Rare Complication of Carotid Stenting: New-Onset Refractory Status Epilepticus: A Study of Five Patients

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Abstract

Introduction: New-onset refractory status epilepticus (NORSE) is uncommon and almost 50% of cases are cryptogenic. We report the rare development of NORSE following carotid artery stenting (CAS), a procedure which is increasingly being used to treat the carotid stenosis. **Materials and Methods:** Patients who developed NORSE following CAS for the prevention of stroke over a period of 5 years were analyzed retrospectively. The degree of internal carotid artery stenosis (ICA) was estimated as per the NASCET criteria. **Results:** We analyzed five patients (age: 56–83 years). NORSE was reported within 30 min to 14 days post-CAS. Status epilepticus was focal in two patients, generalized in two, and one had nonconvulsive status epilepticus. All patients were treated with multiple antiepileptic drugs. Four patients recovered and survived and one succumbed. Two patients had comorbid hypertension and two had diabetes and hypertension. Four patients had hemiparesis due to the contralateral middle cerebral artery territory infarction and one patient had syncope. Two patients had postinfarction gliosis. **Conclusions:** We report a new cause of NORSE, following CAS. Stroke resulting in gliosis and cerebral hyperperfusion syndrome are the proposed mechanisms.

Keywords: Carotid artery stenting, cerebral hyperperfusion syndrome, new-onset refractory status epilepticus

Introduction

New-onset refractory status epilepticus (NORSE) manifests as a prolonged period of refractory seizures without obvious identifiable cause in otherwise healthy individuals.[1] It is a rare entity, and limited information is available about its etiology.[2] Almost half of the cases are cryptogenic, and the best elucidated pathophysiological mechanism involves immune causation.[1]

We report five patients observed over a period of 5 years, who developed NORSE after the carotid artery stenting (CAS). Few authors have previously described status epilepticus after the carotid endarterectomy as well as CAS.[3-5] However, the development of NORSE following CAS has been rarely reported. As CAS procedure is increasingly being used in the current times, this complication assumes importance.[6]

Case Studies

Clinical details and outcomes of all five patients are mentioned in Table 1. Two patients had comorbid hypertension, two had diabetes and hypertension, and one had neither of diabetes and hypertension. Four patients presented with hemiparesis with contralateral infarction in the middle cerebral artery (MCA) territory with stenosis at the internal carotid artery (ICA) origin, whereas one presented with multiple episodes of syncope and was found to have infarction in the left MCA territory with bilateral ICA stenosis. ICA stenosis at origin was calculated by the NASCET criteria.[7] CAS was done at variable periods ranging from 5 to 60 days postinfarction. NORSE was reported in patients within 30 min postprocedure up to 14 days postprocedure. Two patients had gliosis due to a stroke. Two patients presented with focal convulsive status epilepticus who had ipsilateral ICA stenting, two with generalized status epilepticus, and one with nonconvulsive status epilepticus. All patients required multiple antiepileptic drugs (AEDs), including continuous infusion of AED and anesthetic agent for seizure control. None of the patients had a prior history of seizures. All the patients were treated in intensive care units, underwent neuroimaging– magnetic resonance angiography (MRA) of the brain to rule out new infarction or bleed postprocedure. Figure 1 shows the post-CAS procedure MRA of case 2, with no acute infarction on diffusion-weighted imaging [Figure 1a] and fluid-attenuated inversion recovery sequences [Figure 1b]. Metabolic parameters including serum electrolytes, calcium, magnesium, and ammonia were normal. Electroencephalogram (EEG) monitoring was done in all patients. Figure 2 shows EEG traces of case 2 with the right focal onset [Figure 2a] evolving to generalized status epilepticus [Figure 2b] and termination of seizures followed by the generalized slowing [Figure 2c]. There was one death; one patient was discharged with the modified Rankin Scale (mRS) Grade 4, and three patients were discharged with mRS 0–1 Grade.

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Table 1: Summary of clinical characteristics

Case	Age (year)	Sex	Co-morbid condition	Clinical features	ICA stenosis	Percentage stenosis	ICA stenting time	Status epilepticus	MRI post-CAS	EEG	Outcome of NORSE	AEDs required
1	58	Male	HT	Syncope, Lt MCA infarction	Bilateral ICA origin	Rt - 90, Lt - 86	Lt 5 days, Rt 2 weeks later	14th day of right ICA stenting	No acute infarct	Bilateral Slowing (post treatment)	Recovered (mRS 0)	LZ, PH, VL, LEV, MZ
2	83	Male	HT, DM	Rt MCA infarction with gliosis	Rt ICA origin	84	2 months later	2nd day	No acute infarct	Rt Focal status with secondary generalization	Death* (mRS 6)	LZ, PH, VL, LEV, MZ
3	64	Male	HT, DM	Lt MCA infarction	Lt ICA origin	92	10 days later	5th day	No acute infarct	Lt focal status with secondary generalization	Recovered (mRS 4)	LZ, PH, LEV, MZ, KT
4	56	Male	HT	Rt MCA infarction	Rt ICA origin	90	1 week later	30 min	Tiny periventricular acute infarct	Rt focal slowing (Post treatment)	Recovered (mRS 0)	LZ, PH, LEV, MZ
5	58	Female	None	Lt ICA infarction with Gliosis	Lt ICA origin	88	1 week later	10th day	Lt MCA old gliosis with perilesional edema, no acute infarct	PLEDS (Post treatment)	Recovered (mRS 1)	LZ, PH, MZ

*Patient underwent extensive testing including CSF examination as he continued to worsen. HT=Hypertension, DM=Diabetes mellitus, ICA=Internal carotid artery, MCA=Middle carotid artery, TIA=Transient ischemic attack, PLEDs=Periodic lateralized discharges, Mrs=Modified Rankin score, LZ=Lorazepam, PH=Phenytoin, VL=Valparin, LEV=Levetiracetam, MZ=Midazolam, KT=Ketamine, CSF=Cerebrospinal fluid, NORSE=New-onset refractory status epilepticus, MRI=Magnetic resonance imaging, EEG=Electroencephalography, LT=Left, RT=Right, CAS=Carotid artery stenting

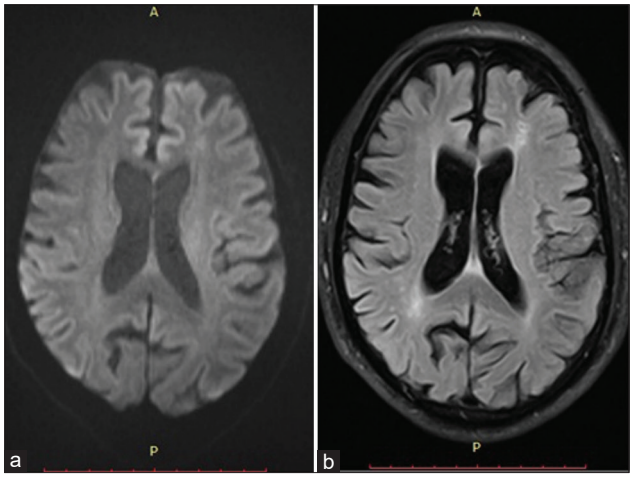

Figure 1: Postcarotid artery stenting procedure magnetic resonance angiogram of case 2. (a) Diffusion-weighted imaging and (b) Fluid-attenuated inversion recovery sequences showing no acute infarction

Discussion

NORSE is a rare condition and has been mostly described in autoimmune conditions. To the best of our knowledge, it has not been described in CAS patients. We postulated cerebral hyperperfusion as a possible mechanism for the development of NORSE in these patients due to its close temporal relationship with carotid stenting.

Cerebral hyperperfusion syndrome (CHS) was first described by Sundt *et al*. It was described following carotid endarterectomy (CEA). Patients presented with the triad of a headache, neurological deficit, and epileptic seizures. These symptoms were not caused by cerebral ischemia.[8] Patients with CHS are symptomatic within the first 4 weeks.

Patients with severe stenosis of ICA are in a state of decreased cerebral perfusion; hence, cerebral autoregulatory mechanisms keep intracranial arteries in the vasodilated state to maintain tissue perfusion. Once the perfusion is reestablished after CAS, there is a sudden increase in cerebral blood flow. This is mainly caused by impaired vasoreactivity. Impairment of cerebral vasoreactivity depends on the duration and intensity of cerebral hypoperfusion. Grade of the ipsilateral carotid stenosis, the presence of contralateral carotid occlusion, and poor collateral flow have been described as the main risk factors for the severity of microvascular autoregulation impairment.[3,8,9]

Another plausible mechanism contributing to NORSE in our series could be CHS in the presence of infarction as well as gliosis. However, larger studies are required to confirm our hypothesis.

The exact mechanism of CHS after CAS or CEA is unclear and appears to be multifactorial. Strict blood pressure control is an important strategy for the management of CHS. Early identification and the prevention of hypertension for prolonged duration are essential during the perioperative period. There are no definite guidelines about blood pressure parameters and therapy needs to be individualized. Patients presenting with seizures and headache should undergo neuroimaging to rule out intracranial hemorrhage and perfusion studies for the early identification of CHS.[10]

Lack of documentation of prestenting and poststenting cerebral blood flow studies is one of the limitations of this study.

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Conflicts of interest

There are no conflicts of interest.

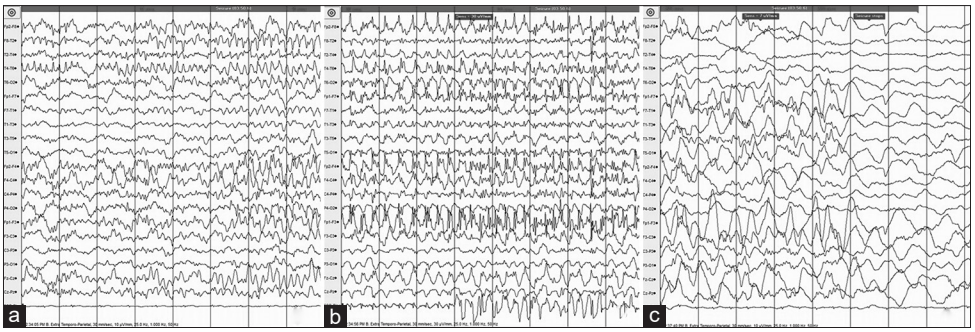

Figure 2: Continuous electroencephalogram monitoring (Temporoparietal montage, Timebase/paper speed of 30 mm/s, high-pass filter 25 Hz, and low-pass filter 1 Hz) of case 2. (a) Right focal onset spike and wave discharges, (sensitivity – 10 μV/cm). (b) Generalized spike and wave discharges suggestive of status epilepticus, (sensitivity –3 0 μV/cm). (c) Termination of epileptic activity followed by generalized slowing (sensitivity – 10 μV/cm)

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