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CEREBRAL MICROBLEEDS AND INTRAVENOUS THROMBOLYSIS

Case report

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ABSTRACT - Intravenous thrombolysis is an important procedure that has significant impact on ischemic stroke prognosis. However, intracranial hemorrhage (ICH) is a feared complication of this procedure. It has been suggested that cerebral microbleeds (CMBs) may increase the risk of ICH after thrombolysis. We report on a 69 years-old woman with multiple CMBs submitted to intravenous thrombolysis without complications.

KEY WORDS: thrombolysis, cerebral microbleeds, amyloid angiopathy, intracranial hemorrhage, stroke.

Micro-hemorragias cerebrais e trombólise endovenosa: relato de caso

RESUMO - A trombólise endovenosa é um procedimento importante que tem impacto significativo sobre o prognóstico de pacientes com acidente vascular cerebral isquêmico. Contudo, a hemorragia intracraniana (HIC) é complicação temida deste procedimento. Foi sugerido que micro-hemorragias cerebrais (MHC) aumentem o risco de HIC após trombólise. Relatamos o caso de mulher de 69 anos com múltiplas MHCs submetida a trombólise endovenosa sem complicações.

PALAVRAS-CHAVE: trombólise, micro-hemorragias, angiopatia amilóide, hemorragia intracraniana, acidente vascular cerebral.

It has been suggested that cerebral microbleeds (CMBs) represent a diffuse hemorrhage-prone angiopathy that may increase the risk of ICH after thrombolysis[1,2] and anticoagulant/antiplatelet treatment[1]. CMBs are often unnoticeable in CT but can be detected as loss of signal on T2*-weighted gradient-echo (GRE) sequences.

We report the case of a patient with multiple CMBs submitted to intravenous thrombolysis without complications.

CASE

We present the case of a 69 year-old woman with a history of arterial hypertension, diabetes mellitus and dyslipidemia. She also had a history of progressive cognitive decline for the past year, two previous strokes (22 years and 5 months earlier) and was taking aspirin 100 mg qd. Family members did not know whether any of the previous strokes had been hemorrhagic and were not sure about previous stroke locations or symptoms. The patient had sudden onset of dysarthria and worsening of a residual right hemiparesis. She had been seen well 83 minutes before arriving at the emergency room presenting global aphasia, dense right and mild left hemiparesis. Her NIH Stroke Scale (NIHSS) score was 11 and her blood pressure, 100/80 mmHg. CT disclosed hypodense areas in the right cerebellar hemisphere and right occipital lobe suggestive of previous strokes as well as subcortical periventricular white matter lesions bilaterally.

Intravenous (IV) thrombolysis with 0.9 mg/kg of rt-PA was performed according to the National Institute of Neurological Disorders and Stroke (NINDS) protocol guidelines[3]. The infusion was started 170 minutes after the last time the patient had been seen well. Two days later, CT disclosed a left occipitoparietal infarct without hemorrhagic transformation; there was marked improvement of aphasia and the NIHSS was 3.

Brain MRI was performed six days after admission (Figure) and revealed a left occipitoparietal acute infarct (A,B), associated to areas of hemorrhagic transformation characterized by high signal on T1-weighted images (T1WI) (C) and

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very low signal on T2*-weighted images (T2*WI) (D). There was also a right cerebellar lesion with very low signal on T1WI and foci of low signal on T2*WI, suggestive of an old infarct with hemosiderin deposition (F); other similar smaller lesions were noticed in the right thalamus and in the putamen bilaterally (E). Another important finding was related to the presence of innumerous punctate foci of marked hypointensity on T2*WI (E, F) in the cerebellum, pons, basal ganglia, thalami and cerebral hemispheres, suggestive of hemosiderin deposition related to previous microhemorrhages not visualized on CT. In addition, there were confluent areas of increased signal on FLAIR (B) and T2-weighted images in the subcortical white matter bilaterally, possibly representing small vessel ischemic disease.

The patient provided informed consent for this publication.

DISCUSSION

Noncontrast CT is a standard imaging method in acute stroke. In the presented case, neurologists relied on CT findings before thrombolysis, in accordance with the NINDS rt-PA study protocol and current guidelines[3,4]. It was assumed that the cerebellar lesion identified on CT corresponded to a previous infarct without associated hemorrhage but MRI performed six days after stroke onset showed that, in reality, this lesion had a past hemorrhagic component. In addition, MRI disclosed small novel foci of hemorrhage in the acutely infarcted area and multiple CMBs. The latter were not present on CT or T1WI and most likely preceded the acute infarct. The patient was on regular use of aspirin before the acute stroke and rt-PA was administered at the edge of the therapeutic window. Nevertheless, no neurological deterioration was observed. On the contrary, the patient presented significant clinical improvement.

It is believed that CMBs are caused by blood leakage from small vessels affected by lipofibrohyalinosis or amyloid angiopathy[5]. T2*WI has greater sensitivity than spin-echo sequences to show CMBs. These lesions are revealed on T2*WI as areas of signal loss due to the paramagnetic properties of hemosiderin, deoxyhemoglobin and ferritin that cause local magnetic field inhomogeneities and are usually not visible on CT[2]. CMBs may be seen even many years after hemorrhage onset and have been associated with age, hypertension, the presence of silent cerebral infarct, white matter hyperintensity and a history of clinical apparent stroke[5,6].

Prevalence of CMBs has varied from 3.1% to 7.7% in healthy subjects but has been higher in patients admitted with ischemic stroke, ranging from 12% to 68%[6,7]. Therefore, if CMBs consistently increase risk of symptomatic ICH in acute stroke after thrombolysis, this procedure should be withdrawn in a considerable proportion of patients. The presented patient had a good outcome after thrombolysis in spite of CMBs and a larger old cerebellar hemorrhage that were not visualized on CT.

Thrombolysis has become a crucial tool in acute stroke management. Symptomatic ICH was reported in 6.4% of patients treated with intravenous rt-PA in the NINDS trial and in 10% of the patients treated with intra-arterial (IA) prourokinase in PROACT II[3,8]. Patients underwent CT but not T2*WI in these trials. In studies in which T2*WI was performed, ICH was shown to occur within or remote from CMBs[1,2,9]. The frequency of symptomatic ICH was not significantly different between cases with and without CMBs

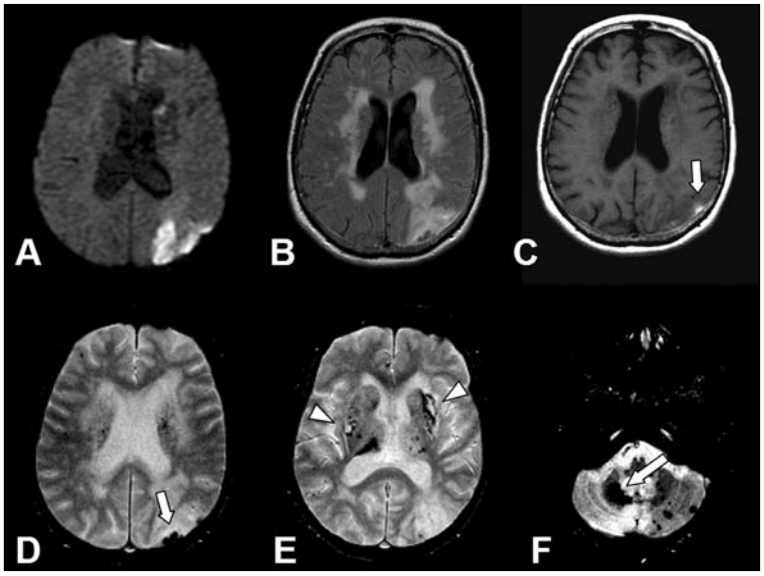

Figure. Axial diffusion-weighted image (A) discloses the left acute occipitoparietal infarct. Axial FLAIR image (B) demonstrates increased signal in the acute infarct area and also confluent areas in the cerebral white matter bilaterally, suggestive of small vessel ischemic disease. Axial T1-weighted image (C) presents foci of high signal in the area of the acute infarct (arrow), presumably related to the presence of hemorrhage (methemoglobin). Axial T2-weighted images show clearly other hemorrhagic areas in the acute infarct, with marked hypointensity (arrow in D) and also innumerous punctate foci of marked hypointensity in the basal ganglia (arrowheads in E), thalami and right cerebellar hemisphere (arrow in F), possibly related to previous microbleeds.*

in 41 patients after IA[2] and in 44 patients after IV thrombolysis[9]. However, in the latter the number of CMBs was small, ranging from one to three, in contrast with the presented patient who had innumerous CMBs along the brainstem, cerebellum, basal ganglia and cerebellar hemispheres. Still, no complications were observed.

Symptomatic hemorrhages after intravenous thrombolysis was were reported by Chalela and colleagues in a patient with higher NIHSS score and older age than the presented patient[1]. Furthermore, preliminary data from the DEFUSE (Diffusion weighted imaging Evaluation For Understanding Stroke Evolution study) suggest that intravenous thrombolysis is safe in patients with CMBs. DEFUSE is a multi-center, prospective oben-label pilot study of IV t-PA therapy administered to stroke patients within 3 to 6 hours after symptom onset[7]. The protocol includes performance of MRI before thrombolysis, 3 to 6 hours after thrombolysis, and 30 days later. Data from patients enrolled in DEFUSE indicated that CMBs were not associated with an increased risk of hemorrhagic complications after thrombolysis. The sample size was relatively small but still, none of the patients with CMBs developed symptomatic ICH after thrombolysis while 11.9% of the patients without CMBs had symptomatic ICH after the procedure. No significant differences were found between rates of either symptomatic or asymptomatic hemorrhages in patients with and without CMBs at baseline.

Novel MRI sequences, more sensitive to detect CMBs than CT, and intravenous thrombolysis have become increasingly available diagnostic and therapeutic tools for neurologists worldwide. Further studies should address the prognostic relevance of CMBs and interactions between imaging results, clinical findings and route of thrombolysis in the decision-making process in acute stroke.

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