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THRESHOLD OF REGIONAL CEREBRAL BLOOD FLOW FOR INFARCTION IN PATIENTS WITH ACUTE CEREBRAL ISCHEMIA

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SUMMARY

Threshold of regional cerebral blood flow (rCBF) for cerebral tissue survival in relation to time was studied in patients with acute cerebral ischemia with xenon-enhanced computed tomography (XeCT). Case 1: A 58-year-old man with right hemiparesis, total aphasia and a high intensity area of 1cm² in the left insula on diffusion weighted image underwent XeCT CBF study before and after intra-arterial local thrombolytic therapy (IALT) on the occluded middle cerebral artery (MCA) 4 hours and 7 hours after stroke onset, respectively. Case 2: A 65-year-old woman with recurrent transient ischemic attacks (TIAs) caused by severe stenosis of the left MCA underwent XeCT CBF study 5 hours after onset of the last attack. XeCT was conducted by 5-min wash-in method. In Case 1 the rCBF in the pre-IALT MCA territory was 4 to 19ml/100g/min. The area where rCBF in the post-IALT increased to above 15ml/100g/min evolved into infarct on subsequent CT scan/MR (magnetic resonance) imaging. The patient was discharged with only mild motor dysphasia. In Case 2 the left corona radiata showed rCBF of 7ml/100g/min and this area evolved into infarct on XeCT and IRM. The patient was discharged home with right hemiparesis. Our results showed validity of the rCBF threshold in acute cerebral ischemia reported by Jones et al. Residual rCBF in the acute stage of cerebral ischemic stroke can predict the fate of the lesion.

Key words: acute cerebral ischemia, cerebral infarction, flow threshold, ischemic penumbra, xenon CT.

RéSUMÉ

Seuil de débit sanguin cérébral correspondant à un infarctus chez les patients ayant une ischémie cérébrale aiguë

Le seuil de débit sanguin cérébral (DSC) pour la survie tissulaire en fonction du temps était étudié par le scanner au xénon (XeCT) chez les patients présentant une ischémie cérébrale aiguë. Cas n°1 : un XeCT a été réalisé chez un homme de 58 ans avec une hémiplégie droite, une aphalie mixte et une zone hyperintense de 1cm² à la 4ème et 5ème heure de l'accident ischémique. Les zones avec un DSC > 15 ml/100g/min ont été récupérées et celles < 9 ml/100g/min ont évoluées vers l'infarctus aux XeCT et IRM de contrôle. Le patient est sortie de l'hôpital avec une hémiplégie modérée. Dans le cas n° 2, le DSC de la corona radiata gauche était 7 ml/100g/min avec une évolution vers l'infarctus à l'IRM. La patiente est sortie de l'hôpital avec une hémiplégie droite. En conclusion, nos résultats valident le seuil d'ischémie cérébrale rapporté par Jones et al. Le DSC résiduel dans la phase aiguë de l'ischémie cérébrale peut prédire l'évolution de la lésion.

Mots-clés : ischemie cérébrale aigue, infarctus cérébral, seuil de perdusion, pénombre ischémique, Xénon CT.

INTRODUCTION

Since the revolutionary concept of “time is brain” was introduced, whether or not thrombolysis is needed in the treatment of patients with acute cerebral ischemia remains a matter of concern [2, 13]. For decision-making within the therapeutic time window computed tomography (CT) scan, magnetic resonance imaging, cerebral angiography and regional cerebral blood flow (rCBF) studies such as single photon emission tomography, positron emission tomography and xenon-enhanced CT (XeCT) are used, often in combination. It is well known that recovery of ischemic brain or development of infarction is largely dependent on the residual blood flow and the duration of ischemia [1, 7]. However, reports on the critical flow and the period of ischemia that can be tolerated in humans are scarce. We report two cases of acute ischemic stroke in which XeCT was used to assess the rCBF and correlated with cerebral angiography, CT scan and MR imaging.

METHODS

XeCT was performed with a 5-min wash-in protocol. After base scan the patient started to inhale a mixture of gas (28% Xe, 30-50% oxygen and balance air) made in the stable Xe gas rebreathing system (AZ-725, Anzai Medical) and delivered by a mask, and underwent CT scans (Asteion, Toshiba) every one min for 5-min inhalation period. Quantification of rCBF was achieved by the image processing software (AZ-7000W, Anzai Medical).
Case reports

Case 1

A 58-year-old man developed right arm weakness and difficulty in speech and was admitted to our department 2 and a half hours after onset. On admission he had motor and sensory aphasia (jargon) and right hemiparesis. The National Institute of Health Stroke Scale (NIHSS) score [3] was 12. He was on medication for diabetes mellitus and had a habit of smoking. CT showed the early signs of ischemic infarction such as hyperdense middle cerebral artery (MCA) sign and blurring of insular ribbon on the left (figure 1a). MR imaging at 3 hours after symptom onset revealed a small distinctly hyperintense lesion in the left insula on diffusion weighted image (DWI) and mild hyperintensity in the insula and closing of the sylvian fissure on fluid-attenuated inversion-recovery (FLAIR) image (figures 2a and 2b). MR angiography disclosed MCA occlusion at its distal trunk (figure 1b).

XeCT CBF study at 4 hours after onset showed a wider area of decreased perfusion than DWI in the left frontoparietotemporal region corresponding to the territories supplied by the operculofrontal, posterior parietal, angular and posterior temporal arteries (figures 2c, 3a and 3b). The rCBF values in these areas were 4.3 to 18.9 ml/100g/min while those in the corresponding areas in the contralateral hemisphere were 29.6 to 43.7 ml/100g/min. The MCA occlusion at the distal segment of the main trunk was confirmed by cerebral angiography (figures 3a and 3b). Five hours passed since the symptom onset. Neurological deficits did not show any improvement. We decided to go on to intra-arterial thrombolysis after informed consent. Urokinase, 120,000 U, was directly infused into the occluded segment of the MCA. It was repeated two more times for a total dose of 360,000 U. The posterior parietal and posterior temporal arteries and the proximal part of the angular artery were recanalized (figures 3c and 3d). No further thrombolysis was attempted because 6 and a half hours, longer than the therapeutic time window of 6 hours, had passed. XeCT at 7 hours after onset showed that the central portion of the ischemic area regained flow of 36.6 to 47 ml/100g/min, mildly hyperemic compared to the corresponding area in the contralateral hemisphere (figure 4a). This hyperemic area corresponded to the reperfused posterior parietal artery territory. The other areas supplied by the non-recanalized arteries remained at low flow level of 8.8 to 17.9 ml/100g/min.

On Day 3, CT showed a low density area in the posterior insula and the adjacent areas where rCBF remained at low level, 8.8 to 14ml/100g/min (figures 4a and 4b). On Day 6, FLAIR image showed a hyperintense lesion in the same area and it was a little larger with mixed intensity in the upper level where thrombolysis failed and rCBF remained at 14 ml/100g/min (figures 4a and 4c). The patient was
THRESHOLD OF REGIONAL CEREBRAL BLOOD FLOW FOR INFARCTION IN PATIENTS

339

Case 2
A 65-year-old woman was admitted with recurrent TIAs over a 3-day period. On admission, 4 hours after onset of the last attack, she was aphasic and hemiparetic on the right side. The NIHSS score was 5. DWI showed a hyperintense lesion in the left putamen extending to the corona radiata (figure 5b). MR angiography revealed no visualization of the left MCA bifurcation and distal branches. The rCBF values at 5 hours after the last symptom onset were 6.8 ml/100gm/min in the left corona radiata, 17 ml/100gm/min in the surrounding white matter and 25 ml/100gm/min in the cortical/sub-
cortical area of the left MCA territories (figure 5a).
Cerebral angiography revealed severe stenosis of the left MCA trunk and no filling of the major branches, but fairly good peripheral filling through leptomeningeal collaterals. An unruptured aneurysm was found at the contralateral MCA bifurcation. Thrombosis was not attempted because of mild neurological deficits, being close to the end of therapeutic time window and the angiographic findings. After returning to the ward her neurological status worsened to a NIHSS score of 15 in spite of intravenous anticoagulation and antiplatelet treatment. MR imaging 24 hours later showed that the hyperintense lesion was slightly larger in the left corona radiata that evolved into infarction on follow-up MR imaging (figure 5c). The white matter with rCBF of 6.8 ml/100g/min evolved into infarction, but brain tissue with more than 17 ml/100g/min was saved. Her neurological deficits started to improve in 4 days. Two months later she was discharged with NIHSS score of 4.

DISCUSSION

Our results show that the ischemic area measured by XeCT is more extensive than that indicated by CT scan or MR imaging in the early hours after symptom onset. Perfusion CT or perfusion MR could detect it as XeCT did. However, those modalities have difficulties in quantification of rCBF. In the clinical setting where prompt decision-making is required whether going on to thrombolysis or not, XeCT CBF measurement is superior to CT and MR perfusion. XeCT enables quantitative measurement of rCBF with relatively high spatial resolution and correlation to anatomical structures [5, 15], although some drawbacks [11, 15, 16] are reported.

Intra-arterial delivery of thrombolitics has been shown to be effective in recanalizing occlusions of the MCA [4]. But only a select group of patients falls into this category. XeCT not only can determine whether or not the collateral supply is present but also can distinguish which patients have reversible or irreversible flow levels [9].

Retrospective analysis of Case 1 indicated that the 4-hour-old ischemic area with rCBF of 15.5 to 18.9 ml/100g/min was partly salvaged by intra-arterial thrombolysis. While the ischemic areas with pre- and post-thrombolysis flows of 4.3 and 7.4 ml/100g/min, respectively, and of 10.6 and 8.8 ml/100g/min, respectively, evolved into dense infarction, the areas with post-thrombolysis flow of ≥15.5 ml/100g/min were salvaged. This flow level falls in the border zone of the threshold curve between the penumbra and infarction [7]. The ischemic tissue that remained in low rCBF level of 14 ml/100g/min at 7 hours evolved into mottled pattern infarction on later imaging. Here, the rCBF value of 14 ml/100g/min was an averaged figure in data processing from a rather wider region of interest that should be a mixture of the tissue with flow as low as 6 ml/100g/min destined to infarction [8] and the salvaged tissue with higher flow than 14 ml/100g/min. Functional recovery of the patient was eventually very good. Thus, rCBF of approximately 15 ml/100g/min may be the threshold for reversibility of the ischemic mixed cortical gray and white matter at 4 to 7 hours after symptom onset.

In Case 2 the white matter with rCBF of 6.8 ml/100g/min at 5 hours after symptom onset evolved into infarction. This result is contrary to the report that white matter has greater tolerance to low flow level like this than gray matter [8], although the value itself fits well to the Jones’ curve [7]. Since this patient had repeated TIs before the last stroke, low perfusion could have persisted much longer than 5 hours.

We observed mild hyperemia after thrombolysis in Case 1. This area did not show abnormalities on later imaging. The prognostic significance of hyperemia remains unclear, although it is reported that postischemic hyperemia resulted in neurological deficit [6]. Hyperemia per se may not carry a uniformly consistent prognosis [17].

Although we have to be careful to apply the experimental results to clinical practice and data are scarce, our results seem to agree well with the threshold curve reported by Jones et al. [7] (figure 6). Levy et al. [10] suggested that the posterior CBF of 6 ml/100g/min at 90 min of basilar artery occlusion might be the threshold for reversible ischemia. We need to accumulate more data on this critical issue.

CONCLUSION

We suggest that a rCBF of 15 ml/100g/min at 4 to 7 hours after symptom onset may be the threshold of mixed cortical gray and white matter for reversible ischemia. Detection of irreversibly damaged tissue and salvageable tissue in the early hours of acute
cerebral ischemia is important for therapeutic interventions. XeCT is a powerful tool for this purpose.

REFERENCES