnormalities in splenium of the corpus callosum (SCC). However, the clinical implications of this lesion are unclear and are not always consistent with ischemic infarctions. We performed this study to clarify the clinical and radiological implications in patients with SCC lesions. *Methods*: We retrospectively reviewed consecutive patients with MRI-reported SCC changes between 2009 and 2012. We analyzed clinical and radiological findings, etiologies, cognitive impairment, and clinical outcomes. *Results*: We found 30 patients (16 females; mean 50.5 years) who had SCC lesions on MRI. Confusion was the most common clinical finding in 50% of cases. Cerebral infarction was the most common etiology (50%). The most consistent SCC changes on MRI were low signal in T1WI, high signal on T2WI and FLAIR, and high signal on DWI. We classified SCC lesions into *in situ* SCC lesions (SCC only) and multiple (SCC plus) lesions for patients with multiple lesions. The clinical symptoms of SCC only lesions were relatively mild. Cognitive functions were evaluated by Mini Mental State Examination (MMSE) and clinical dementia rating (CDR) scale at the time of discharge and patients with SCC only lesions showed less impaired cognition compared with those with SCC plus lesions. Clinical outcomes were evaluated by the modified Rankin scale at 1 month and patients with SCC only lesions revealed good clinical outcomes compared with those with SCC plus lesions.
Conclusions: MRI-reported SCC lesions may have heterogeneous etiologies and present with various symptoms. The clinical course and outcome are relatively good, particularly in small isolated and oval shaped SCC lesions.

INTRODUCTION

Splenium of the corpus callosum (SCC) abnormalities on magnetic resonance imaging (MRI) have been reported commonly and unexpectedly in many cases. Such SCC lesions are usually reversible and associated with many etiologies and clinical symptoms. However, the implications of an SCC abnormality are unclear and are not always associated with ischemic infarctions. Possible causes of SCC abnormalities include infarction, trauma, tumor, alcohol abuse, seizure, heat stroke, multiple sclerosis, epilepsy, drug intoxication, and panhypopituitarism.[1-13]

Many studies have been performed on this topic but most studies are limited to case reports of SCC lesions or special diseases and reviews with published cases. Thus, knowledge about SCC lesions is fragmentary. We undertook this study to evaluate clinical and radiologic findings, etiologies, cognitive impairment, and outcomes of patients with SCC abnormalities noted on brain MRI.

METHODS

The design of this retrospective study was approved by our Institutional Review Board. This study was performed at a university hospital. We retrospectively evaluated clinical and radiologic findings, main etiologies, cognitive impairment, and outcomes of consecutive patients with SCC lesions on brain MRI who visited our hospital from January 2009–June 2012.

Final diagnoses of an SCC lesion on brain MRI were confirmed by neurologists and a neuroradiologist.

Cognitive functions were analyzed by the Mini-Mental State Examination (MMSE) and the clinical dementia rating (CDR) scale at discharge. Clinical outcomes were evaluated with the modified Rankin Scale (mRS) at 1 month.

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A 1.5 Tesla MRI scan (Intera, Philips Medical Systems, Best, The Netherlands) was used (5 mm slice thickness; 2.5 mm interslice gap; 23 axial slices; 230 mm field of view). MRI included T1 (TR/TE 550/11 ms), T2 (TR/TE 4442/100 ms), fluid attenuated inversion recovery (FLAIR; TR/TI/TE 11000/2800/140 ms), and diffusion-weighted magnetic resonance imaging (DWI; TR 4,032 msec, TE 80 msec; matrix number of 192 × 192; two b values of 0 and 1,000 sec/mm^2), and an apparent diffusion coefficient (ADC) map were generated.

MRI scans and all other imaging modalities were performed on all patients. The image analysis included the distribution of involvement and the shape of the corpus callosum (CC) lesion.

According to the location and number of lesions, SCC lesions were classified into: SCC *in situ* (SCC only) and multiple (SCC plus) involvement (including extra-splenial involvement). SCC *in situ* (SCC only) meant that the lesion was localized only at the splenium. Multiple involvement (SCC plus) indicated that SCC involvement included accompanying lesions in the genu, or body of the CC or an extra-CC lesion such as basal ganglia, periventricular white matter, or cerebral cortex. We divided the shape of the SCC *in situ* (SCC only) lesion into oval and elongated shaped. The oval shape described a round small lesion within 1 cm in length of an SCC on one or both sides of the midline. The elongated shape described a large lesion involving most of the splenium. We also divided multiple (SCC plus) lesions into SCC *in situ* lesions with a genu or body lesion (intra CC) and SCC *in situ* lesions with basal ganglia, brainstem, cerebral cortex, or white matter lesions (extra CC).

We analyzed clinical symptoms and clinical outcomes according to the two types of shapes and two categories for the number of lesions.

RESULTS

We retrospectively reviewed 5,078 consecutive brain MRIs showing abnormal lesions from January 2009–June 2012. During the 42-month study period, 30 consecutive patients with SCC lesions on brain MRI were included.

Demographic and general clinical findings of the patients with SCC lesions are shown in Table 1. Fourteen men and 16 women (mean age, 50.53 ± 20.44 years; range, 6–89 years) were

Table 1: Demographic and general clinical findings of patients with splenium of the corpus callosum lesions

		No. (%) of Patients (n=30)
Age (years)		50.53 ± 20.44
Sex (M/F)		14 (46.7%) /16 (53.3%)
Clinical findings	Confusion, irritability	15 (50%)
	Dysarthria	13 (43.3%)
	Disconnection syndrome	12 (40%)
	Ataxia	10 (33.3%)
	Hemiparesis	8 (26.7%)
	Headache	7 (23.3%)
	Mutism	3 (10%)
	Seizure	3 (10%)
	Dizziness	3 (10%)
	Increased muscle tones	2 (6.7%)
Etiology	Infarction	15 (50%)
	Trauma	4 (13.3%)
	Tumor	3 (10%)
	Alcohol abuse	2 (6.7%)
	Seizure	2 (6.7%)
	Heat stroke	1 (3.3%)
	Multiple sclerosis	1 (3.3%)
	Substances abuse	1 (3.3%)
	panhypopituitarism	1 (3.3%)

included. Etiologies included cerebral infarction (50%), trauma (13.3%), tumor (10%), alcohol abuse (6.7%), seizure (6.7%), heat stroke (3.3%), multiple sclerosis (3.3%), drug intoxication (3.3%), and panhypopituitarism (3.3%). Cerebral infarction was the most common etiology.

MRI findings

MRI findings of the patients with SCC lesions with and without extra-splenial involvement are given in Table 2. Extra-splenial involvement was located in the frontal or parietal cortex, basal ganglia, thalamus, pons, and midbrain. The most consistent splenium changes on MRI were low signal intensity on T1-weighted image (T1WI) and high signal intensity on T2WI, FLAIR, and DWI. DWI and an ADC map were completed in all 30 patients. T2WI and FLAIR noted high signals in all patients. T1WI revealed low signals in all patients. DWI showed high signals in 29 patients, whereas one pateint showed low signal intensity. In particular, hyperacute splenium abnormalities were most easily found on DWI. Only one of the 30 patients had low signal intensity on the ADC map. Seventeen of 21 patients had oval shaped lesions in the splenium and four had elongated lesions. T2WI and FLAIR noted high signal intensity in all 17 patients who had oval shaped SCC lesions. DWI revealed high signals, and the ADC map showed low signals for patients with small oval shaped SCC lesions. Among the elongated SCC lesions, only one patient had low signal intensity on DWI and high signal intensity on the ADC map. All four elongated shaped large lesions showed high signal intensity on T2WI and FLAIR.

We found 9 multiple (SCC plus) lesions and divided them into SCC *in situ* lesions with the genu or body lesion (intra CC) and SCC *in situ* lesions with basal ganglia, brainstem, cerebral cortex, or white matter lesions (extra CC). Among the 9 SCC plus patients, 5 intra CC patients had body (3 patients) or genu (2 patients) lesions in the CC and 4 extra CC patients showed lesions in the basal ganglia, internal capsule, and periventricular white matter. T2WI and FLAIR noted high signal intensities in all 9 patients who had an SCC plus lesion. DWI revealed high signal intensity, and the ADC maps showed low signal intensity in all patients with SCC plus lesions.

Contrast-enhanced MRI was performed in 5 of the 30 patients and revealed no prominent enhancement of the splenium lesions. MRI imaging of a typical patient with SCC involvement is presented in Figure 1.

Clinical findings

The most frequent symptom was confusion (50%). Other clinical findings were dysarthria (43.3%), ataxia (33.3%), headache (23.3%), hemiparesis (16.7%), disconnection syndrome (13.3%), dizziness (10%), seizure (10%), and increased muscle tone (6.7%) (Table1). The clinical characteristics of patients with SCC lesions with and without extra-splenial involvement are given in Table 3. The clinical symptoms of patients

Table 2: MRI findings of lesions in the splenium of the corpus callosum with and without extra-splenial involvement

Location	Shape	No.	T1WI	T2WI	FLAIR	DWI	ADC
Splenium in situ (SCC only, n=21)	**oval**	17	H 0 L 17	H 17 L 0	H 17 L0	H 17 L0	H 0 L17
	elongated	4	H 0 L 4	H 4 L 0	H 4 L 0	H 3 L 1	H 1 L 3
Multiple (SCC plus, n=9)	**intra CC**	5	H 0 L 5	H 5 L 0	H 5 L 0	H 5 L 0	H 0 L 5
	extra CC	4	H 0 L 4	H 4 L 0	H 4 L 0	H 4 L 0	H 0 L 4

Splenium in situ, splenium lesion only; multiple or SCC plus, SCC lesion + extra-splenial lesion or extra-corpus callosal lesion; T1WI, T1 weighted image; T2WI, T2 weighted image; Flair, fluid attenuated inversion recovery; DWI, diffusion weighted image; ADC, apparent diffusion coefficient map; Intra CC, lesions in the corpus callosum; extra CC, lesions including area other than corpus callosum; H, high signal; L, low signal

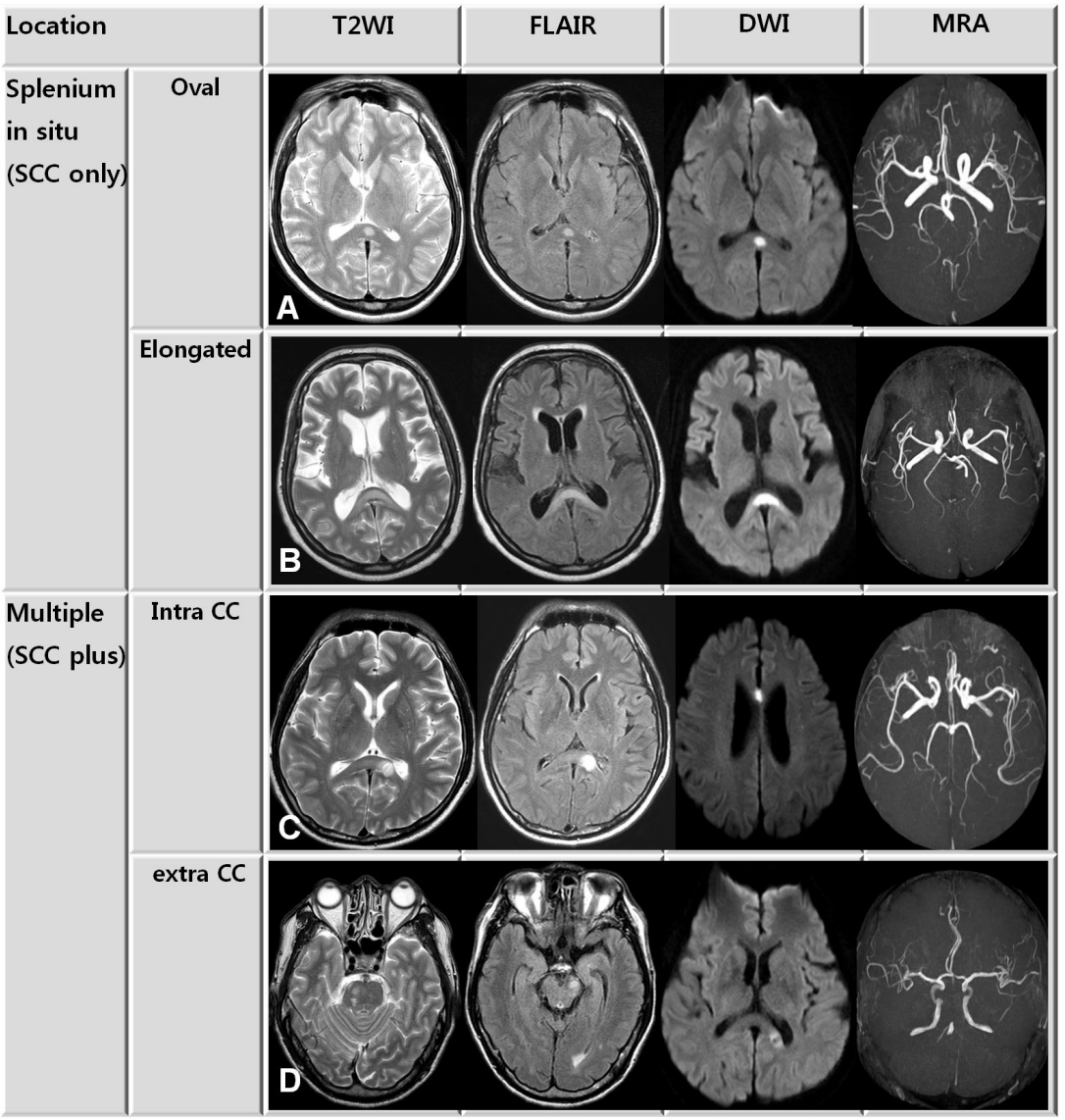

Figure 1. Typical MRI findings of lesions in thesplenium of the corpus callosum (SCC) with and without extra-splenial involvement. A. SCC lesion with oval shape. Axial T2WI, FLAIR image and DWI show increased focal signal intensity in the SCC. MRA shows well visualized intracranial vessels. **B. SCC lesion with elongated shape.** Axial T2WI, FLAIR image and DWI show increased signal in the long area of the SCC. MRA shows no significant stenosis in intracranial vessels. **C. SCC lesion with other CC part lesion.** Axial T2WI and FLAIR image show increased signal in the SCC. Axial DWI shows increased focal signal intensity in the anterior body of CC and SCC (not shown). MRA shows no significant stenosis in intracranial vessels. **D. SCC lesion with extra CC lesion.** Axial T2WI image shows increased signal in right upper pons. Axial FLAIR image shows increased signal in left midbrain and left occipital white matter. Axial DWI shows increased signal in the SCC and midbrain and pons (midbrain and pons lesion were not shown). MRA shows non-visualized PCAs. DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient; FLAIR, fluid-attenuated inversion recovery; T2WI, T2-weighted imaging; MRA, magnetic resonance angiography; PCA, posterior cerebral artery

Table 3: Clinical characteristics of patients with lesions in the splenium of the corpus callosum with and without extra-splenial involvement

Location	Shape	Symptoms	No
Splenium in situ (SCC only, n=21)	**Oval (n=17)**	Confusion, irritability	8(46%)
		Headache	5(29%)
		Disconnection syndrome	4(23%)
		Dysarthria	4(23%)
		Dizziness	1(6%)
		Seizure	1(6%)
	Elongated (n=4)	Confusion, irritability	3(75%)
		headache	2(50%)
		dysarthria	2(50%)
		Disconnection syndrome	2(50%)
		ataxia	1(25%)
		Hemiparesis	1(25%)
Multiple (SCC plus, n=9)	**intra CC (n=5)**	Confusion, irritability	4(80%)
		Disconnection syndrome	3(34%)
		Hemiparesis	2(22%)
		ataxia	2(22%)
		Dysarthria	2(22%)
	extra CC (n=4)	Confusion, irritability	4(100%)
		dysarthria	4(100%)
		Disconnection syndrome	3(75%)
		Hemiparesis	3(75%)
		Ataxia	3(75%)
		seizure	2(50%)

SCC, splenium of corpus callosum; CC, corpus callosum

with SCC *in situ* lesions were relatively mild and included headache, confusion, and dysarthria. In contrast, patients with multiple (SCC plus) lesions showed somewhat more severe symptoms such as disconnection syndrome, hemiparesis, and ataxia. Patients with extra-splenial lesions or multiple lesions showed more severe and various symptoms than those with SCC only lesions.

Cognitive impairment

All patients with SCC lesions had somewhat deteriorated cognition (CDR 0.58 ± 0.66; MMSE 25.03 ± 1.82). The cognitive values of patients with SCC lesions with and without extra-splenial involvement are given in Table 4. Patients with SCC *in situ* (SCC only) lesions showed less impaired cognition compared with those with multiple lesions (SCC plus lesion) (CDR 0.19 ± 0.25 vs. 0.78 ± 0.57, $P = 0.002$; MMSE 26.95 ± 1.47 vs. 24.00 ± 1.32, $P = 0.001$, respectively). Among patients with SCC *in situ* (SCC only) lesions, the oval shaped lesions tended to result in a lower CDR and a higher MMSE score compared to those with elongated SCC lesions, but the result was not significant (CDR 0.18 ± 0.25 vs. 0.25 ± 0.29, $P = 0.50$; MMSE 27.24 ± 1,44 vs. 25.75 ± 0.96, $P = 0.059$, respectively). Among patients with multiple lesions (SCC plus), those with an intra CC lesion tended to show lower CDR and higher MMSE scores than those with extra CC lesions, (CDR 0.50 ± 0.35 vs. 1.13 ± 0.63, $P = 0.09$; MMSE 24.60 ± 1.14 vs. 23.25 ± 1.26, $P = 0.128$, respectively).

Clinical outcomes

The clinical outcomes were relatively good. Of the 30 patients, 22 had favorable outcomes (mRS, 0–2); 13 had complete resolution (mRS, 0), and 9 improved partially (mRS, 1–2). Eight patients had unfavorable outcomes (mRS, 3–6); 7 with left partial disability (mRS, 3–5), and one died (mRS, 6). The clinical outcomes of the patients

Table 4: Cognitive values of patients with lesions in the splenium of the corpus callosum with and without extra-splenial involvement

Location	CDR	MMSE	Shape or location	CDR	MMSE
Splenium in situ (SCC only, n=21)	0.19±0.25*	26.95±1.47†	**Oval (n=17)**	0.18±0.25‡	27.24±1.44§
			Elongated (n=4)	0.25±0.29‡	25.75±0.96§
Multiple (SCC plus, n=9)	0.78±0.57*	24.00±1.32†	**intra CC (n=5)**	0.50±0.35□	24.60±1.14¶
			extra CC (n=4)	1.13±0.63□	23.25±1.26¶

*, *P*=0.002; †, *P*=0.001; ‡, *P*=0.59; §, *P*=0.059;□, *P*=0.09; ¶, *P*=0.128, Mann-Whitney U test; CDR, clinical dementia rating scale; MMSE, mini-mental status exam; mRS, modified Rankin scale; SCC, splenium of corpus callosum; CC, corpus callosum.

with SCC lesions with and without extra-splenial involvement are given in Table 5. Patients with SCC *in situ* (SCC only) lesions revealed good clinical outcomes compared with those with multiple (SCC plus) lesions (mRS 0.24 ± 0.44 vs. 2.00 ± 1.66, $P = 0.001$). Among patients with SCC *in situ* (SCC only) lesions, those with oval shaped lesions tended to show better outcomes compared to that in patients with elongated SCC lesions, but the result was not significant (mRS 0.18 ± 0.39 vs. 0.50 ± 0.58, $P = 0.182$). Among patients with multiple (SCC plus) lesions, those with an intra CC lesion tended to have more favorable outcomes compared to those with an extra CC lesion (mRS 1.20 ± 0.45 vs. 3.00 ± 2.16, $P = 0.08$).

DISCUSSION

The present study was a relatively larger retrospective analysis that focused on SCC lesions on brain MRI compared to other studies[1,9,14] (Doherty *et al*., 9 patients; Hackett *et al*., 17 patients; Maeda *et al*., 8 patients). Most previous studies were case reports on several patients with SCC lesions, published cases, or medical recordings. We investigated 30 patients with SCC abnormalities including 21 patients with

Table 5: Clinical outcomes of lesions in the splenium of the corpus callosum with and without extra-splenial involvement

Location	mRS	Shape or location	mRS
Splenium in situ (SCC only, n=21)	0.24±0.44*	**Oval (n=17)**	0.18±0.39†
		Elongated (n=4)	0.50±0.58†
Multiple (SCC plus, n=9)	2.00±1.66*	**intra CC (n=5)**	1.20±0.45‡
		extra CC (n=4)	3.00±2.16‡

*, *P*=0.001; †, *P*=0.182; ‡, *P*=0.08, Mann-Whitney U test; CDR, clinical dementia rating scale; MMSE, mini-mental status exam; mRS, modified Rankin scale; SCC, splenium of corpus callosum; CC, corpus callosum.

lesion in splenium *in situ* (SCC only), and 9 patients with multiple (SCC plus) lesions. This investigation was performed to clarify the clinical and MRI findings, etiologies, cognitive values, and outcomes.

Etiology

All diagnoses were considered after analyzing the clinical situation, laboratory data, and results of neurological examinations. In addition, all cases underwent sufficient and adequate imaging studies confirmed by a neuroradiologist blinded to the clinical data.

SCC abnormalities are related to various conditions including hypernatremia[1], hypoglycemic encephalopathy[2,3], bacterial or viral meningoencephalitis[4-6], hemolytic uremic encephalopathy[7], radiation therapy[8], high-altitude cerebral edema[9,10], Marchiafava–Bignami disease[11], cerebral infarction[12], and epilepsy.[13] Similar to previous reports and studies of SCC lesions, the diseases and conditions associated with SCC abnormalities in our 30 patients varied, including cerebral infarctions, trauma, tumor, history of alcohol abuse and malnutrition, seizure, multiple sclerosis, medications or substance abuse, and other medical conditions.

Alcohol-related disorders were the most common cause of SCC damage in a previous study.[1] In the present study, cerebral infarction was the most common by 50% and the next were trauma and tumor. In contrast, alcohol and alcohol-related disorders were each 6.7%. This finding is interestingly different from past studies. Vascular lesions of the corpus callosum are rare events and only a few demonstrations of CC infarction are available.[15,16]

The resistance of the CC to small vessel ischemic changes is well known.[16] The CC constitutes the largest white matter bundle and connects the two cerebral hemispheres. The CC receives blood supply form three main sources.[12] The subcallosal and medial callosal arteries or branches of the anterior communicating artery supply the anterior portion of the corpus callosum. The pericallosal artery or branches of the anterior cerebral artery (ACA) are the main blood supply to the body. Finally the posterior pericallosal artery, branches of the posterior cerebral artery (PCA), supplies the splenium. A detailed description of the relevant microsurgical anatomy has been provided by Perlmutter *et al*.[17,18] Anastomoses of the ACA and PCA callosal branches occur near the tip of the splenium. Such communications become evident by angiography in states of occlusive disease.[19,20] The PCA also sends branches to the CC and specifically the splenium. Single or multiple rami arise at the level of the quadrigeminal plate cistern usually from the PCA or its parieto-occipital division. These vessels (called splenial or posterior PCA) take off at almost right angles from the parent arteries.[18]

We performed longitudinal MRI studies on most patients. Cases with longitudinal MRI that demonstrated sustained changes suggestive of irreversible axonal compromise were considered cerebral ischemic infarction, and these MRI findings were confirmed by neuroradiologist.

In the present study, the reason why cerebral infarction was the most common cause of the SCC lesion is not easy to explain. We believe that this result might be because we performed this study in a tertiary university hospital with a stroke center. Because patients with alcohol-related diseases are usually managed in the psychiatry department, patients with alcohol problems are rarely referred to the neurology department. Previous studies were analyzed by groups composed of literature-based case series. Thus, the etiology of past studies might not parallel the etiology distribution of our study.

However, one study showed similar results to our study. Chrysikopoulos *et al*.[12] retrospectively reviewed 352 consecutive cranial CT and MR scans showing cerebral infarcts and concluded that infarction of the CC may be more common than previously thought and is most often the result of cerebral embolism. MRI is better suited than CT for the detecting vascular lesions of the CC. As in the present study, that report showed that cerebral infarction was a common etiology of the SCC lesions.

Despite numerous reports of CC abnormalities, it is uncertain why different etiologies can result in similar MRI findings, and what exactly are the common pathophysiological mechanisms that associate to these many etiologies. The exact underlying pathophysiology of SCC lesions is not fully understood and they may represent nonspecific endpoints of different disease processes. Several presumptive mechanisms have been proposed, including perturbed cellular fluid mechanism, intramyelinic edema and inflammatory infiltration.[4] The splenium may have easily perturbed cellular fluid mechanics when compared with that of surrounding tissues. The etiologies associated with SCC lesions that may compromise cellular fluid regulation include

hypernatremia, hyponatremia, renal failure, infection, altitude sickness, hypoglycemia, thiamine deficiency, and alcoholism.[1] Convulsions might transiently impair available glucose, leading to brief, reversible failures of cellular fluid regulation. A similar mechanism could explain why hypoglycemic patients develop reversible splenium changes.[3]

MRI findings

The most consistent SCC changes evident from MRI were reduced T1 signal intensities, increased T2 and FLAIR signals, and increased DWI as previously published.[1] DWI showed hyperacute or acute splenium abnormalities better than that of the other two modalities. Most cases in the present study presented with acute symptoms and the subsequent brain MRI revealed high signal intensity on DWI indicating an acute lesion. The high signal changes on DWI with reduced ADC values suggest cytotoxic edema. Patients with increased DWI and decreased ADC values in the splenium may normalize with additional imaging, perhaps suggesting the absence of cytotoxic edema. Reversible corpus callosum lesions on DWI are representative of cytotoxic edema, significant vascular spasm, or underlying atherosclerosis possibly implicated in the pathophysiology of a splenium abnormality.[1,14,21] Increased ADC value are suggestive of vasogenic edema. The present study had one patient with an SCC only lesion (elongated lesion) with an increased signal on the ADC map.

Persistent SCC changes (low signal T1WI and high signal T2WI) included cystic lesions, although pathologic confirmation was limited. Patients with longitudinal MRI demonstrating sustained SCC changes suggestive of irreversible axonal compromise were usually considered to have cerebral ischemic infarction.

Clinical findings

The CC is a thick band of nerve fibers that divides the cerebrum into left and right hemispheres. It connects the left and right sides of the brain allowing for communication between the hemispheres. The CC transfers motor, sensory, and cognitive information between the brain hemispheres.

A recent study by Doherty *et al*.[1] who analyzed 9 patients, and 60 additional published cases showed that confusion (35 patients), ataxia (25 patients), and seizure (23 patients) were common. Consistent with previous reports, the most common clinical symptoms in the present study were confusion and irritability (50%). Other frequent clinical manifestations were dysarthria, disconnection syndrome, ataxia, and headache.

Mutism, hallucinations, psychosis, and hemispheric disconnection are more specific findings of SCC lesions. Still unclear is if and how the splenium regulates mutism or hallucinations. Perhaps the right and left hemispheres generate independent nonsense, the censure of which is necessary and normal, and requires an intact splenium. Nonspecific common findings such as ataxia, dysarthria, increased tone, and delirium, do not easily localize.[1]

Disconnection syndrome is a neurologic disorder due to blocking of impulse transmission along a cerebral fiber pathway, mainly interrupted in the uncinate temporal-frontal fasciculus and occipito and temporo parietal tract and develops into apraxias of the left hand, pseudoneglect, alien left hand, astereognosis, agraphia, alexia, visual apraxias, and hemianopsia. Clinical findings of hemispheric disconnection were not common in the study of Doherty *et al*.[1] or the present study.

As study by Maeda *et al*.,[14] revealed that reversible SCC lesions with restricted diffusion are apparent in a wide spectrum of diseases, conditions, and neurological courses and outcomes are good, particularly in patients with isolated SCC lesions.

The present study showed that patients with SCC only lesions including oval or elongated lesions usually presented with confusion, irritability, and headache. In contrast, patients with SCC plus lesions including intra CC or extra CC lesions usually developed dysarthria, disconnection syndrome, hemiparesis, and ataxia other than confusion. These findings are not related to a specific etiology, but the lesional shape or multiplicity of the SCC lesions. Nine patients with SCC plus lesion (extra-splenial lesions or multiple CC lesions) in the present study showed more severe and various symptoms than patients with lesions in the splenium *in situ*. These findings may be applied to patients with extra-splenial lesions or multiple lesions who have lesions in other sites of the splenium of the CC or basal ganglia, internal capsule, and periventricular white matter. Damage to these callosal interhemispheric connections and corticospinal pathways might result in marked dysarthria, hemiparesis, ataxia, and increased tone.

Cognitive impairment and clinical outcome

Given the complexity of cognitive pathways, it is difficult to identify a single domain for cognitive skill. Among the cognitive skill domains, the CC connects the cortical and subcortical regions of the brain hemispheres interconnecting auditory, sensory-motor, and memory information and plays a critical role in interhemispheric communication, taking part in most of the cognitive pathways. It is conceivable that cognitive impairment due to an SCC lesion could be related to commissural disconnection.

Microstructural changes in the CC correlate with cognitive dysfunction in patients with early stage relapsing-remitting multiple sclerosis. That study used diffusion tensor imaging (DTI) for microstructural organization of the white matter. Demyelination and incipient axon loss was slightly higher in the patients with multiple sclerosis and cognitive impairment. The cognitive changes correlated with the DTI parameters, suggesting that loss of complexity in CC connections can impair neural conduction. Thus, cognitive impairment can be related to callosal disconnection.[22] Moreover, a higher integrity of the splenium of the CC predicted better cognitive ability in old age.

We divided SCC lesions into two categories such as the SCC *in situ* lesion group and the SCC plus lesion (other CC lesion or extra CC lesion plus) group. Cognitive impairment levels were different in both categories. However, the subcategories such as patients with oval shaped SCC lesions and elongated SCC lesions in the SCC *in situ* group and the intra CC lesion and extra CC lesion in the SCC plus group showed a tendency for impaired cognition in the elongated SCC lesional and extra CC lesional subcategories.

The present study showed that patients with SCC *in situ* lesions had less impaired cognition compared with those with multiple lesion (SCC plus lesion) (CDR 0.19 ± 0.25 vs. 0.78 ± 0.57, $P = 0.002$; MMSE 26.95 ± 1.47 vs. 24.00 ± 1.32, $P = 0.001$, respectively). Usually, SCC lesions are related to relatively mild or modest symptoms of mentality or cognition. However, marked cognitive impairment can be caused by multiple lesions such as body or head of the CC and regions other than CC develop lesions.

Yaldizli *et al*.[23] investigated the relationship between total and regional CC atrophy, neuropsychological test performance in patients with MS. Total and regional CC atrophy was assessed using the corpus callosum index (CCI). The CCI correlated more strongly with T2- and T1-lesion volume and whole brain volume than with disease duration or Expanded Disability Status Scale score. The CCI correlated strongly with several cognitive function tests. A multivariate regression analysis revealed that atrophy of the posterior CC segment (particularly the SCC) was significantly associated with poor outcome on cognitive function tests. These results also supports the results of the present study in that SCC lesions were associated with cognitive decline and more large or extensive lesions of CC correlated with more cognitive impairment than small or *in situ* SCC lesions.

Complete resolution was observed in 43.3% (13/30) of cases and partial improvement was observed in 30% (9/30). More than 70% of patients with SCC lesions showed relatively good outcomes. According to the study by Doherty *et al*.,[1] 52 of 69 patients had clinical outcomes recorded: 28 had complete resolution, 23 improved, and one died, and outcomes were relatively good. SCC lesions are usually related to relatively favorable clinical outcomes. However, multiple lesions such as on the body or head of CC or in regions other than CC can cause unusually poor clinical outcome.

Several limitations in this study should be mentioned. We had a large sample size in each group but a larger sample is needed analyses of etiology, clinical findings, cognitive impairment assessments and outcomes. This might dampen the reliability of the results. A second limitation was the relatively short follow-up time to evaluate cognitive function and clinical functional outcomes. A third limitation is that we did not perform more structural cognitive indices and specific diffusion MRI techniques such as DTI imaging modalities for insight into tissue organization, evaluation of tissue microstructure and reconstruction of white matter tracts to correlate with the lesions and function.

In conclusion, according to previous observations and our study, many events can result in SCC changes. The MRI-reported SCC lesions may have connections with various clinical findings, including altered mentality, ataxia, dizziness, hemispheric disconnection features, dysarthria, and convulsive movements. Etiologies have been ascribed to ischemic insults, traumas, glucose and electrolyte abnormalities, seizure and infectious process. The clinical courses, cognitive functions, and outcomes are comparatively good, particularly in patients with isolated splenium lesions. Further descriptive studies on splenium abnormalities

are needed, particularly in the setting of new-onset altered mental status. Moreover, further study should include more structural cognitive indices, specialized perfusion imaging studies, and longitudinal data.

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