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Orolingual angio-oedema after alteplase therapy in a stroke patient concurrently using angiotensin II receptor blocker

An 82-year-old female with history of hypertension, atrial fibrillation and rectosigmoid cancer status postoperation without recurrence had a sudden onset of right hemiparesis and aphasia. She had regularly taken irbesartan, atenolol, propafenone and indapamide. On arrival at the emergency room, she was globally aphasic and had right hemiparesis, hemihypoaesthesia and homonymous hemianopia. Her initial National Institutes of Health Stroke Scale Score was 20. Head CT 65 min after onset of symptoms showed a left hyperdense middle cerebral artery sign. A left middle cerebral artery infarction was diagnosed. She received recombinant tissue plasminogen activator (rt-PA) (alteplase, 0.75 mg/kg) 140 min after onset of symptoms. Thirty minutes after completion of alteplase therapy, she was noted to have a large, swollen and protuberant tongue (figure 1). Urticaria and flushing were also seen on her trunk. Mild hypoxaemia was noted and was managed with oxygen delivery through a mask. Orolingual angio-oedema was diagnosed, and the patient was treated with 30 mg of diphenhydramine and 100 mg of hydrocortisone. The symptoms resolved gradually in 4 h. Levels of the complements (C3, C4) and a complete blood count checked on the next day were within normal limits. Reviewing her history, she had taken irbesartan 150 mg per day for 6 months without a similar episode. Her family also denied any known allergy or angio-oedema in the patient and the family. Seven days after development of angio-oedema, she resumed irbesartan. Her other previous medication was also gradually resumed, and no angio-oedema recurred.

DISCUSSION

Orolingual angio-oedema is an uncommon but potentially life-threatening complication of rt-PA treatment in acute ischaemic stroke. The mechanisms underlying the development of angio-

oedema are mainly histamine- and bradykinin-related. The activation of the complement system by rt-PA can elevate the levels of C4a, C3a and C5a, resulting in the release of histamine.¹ In addition, rt-PA may increase the generation of bradykinin, possibly through the plasmin-mediated pathway.²

Previous studies showed that concurrent ACE inhibitor usage is a major risk factor of developing orolingual angio-oedema for rt-PA-treated patients with a RR of 13.6.³ Similar to the ACE inhibitor, angiotensin II receptor blocker (ARB) has been shown to increase levels of bradykinin, as a result of reduced metabolism by ACE and neutral endopeptidase.⁴ In addition, compared with ACE inhibitor alone, the incidence of development of angio-oedema is lower, but it is still present in patients treated with ARB alone.⁵ Therefore, it is theoretically possible that ARB usage is susceptible for development of angio-oedema in patients receiving rt-PA, and further studies should be performed to clarify the exact incidence. Based on our reported case, we suggest that patients receiving rt-PA treatment with simultaneous use of ACE inhibitor or ARB should be closely monitored of this potentially life-threatening complication.

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Competing interests None.

Patient consent Obtained.

Ethics approval Ethics approval was provided by the Ethics Committee of National Taiwan University Hospital.

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Figure 1 Large, swollen, and protuberant tongue with mild hypoxaemia, 30 min after completion of the alteplase therapy, suspected as being due to airway obstruction.

Neurological picture

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