BMJ Case Reports

Unexpected outcome (positive or negative) including adverse drug reactions

Angioneurotic orolingual oedema following thrombolysis in acute ischaemic stroke

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Summary

Alteplase used for thrombolysis in ischaemic stroke may be complicated by orolingual acute angioedema (OAA), a rare but potentially life-threatening side effect. We report the case of a 32-year-old woman who over 24 h experienced OAA after thrombolysis for an acute ischaemic left hemispheric stroke. We discuss the pathophysiology of this rare phenomenon.

CASE PRESENTATION

The administration of alteplase, used in thrombolysis for ischaemic stroke, may be complicated by a rare but potentially life-threatening side effect. Orolingual acute angioedema (OAA) has been reported in several cases after recombinant tissue plasminogen activator (rtPA) infusion in patients often also treated with angiotensin converting enzyme (ACE) inhibitors.[1–3]

A 32-year-old woman without known allergy and not undergoing any medical treatment (other than oral contraception) had an acute ischaemic left hemispheric stroke. After exclusion of intracranial haemorrhage, she received alteplase 140 min after symptom onset. Forty-five minutes after infusion, she presented lingual oedema and hypersialorrhoea. Lingual protrusion was impossible but the lips remained untouched (figure 1A). No dyspnoea, bronchospasm or urticaria was observed.

TREATMENT

The patient was immediately treated with intravenous clemastine, methylprednisolone infusion and budesonide nebulisation.

OUTCOME AND FOLLOW-UP

The angioedema subsided within 24 h without sequelae (figure 1B). The next day, a blood test revealed low fibrinogen concentration and prolongation of prothrombin time (35%) and detected soluble fibrin in the plasma. However, the platelet count remained normal (243 000). These abnormalities disappeared within 24 h.

DISCUSSION

Orolingual angioedema after treatment of acute ischaemic stroke with alteplase is observed in 5.1% of treated patients.[2] Two main risk factors are well known: concomitant ACE inhibitor treatment (RR 13.6) and early MRI evidence of an acute middle cerebral artery ischaemic stroke (RR 6.4).[3] Other risk factors are suspected, such as concomitant blocker treatment.[1] In this case, the patient was not on any medical treatment, however CT scanning detected early evidence of middle cerebral artery stroke confirmed by the MRI-DWI. The hypothesis about the pathophysiology of OAA suggests simultaneous activation of the complement system and kinin cascasdes by plasmin, produced by alteplase-induced cleavage of plasminogen.[2] The

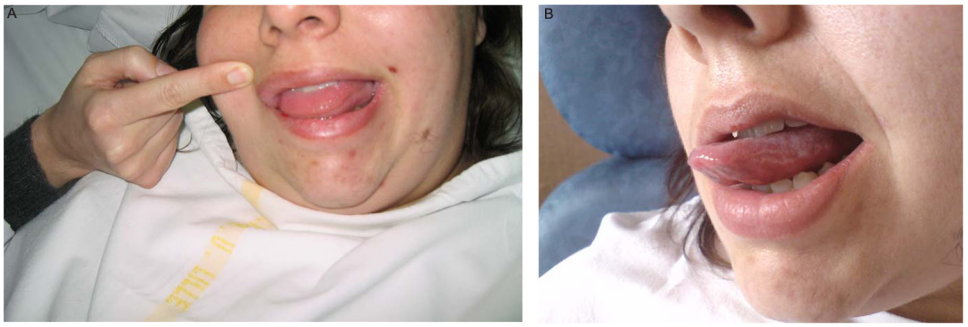

Figure 1 Angioneurotic orolingual oedema following thrombolysis for ischaemic stroke. (A) Angioneurotic orolingual oedema at the acut-estage. Note the lingual oedema. (B) Vanishing of the symptoms of angioedema in 24h.

direct activation of the complement cascade causes histamine liberation and mast cell degranulation[4] followed by a raised bradykinin level (due to the kinin cascade).[5] The combination of these two biological pathways leads to significant vasodilatation. ACE inhibitors are associated with more severe OAA because they may induce inhibition of plasma kinases which are responsible for bradykinin degradation. The next day, our patient's blood test revealed disseminated intravascular coagulation (DIC). The literature does not mention any effects following alteplase infusion but the 14th edition of *Meyler's Side Effects of Drugs* reports possible DIC with fibrinolytics and specially urokinase. The pathophysiology is unknown but involvement of a urinary thromboplastin is suspected. OAA and DIC are rare but potentially life-threatening complications of thrombolysis requiring control of clinical and biological signs with immediate initiation of specific treatment.

Learning points

- Orolingual acute angioedema (OAA) after treatment of acute ischaemic stroke with alteplase is observed in around 5% of treated patients.
- The pathophysiology of OAA suggests simultaneous activation of the complement system and kinin cascasdes by plasmin, produced by alteplase-induced cleavage of plasminogen.
- Angiotensin converting enzyme inhibitors are associated with more severe OAA.

Competing interests None.

Patient consent Obtained.

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