Intravenous thrombolysis and thrombectomy in young patients with ischaemic stroke due to undetected atrial myxoma: Do recent clinical trials provide sufficient evidence to support reperfusion in these cases? a, b, c

Trombólisis intravenosa y trombectomía en paciente joven con ictus isquémico por mixoma auricular desconocido: ¿hay suficiente evidencia en los recientes ensayos clínicos de reperfusión para estos casos?

Dear Editor,

Cerebral embolism caused by a myxoma in the left atrium is a rare but usually fatal event. Atrial myxomas represent 50% of all primary cardiac tumors; 75% of them are located in the left atrium.1 Myxomas usually appear between the ages of 30 and 60. Pedunculated myxomas, which have an irregular morphology, are the type of myxoma most likely to cause embolism since they are mobile.2 Transoesophageal echocardiography is a safe, accurate, and non-invasive means of diagnosing these myxomas.3 Treatment with intravenous fibrinolysis or rescue mechanical thrombectomy is based on previously published cases.4,5 However, no guidelines or studies provide reliable evidence supporting use of these techniques.

We present the case of a 17-year-old adolescent who was admitted to our hospital’s emergency department due to sudden loss of consciousness while he was exercising. He had no known drug allergies, history of drug use, or any other relevant medical history. The general examination showed a blood pressure of 110/60 mm Hg, 110 bpm, and no fever. Cardiac auscultation revealed a rhythmical heart sound with a systolic murmur that could be heard in all areas and radiated to both carotid arteries. In the neurological examination, the patient scored 32 on the NIHSS (2+2+2+2+2+3+3+4+3+4+0+2+0+2+1). Time from symptom onset to assessment by a neurologist was 45 minutes. The emergency department performed a complete blood count, which yielded normal results, and an ECG, which revealed sinus tachycardia at 108 bpm and no signs of acute ischemia. A simple cranial CT scan showed no anomalies (Fig. 1). A CT angiography performed before the intravenous fibrinolysis showed occlusion of the distal segment of the right internal carotid artery (ICA) and stenosis of the distal basilar artery, affecting the exit of the right posterior cerebral artery (PCA). In view of these findings, we decided to administer intravenous fibrinolysis; our patient’s guardians signed the informed consent form. At this point, door-to-needle time was 50 minutes. While receiving fibrinolytic treatment, the patient underwent a transthoracic echocardiography which revealed a large pedunculated mass with irregular borders in the left atrium. A few days later, a thoracic CT scan confirmed the presence of an intracardiac mass (Fig. 1). After thrombolytic treatment, our patient scored 26 on the NIHSS and we opted to conduct a rescue mechanical thrombectomy. Door-to-femoral puncture time was 130 minutes. When the patient arrived at the interventional neuroradiology department, his lower limbs were pale, cold, and livid. As we were unable to register his blood pressure, we administered norepinephrine before starting the procedure. An angiography study revealed occlusion of the proximal left subclavian artery (SA) due to a thrombus which penetrated the origin of the left vertebral artery (VA). It also revealed occlusion of the right ICA, right middle cerebral artery (MCA), and the proximal segment of the right PCA, with a partially recanalised thrombus in the M1–M2 segment of the left MCA (Fig. 1). To address the multiple occlusions, we performed thrombectomies in the following order: right ICA, right MCA, and left MCA (2 passes in each) with a Solitaire FR device (4×20). We also coiled the left VA at V3–V4 below the left posterior inferior cerebellar artery to prevent new embolic events in the basilar artery due to the thrombus in the left SA (Fig. 2). An angiography study conducted after embolectomy revealed occlusion of the abdominal aorta (Fig. 2), both iliac arteries, both femoral arteries, and the left SA (Fig. 1). The patient subsequently underwent thromboendarterectomy of the abdominal aorta, the iliac and femoral arteries, and the axillary and humeral circumflex arteries, all of which achieved partial recanalisation. Despite the above procedures, a neuroimaging study taken 24 hours after admission revealed diffuse hemorrhagic transformation in the right temporoparietal area affecting the basal ganglia and causing a mass effect leading to a midline shift of approximately 10 mm. An ischaemic area was also found in the territory of the right PCA (Fig. 2). The patient died due to multiple systemic complications. The samples of the material removed during mechanical thrombectomy confirmed a myxoma as the source of the emboli (Fig. 2).

Systemic embolism is a potential complication of atrial myxomas, especially those located in the left atrium; emboli travel to the cerebral arteries and are the cause of 0.5% of all ischaemic strokes.6 Emboli usually consist of tumor tissue or thrombi that form on the surface of the myxoma. The effectiveness of intravenous fibrinolysis varies, and it may depend on the composition of the thrombus; for example, thrombi of myxomatous tissue are more difficult to break down.7 Likewise, as fibrinolysis may break down any thrombi on the surface of the myxoma, the treatment may increase the risk of embolism. Lastly, some authors state that patients with cardiac myxoma receiving intravenous systemic thrombolytic therapy are at high risk for hemorrhage due to the high incidence of preexisting brain microaneurysms.8 Regarding use of mechanical thrombectomy in these patients, recently published cases report good

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a Please cite this article as: Zapata-Arriaza E, Pardo-Galiana B, González-García A, Montaner Villalonga J. Trombólisis intravenosa y trombectomía en paciente joven con ictus isquémico por mixoma auricular desconocido: ¿hay suficiente evidencia en los recientes ensayos clínicos de reperfusión para estos casos? Neurología. 2017;32:404–407.
b This study has not been presented at any scientific conferences.
rates of recanalisation and functional improvement. In one of these cases, the authors used a stent retriever plus a Penumbra® aspiration pump to prevent distal migration of the thrombus, and achieved recanalisation of the occluded segment.

Rescue endovascular treatment, which was shown to be effective in recent studies, was not successful in our case. Patients under 18 will require an aetiological diagnosis as quickly as possible because of lack of evidence on the safety and effectiveness of intravenous fibrinolysis and rescue mechanical thrombectomy for this age group. Given that the cause of ischaemic symptoms in young patients may contraindicate fibrinolysis, they will need quick screening tests to help prevent any potential complications of fibrinolytic treatment. In any case, diagnostic tests should never delay reperfusion treatment.

In our case, performing a heart ultrasound before intravenous fibrinolysis would have revealed the cause of multiple embolism and helped in therapeutic decision-making. Intravenous fibrinolysis was not fully effective, which was probably due to the composition and aggressiveness of the source of embolism. This treatment could have been omitted in favor of thrombectomy with aspiration devices that may have extracted myxomatous material more easily. This approach would have been a more effective means of reperfusing occluded vessels.

Given the low incidence of this type of stroke, establishing diagnostic and treatment criteria is a complex task. The final decision resides with the neurologist or neuroradiologist responsible for each specific case. Multicentre studies and clinical trials should be conducted in this population to provide scientific evidence on treatment of this entity.
Figure 2  (A) Angiogram of the right internal carotid artery (anteroposterior projection) showing complete recanalisation after the second pass. (B) Left internal carotid artery angiogram (anteroposterior projection) showing complete recanalisation of the middle cerebral artery after the second pass. (C) Left vertebral artery angiogram (anteroposterior projection) showing coil occlusion. (D) An infrarenal abdominal aorta angiogram (anteroposterior projection) conducted after embolectomy revealed occlusion. (E) Thrombus with myxomatous material removed in the embolectomy. (F) Simple, non-contrast CT scan (axial slice) at 24 hours. The image reveals hemorrhagic transformation in the right temporoparietal area.

Funding

This study has received no public or private funding.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

Continuous infusion of apomorphine in patients with advanced Parkinson’s disease and different degrees of functional disability

Apomorfina en bomba de perfusión continua en pacientes con enfermedad de Parkinson avanzada con diferente grado de afectación funcional

Dear Editor:

Progression of Parkinson’s disease (PD) is associated with significantly decreased mobility, increased risk of falls, and such non-motor symptoms as cognitive and psychotic disorders. The main phenotypic manifestations of advanced PD (APD) are motor fluctuations, severe dyskinesia, axial motor symptoms resistant to levodopa, and non-motor symptoms such as cognitive impairment. Conventional treatment, which fails to control symptoms satisfactorily in these patients, is usually administered to patients on H&Y stages 4 or 5. Approximately 50% of patients with PD display alterations characteristic of APD 5 years after clinical diagnosis; such alterations include motor fluctuations, non-motor symptoms, and treatment-induced dyskinesia. Treatment with continuous infusion of apomorphine (CIA) has been found to effectively improve motor symptoms and overall function in patients with APD. However, the literature provides little information on the effectiveness of CIA according to the degree of functional disability in these patients. With this in mind, we conducted an observational study to determine the effectiveness and tolerability of CIA in patients with APD and different degrees of functional disability. We believe that our partial results are worth publishing.

Patients and methods

We included consecutive patients with PD, diagnosed according to the Queen Square Brain Bank diagnostic criteria, who were attended in the Parkinson’s and movement disorders unit at Consorci Sanitari de Terrassa (Barcelona, Spain); all patients were in advanced stages of the disease. The included patients had motor and non-motor fluctuations and experienced disabling ‘off’ periods. These patients were offered initiation of treatment with continuous subcutaneous infusion of apomorphine in line with the indications listed on the summary of product characteristics. All patients signed informed consent forms before inclusion. Our study was approved by the hospital’s Clinical Research Ethics Committee.

Assessment of functional disability and patient classification

Participants were categorised in 2 groups: a) patients with APD and moderate functional disability, defined as rates of 60% to 80% on the Schwab & England Activities of Daily Living Scale (S&E) and H&Y stages 2 to 3 (group A); and b) patients with APD and severe functional impairment, defined as S&E rates < 60% and H&Y stages > 3 (group B).

Procedure

We tested CIA in all patients for 3 to 4 days. The initial infusion rate of apomorphine (Apomorfina Archimedes® 10 mg/mL, infusion solution; Archimedes Pharma Ibérica S.L., Madrid, Spain), at a concentration of 5 mg/mL, was 0.20 mL/h. Infusion speed was adjusted according to clinical response in increments of 0.20 mL/h until either symptom control was achieved or patients displayed side effects.