When rt-PA goes with the flow: role of collateral circuits in concurrent carotid and middle cerebral artery occlusion

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Abstract

Background: *Patients with internal carotid artery (ICA) occlusion treated with rt-PA have higher rates of unfavorable outcomes. When a middle cerebral artery (MCA) embolization is also present, it has been hypothesized that the MCA recanalization could have an important role in clinical recovery.*
Aims: *Our aim is to illustrate the clinical and prognostic importance of the activation of Willis' Circle collateral flows, studied by transcranial colordoppler, in patients with ICA and concurrent MCA embolization.*
Patient: *A 74-year-old man presented with right facio-brachio-crural hemiplegia, global aphasia and right campimetric deficit. Emergency CT showed left MCA hyperdensity. The patient was treated with rt-PA, with resolution of the hyperdensity at the control-CT. Neck vessels and transcranial colordoppler revealed MCA reperfusion and persistent left carotid occlusion with intracranial hemodynamic compensation ensured by the right anterior cerebral artery (ACA) through the anterior communicating artery. The patient had a remarkable clinical recovery (three months later modified Rankin Scale 0) and underwent to carotid endoarterectomy, because of ultrasound finding of carotid late-reperfusion.*
Conclusions: *The case highlights a possible role of intracranial collateral flows in MCA reperfusion and clinical recovery of rt-PA-treated patients with concurrent ICA and MCA occlusions and could stimulate an extensive study on this issue.*
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Keywords: *cerebrovascular disease; neuroimaging; neurosonology; strokes.*

Clinical history

A 74-year-old man was admitted to our hospital for sudden development of facio-brachio-crural hemiparesis of his right side, severe global aphasia and right campimetric deficit. His NIHSS (National Institutes of Health Stroke Scale) was 14. The patient had been healthy until this event, except for an abdominal hernia, surgically treated several years before.

His risk factors for vascular disease were smoking and dyslipidemia in treatment with statins. He had no hypertension nor diabetes mellitus. Emergency cranial computed tomography (CT) showed hyperdensity of the distal M1 tract of left Middle Cerebral Artery (MCA) **(Fig. 1A)**, no sign of acute ischemic lesion, hemorrhage or space occupying lesion.

The patient was treated with 72 mg of intravenous recombinant tissue plasminogen activator (rt-PA), post-treatment NIHSS was 12. Left MCA hyperdensity was no longer showed by the 24 hours control CT (**Fig.1B**).

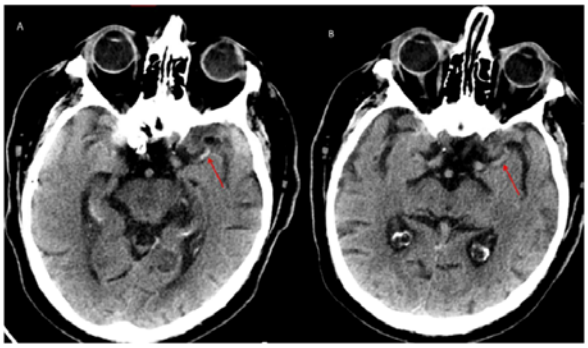

Figure 1A. Emergency cranial CT showing hyperdensity of the distal M1 tract of left MCA -1B. Control CT performed 24 hours after rt-PA treatment showing absence of hyperdensity of the left MCA.

Color doppler ultrasonography (CDU) of neck vessels showed occlusion of extracranial left ICA (**Fig. 2A-2B**). Transcranial colordoppler (TCCD) showed flux acceleration in right anterior cerebral artery (**Fig. 2C**) and flux inversion in left anterior cerebral artery (ACA) (**Fig. 2D**), normal flux in right MCA (**Fig. 2E**) and reperfusion of left MCA (**Fig. 2F**) served by anterior communicating artery (AComA).

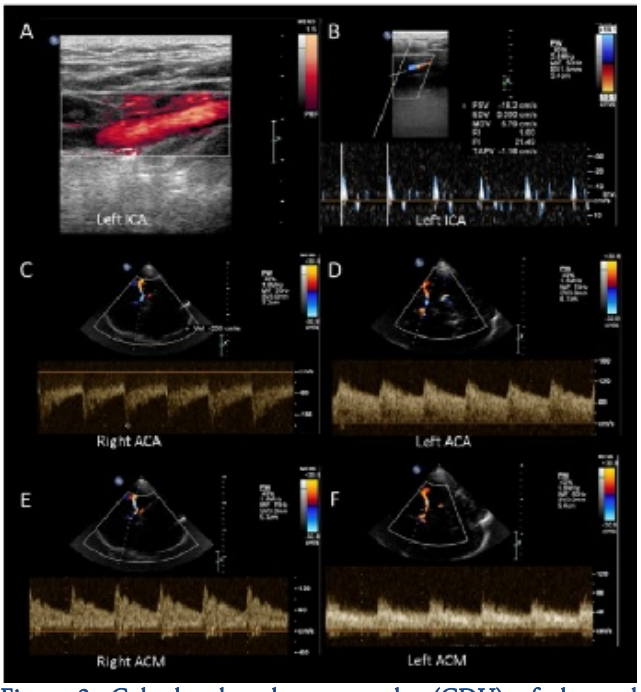

Figure 2. Colordoppler ultrasonography (CDU) of the neck vessels, performed 24 hours after the therapy showed complete occlusion of left ICA (2A, 2B). Transcranial colordoppler (TCCD) showing increased peak velocity in right ACA (2C), blood flow inversion in left ACA (2D), reperfusion of left MCA with reduced blood flow compared to the contralateral vessel (2E-2F).

Magnetic Resonance and Magnetic Resonance Angiography performed four days after the event confirmed CT and CDU findings (**Fig .3A-B**);

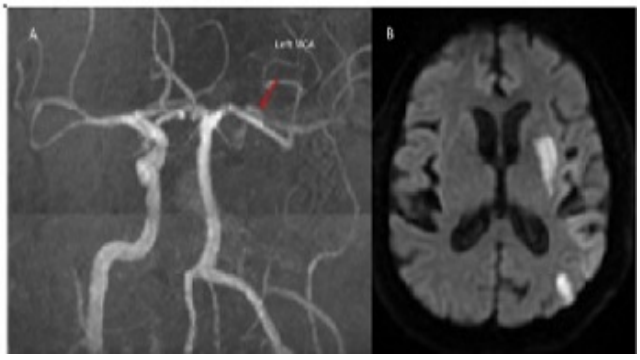

Figure 3A. MRI angiography showing left MCA reperfusion and left ICA occlusion - 3B. DWI sequence showing acute ischemic lesions.

MRI angiography showed left MCA reperfusion while the left ICA was still occluded. Echocardiogram and Holter ECG were normal. All laboratory tests were unremarkable. During the hospital stay, the patient's neurological condition had a good clinical recovery, in particular he presented remarkable improvement of aphasia, persistent drift of upper and lower right limbs, minor facial paralysis and mild sensory lost in the right hemisoma. The patient was transferred to rehabilitation facilities. After rehabilitation cycle, the patient had no longer significant neurological deficits and his mRS (modified Rankin Scale) was 0 at 3 months. The follow-up colordoppler CDU and TCCD, performed three months after the stroke, showed reperfusion of left ICA with a 80% stenosis (300 m/s peak velocity) and a lower flow in left MCA and ACA without flux inversion in left ACA. An angio-CT confirmed the reperfusion of left ICA with residual high grade stenosis and showed a reduced representation of the left MCA vascular tree. After a vascular surgery evaluation, the patient was submitted to carotid endarterectomy, with successful outcome.

Discussion

Generally, ICA recanalization rate after rt-PA treatment is about 30%[1,2] and is observed at a median of 3.5 days after the stroke[3]. Furthermore our patient's good clinical recovery is objectively impressive. In fact, it has been reported that patients with ICA occlusion generally have lower rates of good outcomes (14.9%), higher mortality (28.1%), and higher rates of unfavorable outcomes, like hemorrhages, (59.8%) compared with patients with basilar artery occlusion (28.1%, 23.6%, and 44.9%, respectively) or MCA occlusion (32.6%, 8.8%, and 31.3%, respectively)[4]. In addition, EPITHET study reported that patients with ICA occlusion treated with rt-PA had much worse outcomes compared to placebo-treated patients (high disability was observed three months after the stroke in the 88% of rt-PA treated patients and in the 38% of the placebo treated ones)[5].
It has been hypothesized a possible role of MCA reperfusion in dramatic clinical recovery in patients with ICA occlusion and ipsilateral MCA embolization[2]. In fact it has been reported that a favorable outcome occurs in 100% of patient that present MCA recanalization within 24 hours after rt-PA treatment; if there is no MCA recanalization within this period, a favorable outcome is observed only in 25% of patients. In addition there is no difference in frequency of ICA recanalization between these two group of patients[2].

In our case, the presence of hemodynamic compensation through Willis' Circle, which ensures blood support to the hemisphere served by the occluded carotid, appears crucial. The good recovery of our patient might be related to pivotal hemodynamic features: the communication between the two hemispheres ensured a prompt delivery of rt-PA to the left MCA (which appeared hyperdense at emergency CT) and a consequent fast reperfusion of ischemic regions. In the absence of these characteristics, it's reasonable to hypothesize that the outcome would have been poor and the rt-PA treatment useless since in absence of collateral circuits the local concentration of rt-PA at the left MCA probably would have been low. The variability of activation of collateral circuits could explain the different outcomes observed in patients with the same stroke.

The Willis' Circle's "plasticity" is not only an anatomical, but also a functional parameter, which can be studied through several techniques. Nevertheless TCCD is a fast (and bed-side) exam permitting a functional evaluation of the Willis' Circle. A rapid CDU and TCCD evaluation of these features in patients suitable for thrombolysis with ICA occlusion could be helpful in differentiating two subsets of patients: potential good responders and potential poor responders to rt-PA treatment.

In this view, if a compensation through the anterior communicating artery is not functionally activated, other mechanisms should be evaluated as, for example, those through the posterior communicating artery or through the ophthalmic artery, both evaluable by TCCD.

Obviously, the TCCD evaluation should be performed without delaying the proper treatment; for example it could be performed while the patient is receiving thrombolytic therapy. Furthermore extensive studies should be performed in order to investigate a possible relationship between the presence of Willis' collateral circuits and good outcome in patients with ICA occlusion.

Conclusions

A possible role of MCA reperfusion in good clinical recovery of patients with ICA occlusion and ipsilateral MCA embolization has been hypothesized. In literature, the relevance of active intracranial collateral circuits has not been sufficiently highlighted. In particular the possibility of a rapid, bed-side, non-invasive evaluation of these features through TCCD could have an important diagnostic and prognostic role in such patients.

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