

Contrast-induced Encephalopathy after Coil Embolization of an Unruptured Internal Carotid Artery Aneurysm

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Abstract

A 58-year-old woman developed agraphia and mild right hemiparesis approximately one month after undergoing coil embolization of an unruptured left internal carotid artery aneurysm. MRI performed on day 39 post-coil embolization showed multiple lesions in the white matter with signal hyperintensity on T2-weighted and FLAIR images in the left middle cerebral artery territory. The patient's cerebrospinal fluid exhibited an elevated protein level at 46 mg/dL; however, no other findings suggested another underlying disease. Corticosteroids were administered, and, by day 50 post-coil embolization, the clinical findings and abnormal features on MRI had improved. The patient was therefore diagnosed with contrast-induced encephalopathy after coil embolization.

Key words: contrast-induced encephalopathy, cerebral aneurysm, coil embolization, posterior reversible encephalopathy syndrome (PRES)

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Introduction

Contrast-induced encephalopathy (CIE) due to the use of contrast agents is a rare complication of angiography. This pathology was first reported in 1970 as transient cortical blindness after coronary angiography (1). The clinical manifestations include cortical blindness, seizures and focal neurological deficits. The incidence of CIE ranges between 0.3% and 1.0%, although it can reach 4% when hyperosmolar iodinated contrast agents are used (2). One possible reason for this complication is disruption of the blood-brain barrier. We herein report the case of a patient diagnosed with CIE after coil embolization of an unruptured internal carotid artery (ICA) aneurysm.

Case Report

A 58-year-old woman was diagnosed on brain magnetic resonance imaging (MRI) with an unruptured ICA aneurysm

at another hospital in 2012. Her past and family medical histories were unremarkable. She was referred to the Department of Endovascular Neurosurgery at our hospital for a further assessment. Cerebral angiography revealed an unruptured aneurysm with a maximum diameter of 5 mm at the left ICA-ophthalmic artery junction (Fig. 1A). Coil embolization of the aneurysm was performed at the end of February 2013. The coiling procedure was carried out under general anesthesia with heparinization. The aneurysm was framed with ED coil 14 standard (Kaneka, Osaka, Japan) and one Target 360 Ultra coil, while three Target Helical Ultra coils (Target, Stryker, USA) were placed into the aneurysm while preserving the ophthalmic artery, resulting in a volume embolization rate of 21.9%. A HyperForm 7×7-mm balloon (Micro Therapeutics, Irvine, USA) was intermittently inflated and deflated at the neck of the aneurysm. In order to avoid cerebral ischemia, we discontinued balloon inflation within five minutes and used half inflation when necessary. Postcoiling angiography showed complete occlusion of the aneurysm. Iohexol (316 mL of Omnipaque 300;

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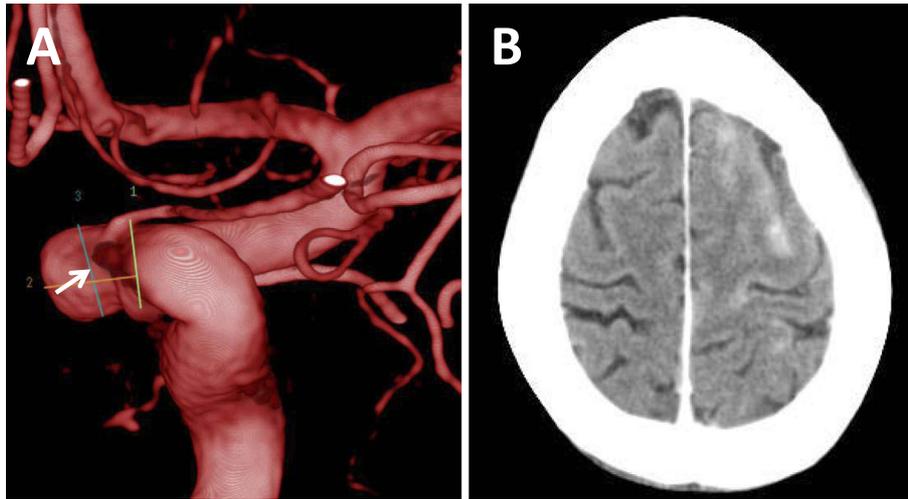


Figure 1. A) Pre-coiling cerebral angiography shows an unruptured aneurysm (arrow) with a maximum diameter of 5 mm at the branch point of the left ICA-ophthalmic artery. B) Brain CT performed immediately after coiling reveals a hyperdense area due to leakage of contrast agent in the left frontal lobe cortex.

Daiichi Sankyo, Tokyo, Japan) was used as the contrast agent during the procedure. Brain computed tomography (CT) performed immediately after the coiling procedure showed leakage of contrast agent into the left frontal subarachnoid space (Fig. 1B). No large fluctuations in blood pressure were noted and no neurological symptoms were apparent during or after the procedure, while brain MRI performed on day 3 post-coiling revealed only a small, acute infarct in the left insular cortex and high frontal cortex (Fig. 2). The patient was discharged without neurological deficits.

At work, approximately four weeks after hospital discharge, her colleagues pointed out that she was making simple mistakes, such as being unable to write or remember kanji (Japanese characters). Brain MRI performed on day 39 post-coiling showed multiple lesions predominantly in the white matter with signal hyperintensity on T2-weighted and fluid-attenuated inversion recovery (FLAIR) imaging in the territory of the left middle cerebral artery (MCA). In addition, post-contrast MRI revealed punctate enhancement within the lesions (Fig. 3). The patient was therefore readmitted to our hospital for a further evaluation and treatment.

A general physical examination performed on admission disclosed no abnormalities. According to the neurological examination, the patient was lucid, although an assessment of the higher brain function showed agraphia. The Mini Mental State Examination total score was 25, with reductions in the scores for attention and calculation with delayed recall. The patient's visual field and other cranial nerves were normal. Her muscle strength in the right upper extremity was mildly decreased. No sensory deficits, abnormal muscle tonus or involuntary movements were identified. All tendon reflexes in the extremities were normal, without any pathological reflexes. An examination yielded negative results for signs of meningeal irritation.

Laboratory studies showed a normal blood cell count, with a white blood cell count of $4.6 \times 10^3/\mu\text{L}$ and an eosinophil count of $1.5 \times 10^2/\mu\text{L}$ (3.3%). Parameters of the liver and kidney functions, electrolytes and coagulation were all normal. The C-reactive protein level was 0.03 mg/dL. In addition, the patient was negative for antinuclear antibodies, anti-SS-A antibodies, anti-SS-B antibodies, anti-ds-DNA antibodies and anti-neutrophil cytoplasmic antibodies. The soluble interleukin (IL)-2 receptor level was 159 U/mL, which is within the normal limits. A drug lymphocyte stimulation test (DLST) to iohexol yielded negative results. A spinal tap revealed an opening pressure of 150 mmH₂O; the cerebrospinal fluid was colorless and clear, with a normal cell count of 15 mononuclear cells/ μL , although the protein level was slightly elevated at 46 mg/dL. The immunoglobulin G index was 0.72, and the level of myelin basic protein was <40 pg/mL (both normal). Testing yielded negative results for oligoclonal bands.

On day 46 post-coiling, with the aim of improving the patient's edema, she was treated with intravenous methylprednisolone at a dose of 1,000 mg/day for three days.

On day 53 post-coiling, fluorodeoxyglucose positron emission tomography showed no areas of abnormal uptake. On day 58 post-coiling, MRI demonstrated a reduction in the size of the lesions, with almost complete resolution by day 90 post-coiling (Fig. 4). The lesions exhibited signal hyperintensity on T2-weighted imaging, mild to low signal intensity on T1-weighted imaging and signal isointensity on diffusion-weighted imaging. The apparent diffusion coefficient was elevated. These findings suggested vasogenic edema.

The mild hemiparesis of the right arm and higher brain dysfunction that had developed approximately four weeks post-coiling improved after hospital admission and were almost completely resolved by day 50 post-coiling. Based on

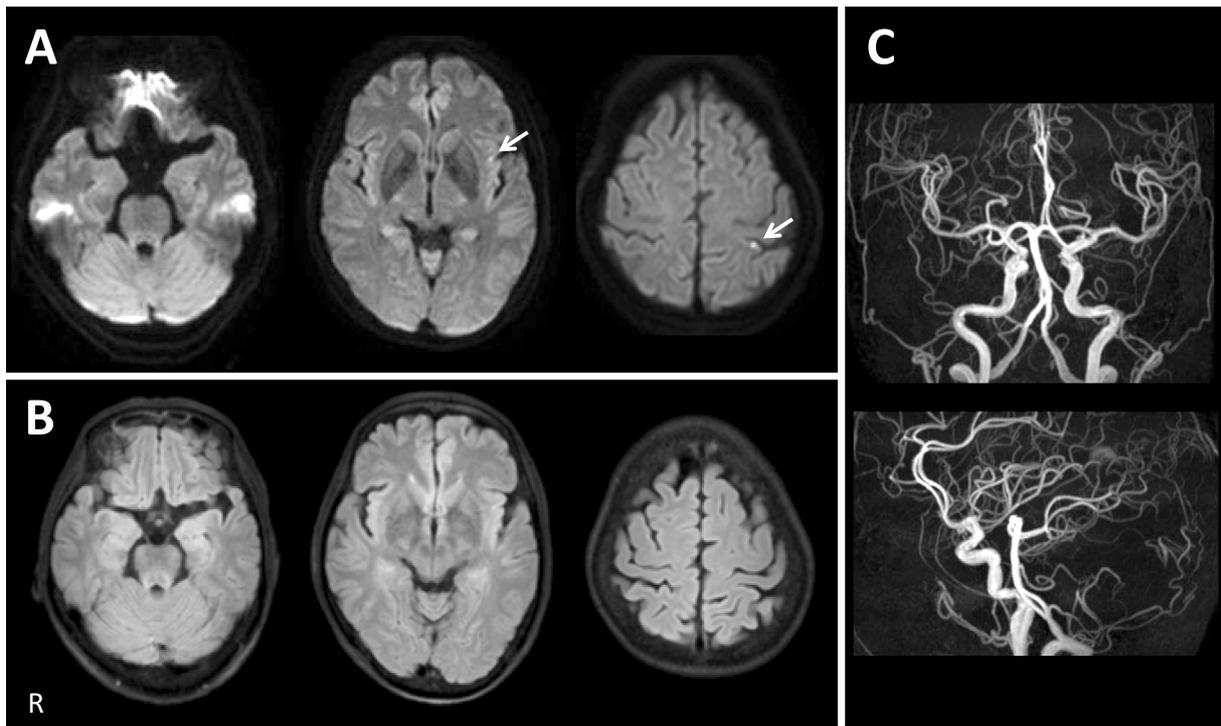


Figure 2. A) Brain MRI performed on day 3 post-coiling shows acute small infarction of the left insular cortex and high frontal cortex on diffusion-weighted imaging (arrows). B) Brain MRI performed on day 3 post-coiling shows no abnormal findings on FLAIR imaging. C) Brain MRA performed on day 3 post-coiling shows no abnormal findings, such as a neck remnant, spasms or occlusion.

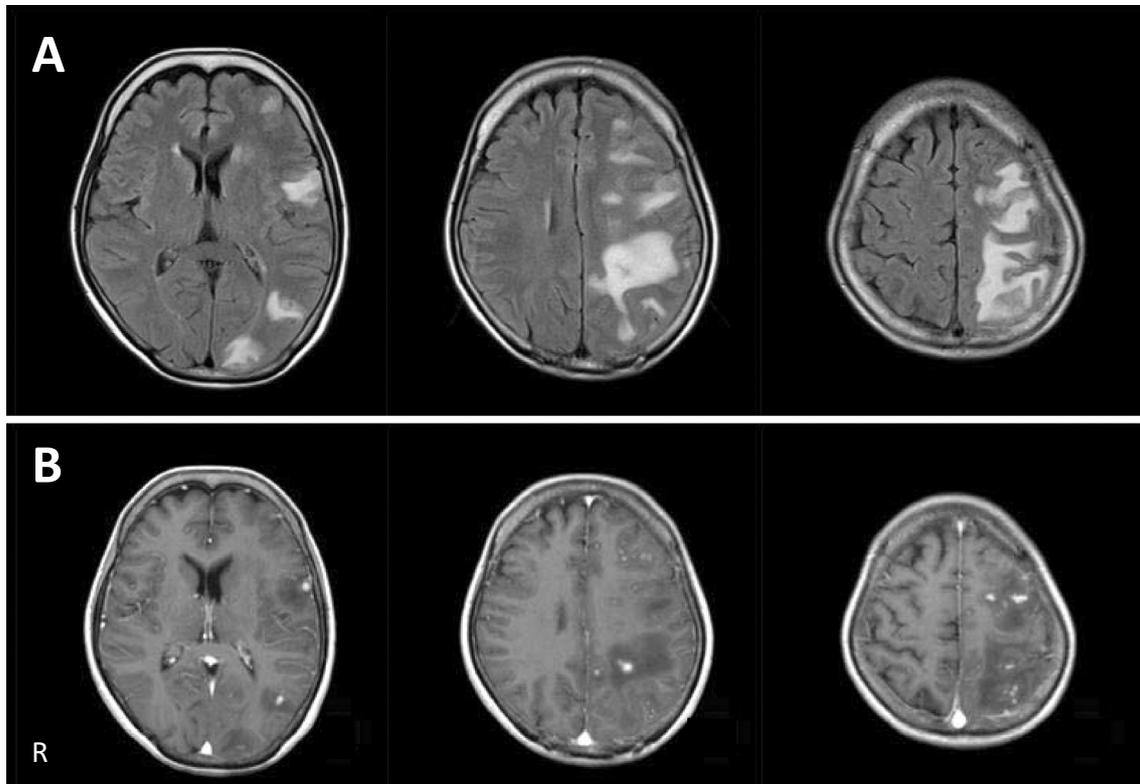


Figure 3. A) Brain MRI performed on hospital admission (39 days post-coiling) shows multiple lesions, predominantly in the white matter, with signal hyperintensity on FLAIR imaging in the area of the MCA in the left cerebral hemisphere. B) Post-contrast MRI reveals punctate enhancement within the lesions.

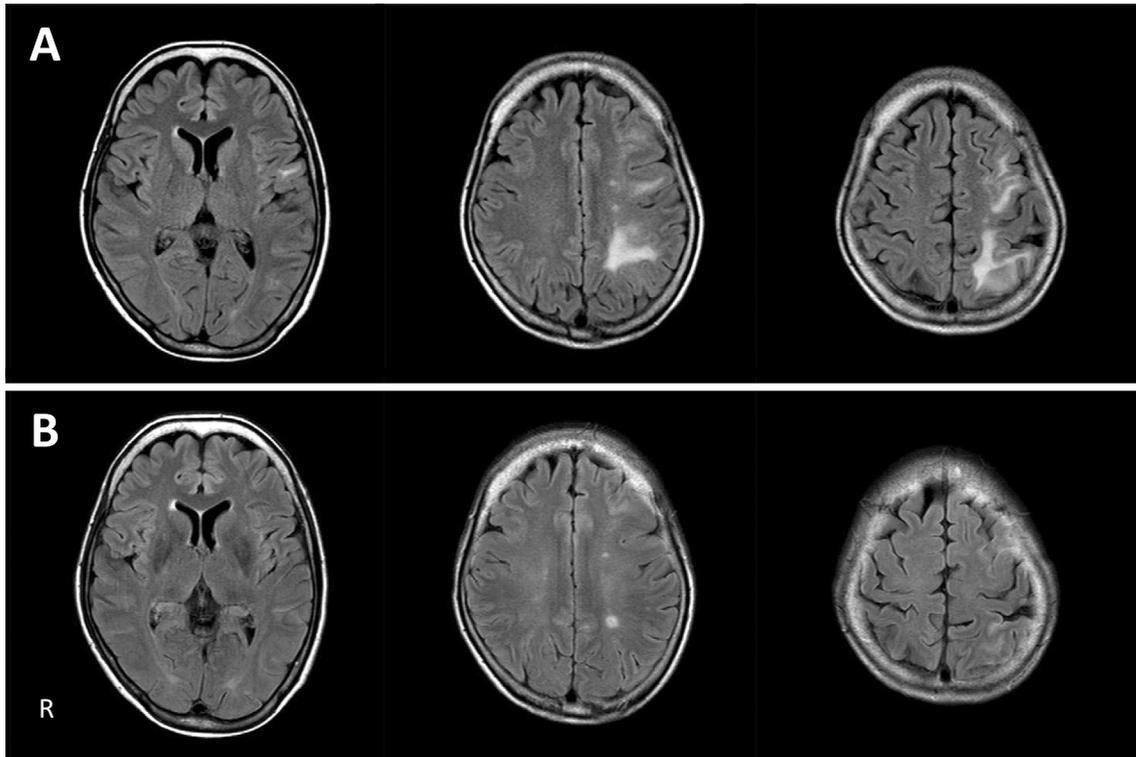


Figure 4. A) Brain MRI performed on day 58 post-coiling shows a reduction in the size of the lesions on FLAIR imaging. B) Brain MRI performed on day 90 post-coiling shows the almost complete resolution of the lesions.

the patient's clinical course and findings on brain MRI, CIE was diagnosed.

Discussion

The features of the present patient included transient right hemiparesis and agraphia following coil embolization for an unruptured ICA aneurysm, lesions on brain MRI consistent with widespread vasogenic edema predominantly in the white matter territory of the left MCA and the identification of reversible changes over time. Table lists reported cases of CIE after cerebral angiography with CT- or MRI-confirmed lesions (3-18).

Among these cases, including that involving our patient, CIE occurred after coil embolization in 13 of 23 patients. These reports include four cases that developed after coil embolization for ruptured cerebral artery aneurysms (8, 12, 14). In addition, five cases occurred after cerebral angiography (3, 4, 15, 17), four after carotid artery stenting (5, 10, 13) and one after placement of a flow diversion stent for an arterial aneurysm (11). Factors associated with CIE include inflammation induced by the coil materials (13), vasospasm and subarachnoid hemorrhage and blood pressure changes after surgery of ruptured arterial aneurysms. Even without specific risk factors, causative factors for CIE include hyperosmolality, neurotoxicity and the vascular toxicity of contrast media.

In reports published to date, the onset of CIE often occurred within a few hours to a few days after coil emboliza-

tion or cerebral angiography. In contrast, our patient developed symptoms approximately 30 days after coil embolization. In three previously reported cases of subacute onset, CIE occurred at approximately one month and three weeks post-procedure, respectively (13, 17). The present patient showed only very mild symptoms of agraphia and right upper extremity hemiparesis and may not have noticed symptoms for some time during daily activities.

Typical radiological findings of CIE include abnormal cortical contrast enhancement and edema, subarachnoid contrast enhancement and striatal contrast enhancement (16). Abnormal findings on brain MRI were identified in 16 of the previously reported cases (3, 6, 7, 9, 11-18). Because abnormal findings on brain MRI are consistent with vasogenic edema, CIE has recently been occasionally included in the category of posterior reversible encephalopathy syndrome (PRES). In previous reports, the prognosis has typically been good, with the exception of one case (16). As observed in those with PRES, clinical sequelae are absent and imaging shows reversible findings in most patients.

A large amount (316 mL) of non-ionic contrast agent was used in the current case. CIE reportedly occurs when great volumes of iodinated contrast are employed (13), while the amount of contrast agent used in the above cases varied from 12 mL to 300 mL (mean, 125 mL). Therefore, no clear correlation exists between the incidence of CIE and the amount of contrast agent.

In the present case, steroid pulse therapy was administered for three days with 1,000 mg of methylprednisolone in

Table. Cases of CIE after Cerebral Angiography with CT- or MRI-confirmed Lesions

Reference	Sex/Age	Back ground	Contrast agent	Volume (mL)	Symptoms	Location of brain lesion	Interval between angiography and symptom onset	Clinical resolution	Normalization of lesion by CT or MRI
3	M/64	Carotid artery stenosis	Iothalamate meglumine	12	Cortical blindness, fluent aphasia	Left occipital	During angiography	3 days	N/A
	M/71	Carotid artery stenosis	Iohexol	38	Cortical blindness, ophthalmoplegia	Bilateral occipital	20 minutes	10 days	N/A
	F/68	PCoA aneurysm	Iohexol	24	Cortical blindness, amnesia	Bilateral occipital	Immediately	6 days	N/A
4	M/70	Carotid artery stenosis	Diatrizoate meglumine	50	Cortical blindness	Bilateral occipital	Immediately	2 days	1 day
5	M/82	Carotid artery stenting	Ioxaglate	50	Left hemiparesis, left neglect	Right fronto-parietal	Immediately	2 days	2 days
6	F/62	Coiling (basilar aneurysm)	Ioversol	150	Restlessness, blindness	Bilateral occipital, left frontal	During angiography	21 days	17 days
7	F/74	Coiling (basilar aneurysm)	Iohexol	None reported	Complete bilateral blindness	Left parieto-occipital	1 hour	1 day	N/A
	F/45	Coiling (basilar aneurysm)	Iohexol	None reported	Confusion, cortical blindness	Bilateral occipital	12 hours	16 days	N/A
	F/73	ICA aneurysm	Iohexol	None reported	Blindness	Bilateral occipital	20 minutes	5 days	N/A
8	M/72	Coiling (ACoA aneurysm)	Iopamidol	260	Right hemiparesis, motor aphasia	Left cerebral cortex, left basal ganglia	1 hour	7 days	N/A
9	F/54	Coiling (basilar aneurysm)	None reported	62	Blindness	Occipital lobe	3 hours	1 month	1 month
10	M/80	Carotid artery stenting	Iohexol	250	Right hemiparesis	Left fronto-parieto-occipital	2 hours	2 days	4 days
11	M/51	Stenting (ICA aneurysm)	Iopromide	300	Gerstmann's syndrome, blindness, left hemiparesis	Right fronto-parieto-occipital	30 minutes	2 days	5 days
12	F/65	Coiling (PCoA aneurysm)	None reported	None reported	Confusion, headache, paresis, blindness	Bilateral temporo-occipital	6 days	9 days	1 month
13	F/46	Coiling (basilar aneurysm)	None reported	None reported	Sotomas, dysmetria, inability to tandem walk	Right pons, middle cerebellar peduncle, occipital	1 month	9 months	9 months
	F/56	Stent and coiling (basilar aneurysm)	None reported	None reported	Paresthesia, difficulty ambulating	Pons, left occipital	1 month	1 month	4 months
14	F/70	Coiling (MCA aneurysm)	None reported	None reported	Altered mental status, seizure	Posterior temporal, occipital	12 days	Improved	18 days
	M/62	Coiling (ACA aneurysm)	None reported	None reported	Altered mental status	Bilateral temporo-occipital	7 days	Improved	24 days
15	F/35	SAH	None reported	None reported	Confusion, headache, seizure, left hemiparesis	Bilateral cerebellum, occipital, left cerebral hemisphere	2 days	Improved	18 days
16	F/50	Coiling (ICA aneurysm)	Iopromide	220	Right hemiparesis, sensory loss, right-sided neglect	Left cerebral hemisphere	Immediately	persistent deficit	N/A
17	F/66	Basilar aneurysm	None reported	None reported	Headaches	Bilateral occipital	3 weeks	3 months	16 weeks
18	F/66	Coiling (ICA aneurysm)	Iomeprol	80	Consciousness disturbance, aphasia, right hemiparesis	Left cerebral hemisphere	Immediately	4 days	29 months
Current report	F/58	Coiling (ICA aneurysm)	Iohexol	316	Right hemiparesis, agraphia	Left fronto-parieto-occipital	About 30 days	50 days	90 days

CT: Computed tomography, MRI: Magnetic resonance imaging, CIE: Contrast-induced encephalopathy, M: Male, F: Female, PCoA: Posterior communicating artery, ICA: Internal carotid artery, ACoA: Anterior communicating artery, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, SAH: Subarachnoid hemorrhage, N/A: Not applicable

order to reduce the patient's edema. Her symptoms improved after treatment, signifying either steroid responsiveness or spontaneous resolution. If we assume steroid responsiveness, then the presence of immune-mediated encephalopathy may also be considered; however, no immediate adverse reactions, such as rashes or nausea, were noted following contrast injection, no eosinophilia was evident at the time of hospital admission or during follow-up and DLST to iohexol yielded negative results. An allergic inflammatory reaction thus seems unlikely.

In conclusion, endovascular coil embolization for unruptured arterial aneurysms is a widely performed neurosurgical intervention. Therefore, the possibility of complications, such as CIE, should be kept in mind in cases involving postoperative abnormal neurological findings, even during the subacute period.

The authors state that they have no Conflict of Interest (COI).

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