Case report

Remote cerebellar hemorrhage after thrombolysis

Hematoma remoto cerebeloso post-fibrinolisis

Abstract

Introduction: Intracerebral haemorrhage after intravenous thrombolysis is a relevant complication of ischaemic stroke. Its mechanisms are not well known; making a distinction between haemorrhagic transformation of the ischemic region and hematomas unrelated to that area, referred to as remote intracerebral haemorrhage (rICH).

Case report: An 84-year-old male, independent in all activities of daily living with hypertension as a cardiovascular risk factor suffers abruptly from aphasia and right faciobrachial hemiparesis. Cerebral Computed Tomography (CT) does not show any findings of bleeding or acute ischemia. Intravenous thrombolysis is administrated in the absence of contraindication. After 24 hours, control CT showed a parenchymatous haemorrhage in the right cerebellar amygdala and no signs of haemorrhagic transformation of the infarct. Follow-up Magnetic Resonance imaging showed the absorption of the cerebellar hematoma, without signs of previous ischemia in that location.

Conclusion: rICH is not an uncommon post-thrombolytic complication and its long-term morbidity and mortality is considerable. The finding would force us to think about small vessel disease with hypertensive microangiopathy as one of the main predisposing factors of cerebellar rICH, in contrast with lobar rICH, more related with leucoaraiosis, amyloid angiopathy and microbleeds.
Resumen

Introducción: La hemorragia intracraneal tras fibrinolisis intravenosa es una de las complicaciones más trascendentales del ictus isquémico. Sus mecanismos precursores aún no son bien conocidos, diferenciando la transformación hemorrágica del área isquémica y los hematomas no relacionados con dicha región, conocidos como hemorragias intracraneales remotas (HICr).

Reporte de caso: Varón de 84 años, independiente en sus actividades diarias e hipertenso. De forma brusca sufre afasia y hemiparesia facio-braquial derecha. En Tomografía Computarizada cerebral no se observan signos de sangrado ni hallazgos isquémicos agudos. Al no existir contraindicación se realiza fibrinolisis intravenosa, observándose en el control tomográfico a las 24 horas una hemorragia parenquimatosa en amígdala cerebelosa derecha, sin transformación hemorrágica del área de infarto. En la Resonancia Magnética de seguimiento se aprecia reabsorción del hematoma cerebeloso sin signos de isquemia previa en dicha localización.

Conclusión: Los HICr no son una complicación tan infrecuente de la terapia fibrinolítica y su morbimortalidad a largo plazo no es despreciable. Su hallazgo en pruebas de imagen nos obligaría a pensar en patología de pequeño vaso, destacando la microangiopatía hipertensiva como uno de los principales factores predisponentes de HICr cerebelosos; a diferencia de las HICr lbrares, en las que la leucoaraiosis, la angiopatía amiloide y los fenómenos de microsangrado estarían más asociados.

Palabras clave
Introduction

Intracranial hemorrhage after intravenous thrombolytic therapy is one of the most clinically relevant complications in the management of ischemic stroke. However, its pathophysiological foundations are still not well known.

In the evaluation of the precursor mechanisms of intraparenchymal brain hemorrhage post-thrombolysis, a distinction has been made between bleeds over areas of cerebral ischemia where revascularization has been tried (ICH) compared to those on regions unrelated to the ischemia causing the initial symptoms, known as remote intracranial hemorrhages (RICH). The latter, less addressed in the literature, carry a higher risk of long-term morbidity and mortality. They may appear isolated or associated with an ICH in patients undergoing thrombolysis, which is between 1.3 and 3.7% of the total number of patients with ischemic stroke.

We present the case of a patient with acute ischemic stroke who, after receiving intravenous thrombolytic therapy, suffered a cerebellar hemorrhage not topographically related to the initial clinical presentation.

Clinical case

An 84-year-old male, functionally autonomous (score 0 in the mRS), with arterial hypertension as the only known cardiovascular risk factor and with no antiplatelet or anticoagulant treatments suffered an abrupt mixed aphasia with motor predominance and mild right faciobrachial hemiparesis scoring 9 in the NIHSS. A simple cerebral computed tomography (CT) shows moderate leukoaraiosis data with no signs of bleeding or acute ischemic findings and a score of 10 on the ASPECT scale. The picture is compatible with a partial anterior circulation infarct (PACI) dependent on a distal segment of the left middle cerebral artery (Figure 1A and 1B). As there was no contraindication, an intravenous thrombolysis was performed at 2h 30min from the beginning of the clinical examination. He was admitted to the stroke unit without clear clinical improvement, maintaining blood pressure values below 180/105 mmHg and with no relevant pathological findings in biochemistry, blood count, or coagulation. In the tomographic control at 24-hours post-thrombolysis, a parenchymal hemorrhage was observed in the right cerebellar amygdala, without hemorrhagic transformation of the infarction area in the left frontal lobe (Figure 2A and 2B).

In the follow-up brain magnetic resonance imaging (MRI), resorption of the cerebellar hemorrhage without signs of previous infarction was observed (Figure 3). Diffuse leukoaraiosis is confirmed in turn with a Fazekas grade 2.

Discussion

Unlike ICHs which are associated with cardioembolic pathology or occlusion of large intracerebral arteries, RICHs seem to have a small vessel disease as a predisposing factor. Alteplase (recombinant tissue Plasminogen Activator r-tPA) would thus act on areas more prone to disruption of the blood-brain barrier, without being able to rule out a possible interaction with undiagnosed base coagulopathies.

Despite discrepancies between some studies, the factors related to small vessel pathology and frequently associated with RICH are leukoaraiosis, amyloid angiopathy, and micro-bleeding phenomena. These hemorrhages are more prevalent in women and patients of more advanced age. According to the latest published series, these factors seem to predispose concretely to lobar RICHs, whereas deep, brainstem, and cerebellar RICHs would be related to hypertensive angioopathy in accordance with the case presented here. However, it could not be ruled out that some of these RICHs were actually ICHs on ischemic areas not visible by the CT brain scan performed at admission.

Our clinical case shows an atypical location of a remote hemorrhage. This location (cerebellar...
**Figure 1.** Initial simple brain CT pre-thrombolysis: supratentorial (A) and infratentorial (B) cut. The supratentorial section shows diffuse periventricular hypodense areas in the context of leukoaraiosis.

![Figure 1](image1.png)

**Figure 2.** Simple brain CT of post-thrombolysis control at 24 hours: supratentorial section (A), where a hypodense area compatible with ischemic stroke is observed (arrow); and infratentorial (B), showing hyperdense area suggestive of hemorrhage in right cerebellar tonsil.

![Figure 2](image2.png)
Remote cerebellar hemorrhage post-thrombolysis

Figure 3. Control brain MRI. An axial section in T2 FLAIR (A) is shown in which a hypointense area is observed in the area of previous cerebellar hemorrhage, compatible with hemosiderin deposits (arrow). In the coronal section in T2 STE (B) there is scarring lesion in the left frontal lobe and a small area of porencephaly with peripheral hyperseal due to a deposit of hemosiderin (arrow) in the right cerebellar hemisphere.

Knowing this association and having the possibility to detect it, several works have analyzed the benefit of r-tPA in these patients. For those in whom the existence of microbleeds is already known from previous MRIs, it is not clear that the increase in risk of ICH or RICH completely exceeds the possible benefit of thrombolysis. Regarding the presence of leukoaraiosis, patients who underwent alteplase showed a better functional prognosis at 3-6 months of the event compared to those who did not. Finally, if we assess the benefit of low doses of fibrinolytic compared to standard doses of 0.9 mg/kg in these patients with the aim of reducing the risk of bleeding, a recent study did not show that the reduced dose of 0.6 mg/kg was equivalent in terms of good functional prognosis at 3 months despite being associated with fewer cerebral hemorrhages, therefore, without trials that take into account groups with signs of small vessel pathology, international guidelines continue to recommend standard doses.

This existing association between RICH and small vessel pathology has led some authors to propose pre-thrombolysis MRI. It is a useful imaging technique to help assess the patient’s previous situation, taking into consideration the greater risk of death and functional dependence (70.3%). However, it is not as accessible in hyperacute stroke care and the assessment of aspects such as the number of microbleeds would be impractical for rapid decision making in daily clinical activity when CT is already able to detect leukoaraiosis associated with intraparenchymal bleeding.

hemorrhage) would suppose between 8.8% to 25% of all RICHs. As already explained, hypertensive microangiopathy would be one of the most plausible predisposing factors. This is unlike what occurs in remote cerebellar hemorrhages associated with a neurosurgical intervention, in which the most feasible explanation would be a hemorrhagic venous infarction due to excessive CSF drainage.
Conclusion

In conclusion, remote hemorrhages are not an infrequent complication of thrombolytic therapy and its long-term morbidity and mortality are not negligible. The finding of one of them in imaging tests would force us to think of small vessel pathology, highlighting hypertensive microangiopathy as one of the main predisposing factors of remote cerebellar hemorrhages.

Conflicts of interest
We declare that this research has no conflicts of interest.

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References
