Simultaneous Occurrence and Interaction of Hypoperfusion and Embolism in a Patient With Severe Middle Cerebral Artery Stenosis

Stefanie Schreiber, MD; Mine Serdaroglu; Frank Schreiber; Martin Skalej, MD; Hans-Jochen Heinze, MD; Michael Goertler, MD

Background and Purpose—The coincidence of hemodynamic and embolic findings in patients with stroke from large artery stenosis has suggested an interaction of both pathologies. This has emerged into the hypothesis of an impaired washout of emboli in the presence of hypoperfusion. We propose an additional link between both pathologies.

Summary of Case—A 48-year-old woman presented with a recurrent symptomatic severe left middle cerebral artery stenosis. MRI depicted left hemispheric ischemic infarcts in the deep and subcortical white matter and in the cortical border zone. One-hour transcranial Doppler monitoring detected 64 microembolic signals distal to the arterial stenosis. Monitoring also revealed recurrent thrombus formation at the stenotic plaque with decline of poststenotic flow velocity followed by embolism with abrupt excessive flow velocity increase and subsequent normalization at the initial baseline level. Cerebrovascular reserve in the distribution territory of the stenosed artery as assessed by transcranial Doppler after carbon dioxide stimulation revealed a normal reserve capacity in periods with baseline poststenotic flow velocity and an exhausted reserve capacity when flow velocity was decreased due to stenotic thrombus formation.

Conclusion—In our patient, adherent thrombus formation resulted in an increasing severity of the stenosis with subsequent vasodilatation and diminution of flow resistance in the depending vascular distribution territory. MRI suggested that adherent thrombi were predominantly washed into terminal supply and border zone brain regions, ie, into regions with supposed maximum vasodilatation and least flow resistance immediately before thrombus avulsion. Preferred wash-in of emboli into regions with low blood flow resistance might be an additional mechanism besides impaired washout in patients with severe large artery disease.

Key Words: embolism ■ hypoperfusion ■ middle cerebral artery stenosis ■ transcranial Doppler sonography

Large artery stenosis accounts for 15.6% of ischemic events in patients admitted to the hospital with an acute stroke or transient ischemic attack. Hemodynamic compromise downstream to severe stenosis and arterial embolism from the stenotic plaque are considered the predominant pathologies in this etiology. We report a patient with symptomatic middle cerebral artery (MCA) stenosis in whom both pathologies were linked together by recurrent thrombus formation at the stenotic plaque and subsequent embolism as detected by real-time transcranial Doppler monitoring.

Materials and Methods

Patient
A 48-year-old woman presented with recurrent dysarthria and paresthesia of her tongue and right hand during the past 4 weeks. On admission, she exhibited a moderate dysarthria and right-sided paresis of her face and arm, which had developed 3 days before. In her medical history, a treated arterial hypertension and an untreated mild hypercholesterolemia were revealed. She did not receive any antiplatelet or anticoagulant medication since symptoms had occurred 4 weeks ago.

Diagnostic Examinations
MRI, including T1, T2, fluid-attenuated inversion recovery, and diffusion-weighted imaging sequences, depicted ischemic infarcts with a rosary-like pattern in the deep and subcortical white matter of the left MCA territory and small cortical infarcts in the left cortical border zone (Figure 1). Transcranial color duplex sonography revealed an isolated high-grade stenosis (peak systolic flow velocity 311 cm/s) in the left MCA. Extracranial duplex sonography, echocardiography, electrocardiography including 24-hour monitoring, and laboratory findings were normal.

Functional Transcranial Doppler Examinations
Transcranial Doppler sonography (Multidop X4, DWL) with carbon dioxide testing was performed to determine cerebrovascular reserve capacity. Mean flow velocity of the MCA distal to the symptomatic stenosis was measured at rest under normal breathing and after stimulation of cerebral vasodilatation by breathing a mixture of 5% carbon dioxide and 95% oxygen. Because stimulation only affects
cerebral resistance vessels, increase of cerebral blood flow correlates with a proportional increase of flow velocity in basal cerebral arteries. An exhausted reserve capacity was assumed at flow velocity increase of <5% per volume percent increase of end-expiratory carbon dioxide, indicating pre-existing vasodilatation due to stenosis induced low cerebral perfusion pressure.6

Subsequently, the patient underwent 1-hour bilateral simultaneous MCA monitoring with dual-gated 2-MHz pulsed-wave probes (Multiplex X4, DWL). Sample volumes were placed distal to the left-sided MCA stenosis. Periods suspicious of embolic signals were assessed automatically and recorded. Subsequent visual offline review of the automatically stored episodes was performed by 2 independent observers.7

Results
Monitoring of the left MCA revealed repeated periods of a spontaneous flow velocity decline. During the presented 4-minute period, mean velocity decreased from 54 to 34 cm/s followed by a loud chirping sound from a passing embolus and accompanied by an abrupt increase to 60 cm/s with subsequent normalization at 54 cm/s. Further, less pronounced sudden flow velocity increases, each initiated with a chirping sound from a passing embolus, could be observed within the 4 minutes. Simultaneously monitored velocity in the right MCA remained stable at 76 cm/s over the whole

Figure 1. Diffusion-weighted MRI scans showing small cortical and deep and subcortical white matter infarcts in the border zone and terminal supply regions.

Figure 2. Flow velocity decline in the left poststenotic MCA resulting from thrombus formation at the stenotic plaque. Transient excessive flow velocity increase after thrombus avulsion as a consequence of preceding hemodynamic compromise with vasodilatation in the depending vascular bed.

Figure 3. Normal (A) and exhausted (B) cerebrovascular reserve distal to left MCA stenosis in the absence (A) and presence (B) of an additional thrombus at the stenotic plaque.
period (Figure 2). Subsequent carbon dioxide testing starting when mean flow velocity was quite stable at 54 cm/s in the left and 76 cm/s in the right MCA revealed a bilateral velocity increase indicating a normal cerebrovascular reserve capacity in both MCA distribution territories (Figure 3A). In contrast, when carbon dioxide testing on the left side was initiated at a dampened mean velocity of 34 cm/s, no velocity increase was observed, consistent with an exhausted cerebrovascular reserve at this time (Figure 3B).

After carbon dioxide testing, transcranial Doppler monitoring was switched from flow velocity recording to Doppler spectrum recording for microembolic signal detection. In a subsequent 1-hour spectrum monitoring, 64 microembolic signals were detected distal to the left MCA stenosis. No signals were observed in the right MCA. Also during spectrum monitoring, velocity spontaneously declined in the left MCA followed by a sudden excessive increase immediately after registration of a loud chirping, utmost high-intense microembolic signal (Figure 4).

After completion of monitoring, antithrombotic therapy was initiated with an intravenous bolus of 500 mg aspirin and a loading dose of 300 mg clopidogrel. A recurrent monitoring 3 hours later revealed cessation of microembolic (and macroembolic) signals, constant left MCA mean flow velocity of 52 cm/s, and normal cerebrovascular reserve capacity at carbon dioxide testing.

Discussion

The clinical importance of MCA stenosis is determined by its potential to cause cerebral ischemic events due to hemodynamic compromise and artery-to-artery embolism. Traditionally, both pathologies were considered to be mutually exclusive. In contrast, Caplan and Hennerici proposed an interrelated and complementary occurrence of hypoperfusion and embolism, which was corroborated by further investigations. They postulated that reduced blood perfusion distal to high-grade stenosis limits the ability of emboli from the stenosis to be washed out of the cerebral circulation and therefore may accumulate in least perfusion pressure regions, i.e., in the terminal supply and border zone areas.

In our patient, adherent thrombus formation at the stenotic plaque resulted in an increased severity of the stenosis with subsequent vasodilatation and diminution of the flow resistance in the depending vascular bed. This was confirmed by the accompanying deterioration of the cerebrovascular reserve and the excessive flow velocity increase immediately after thrombus avulsion. Although not to be discriminated by transcranial Doppler, vasodilatation and diminution of flow resistance in the depending vascular bed may be maximal in the terminal supply and border zone regions. As a consequence and corroborated by MRI findings, flow immediately after thrombus avulsion may be maximal into these regions as well as the probability that embolic thrombi detected as macroembolic signals are washed into these regions. Thus, preferred wash-in of emboli into terminal supply and border zone regions might be an additional mechanism besides an impaired washout to explain coincidental findings of hypoperfusion and embolism in patients with severe arterial stenosis.

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Disclosures

None.

References

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