

Favourable outcome after aggressive treatment of a thrombolysis-associated intra-cerebral haemorrhage

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Summary

Background and importance: Intracerebral haemorrhage (ICH) is the most serious and feared complication of systemic thrombolysis for ischaemic stroke. Symptomatic ICH (sICH) usually occurs within 24–36 hours after thrombolysis (tsICH). Mainly because of the poor prognosis and the lack of clear treatment evidence, patients often are not aggressively treated, nor receive procoagulant therapy. The absence of literature on hemicraniectomy in tsICH and lack of treatment consensus is problematical to direct the care of these patients.

Clinical presentation: We present a 72-year-old gentleman with an acute ischaemic stroke in the left MCA territory who had a severe intravenous thrombolysis-associated intra-cerebral haemorrhage. The patient was promptly treated with procoagulant drugs and hemicraniectomy. The clinical evolution was successful with a 12-month follow-up status with the patient presenting complete independence (modified Rankin Scale of 2).

Conclusion: Despite potentially unfavourable prognosis of tsICH and the frequently nihilistic attitude to this dramatic condition, our report should be reason enough to at least consider aggressive treatment in selected cases and on an individual basis. Prospective studies addressing outcome and treatment of tsICH are needed.

Key words: acute stroke treatment; thrombolysis; symptomatic haemorrhage

Background and importance

Intracerebral haemorrhage (ICH) is the most serious and feared complication of systemic thrombolysis for ischaemic stroke. Symptomatic ICH (sICH) usually occurs within 24–36 hours after thrombolysis. 36 hours after thrombolysis a sICH is to be considered as not related to tissue plasminogen activator therapy (rtPa) [1]. The risk of sICH after IV thrombolysis may vary from 2 to 10% depending upon the single studies and various definitions [1, 2]. In the NINDS-study 6.4% of the patients collectively showed a sICH and this rate was confirmed by the majority of other following studies of systemic thrombolysis within 3 hours of onset of symptoms [1, 3]. Patients with sICH have an increased risk for poor

and/or fatal outcome. The 3-month poor outcome (defined by modified Rankin Scale [mRS] of 5–6) ranges from 6 to 11% and the mortality rate is between 5 and 10%. The in-hospital-mortality is much higher varying from 47 to 75% according to the literature [1, 2]. The acute clinical management of thrombolysis-associated sICH (tsICH) is not uniform [3]. Mainly because of the poor prognosis and the lack of clear treatment evidence, patients are often managed according to the discretion of the treating physician who might not consider an aggressive treatment option nor administer procoagulant therapy. The absence of literature on hemicraniectomy in tsICH and lack of treatment consensus are problematical to direct the care of these patients.

Clinical Presentation

We present the case of a 72-year-old gentleman, with a negative medical history, without any medical treatment, who reaches the emergency room with symptoms of sudden speech-impairment. At clinical exam he presents global aphasia without hemiparesis and a National Institute of Health Stroke Scale (NIHSS) of 5. Clinical and laboratory parameters showed a moderate hypertension at 160 mm Hg, normal blood sugar levels and slightly elevated serum fibrinogen at 6.4 g/l (reference 1.7–4.5 g/l) that dropped to 1.6 g/l during the first 12 hours of hospitalisation. On admission the CT-scan did not show any haemorrhagic or ischaemic signs. The Doppler-Duplex of the pre-cranial blood and intracranial vessels did not show any thrombotic material nor haemodynamically significant stenosis. He receives IV thrombolysis two hours after appearance of the symptoms and is admitted to the intensive care unit. 10 hours after thrombolysis we observe a clinical deterioration: he develops a complete right senso-motoric hemisindrome, right hemianopsia and oculo-motoric paralysis corresponding to a NIHSS of 20. The vigilance at this moment is maintained. The CT-scan (fig. 1) evidences intracerebral haemorrhage at the left parieto-occipital region accompanied by a middle-line shift and compression of the left lateral ventricle. In absence of evident therapeutical consequences/options the patient did not undergo MRI.

The case is discussed with the neurosurgeons who decide not to operate at this point, mainly because of the preserved vigilance status. According to our anaesthesiologists and after having carried out a ROTEM-test, the patient receives 4 × fresh frozen plasma (FFP, with 250 ml of fluid volume) and 1 g of fibrinogen. The cause of the stroke appears to be

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Figure 1

Plain CT-scan of the brain documenting a thrombolysis-associated intra-cerebral haemorrhage with mass effect.



cardioembolic due to an antero-septal hypokinesia with visible thrombus apposition on transthoracic echocardiography, secondary to prior heart infarction. After four days in which the neurologic parameters remain stable, despite progressive radiological expansion of the haematoma, on the fifth day the patient's state of vigilance ultimately degrades accompanied by further augmentation of the haemorrhage's site with greater mid-line shift and beginning transtentorial herniation. On this basis and in consensus with our neurosurgical colleagues we opt for decompression by craniotomy and evacuation of the haematoma. Post-operatively we observe a progressive improvement of the neurological status and radiological regression of the haematoma's expansion and mass-effect. The final neurologic exam two weeks after craniotomy shows a NIHSS of 8 with a residual motor aphasia, a slightly persisting comprehension disorder for complex orders, a right hemianopsia and subtotal regression of the right hemiparesis (for now remains a minimal facial-leg paresis). On the one-year follow-up the patient lives at home with a persisting slight motor aphasia being able to communicate simply structured phrases and excellent verbal comprehension. The hemiparesis is still in regression, the patient is able to walk autonomously and he uses his bicycle. He is independent in his daily activities and considers his quality of life as good. The m-Rankin Scale is 2.

Conclusion

The most feared complication after systemic thrombolysis is intracranial haemorrhage. Its management is not clear since literature and consistent guidelines are lacking. The cur-

rently known predictors of sICH are timing of thrombolysis, age, clinical stroke severity (NIHSS) on admission, high blood pressure, hyperglycaemia, early CT-changes, large-baseline-diffusion-lesion volume and leucoraiosis on MRI. The role of biomarkers is currently being evaluated [1].

Of the various post-lysis haemorrhage-classifications the most commonly used are the NINDS and the ECASS classification. The two types of the NINDS-classification distinguish CT findings, haemorrhagic cerebral infarction and intracerebral haematoma. The four types of the ECASS-classification differentiate between haemorrhagic infarction type 1 and 2, parenchymal haematoma type 1 and 2 and between symptomatic and asymptomatic haemorrhage. The most commonly used parameter for rating sICH is decrease of four or more points on the NIHSS-score [1].

The literature on sICH after thrombolytic management is very poor and the necessity for treatment consensus primarily regards "malignant" sICH being associated with poor prognosis (corresponding to intracerebral haematoma of the NINDS-classification and parenchymal haematoma type 2 of the ECASS-classification). For most authors haemorrhagic infarction and parenchymal haematoma have a different clinical aetiology and pathophysiological significance. "Benign" haemorrhagic infarction could be considered as the natural evolution of cerebral infarction whereas parenchymal haematoma might be linked to the rt-PA itself and in particular to its impact on haemostasis [1].

The American Heart Association (AHA) suggests empirical therapies to replace clotting factors and platelets admitting the lack of evidence to support any specific therapy in sICH 3. One retrospective study analysed the treatment of tsICH (n = 20); 55% of the patients collectively received therapy for coagulopathy: fresh frozen plasma (FFPs), cryoprecipitates, vitamin K₁, platelets, aminocaproic acids or any combination of these. There was no significant association found between use of procoagulant therapy and patients' outcome [3]. No patient had hemicraniectomy and the outcome of these patients was poor: the in-hospital mortality was 75% (15/20), all deaths but one were preceded by a do-not resuscitate order. The long-term outcome of the survivors is unknown. In 40% of the patients with tsICH analysed with serial CT (n = 4) a pattern of continuous intracranial bleeding was observed with an expansion of ICH greater than 33%. This pattern is also observed in our patient, and this raises the question of the best timing for aggressive treatment. This evolution might leave a potential therapeutical window trying to reduce early haematoma expansion and therefore point on improving the clinical outcomes with procoagulants. Our case shows typical ongoing bleeding-behaviour despite procoagulant therapy (FFPs and platelets). Except thrombolysis, we could not identify any clear risk factors or predictors of intra-cerebral haemorrhage.

Surgical intervention has been analysed in spontaneous intracerebral haemorrhage and guidelines have been proposed [4]. For malignant infarction in the mid-cerebral artery territory evidence for early decompressive surgery is also documented. One pooled analysis of three randomised and controlled trials demonstrated the benefit of decompressive surgical therapy within 48 hours of symptom onset in

patients with malignant MCA infarction. Mortality showed to be reduced and the number of favourable clinical patient outcomes increased [5]. Regarding the benefit of surgical haematoma evacuations in tsICH there are no reports or literature available. The growing use of thrombolytic agents due to patients' and doctors' sensibility to the early signs of stroke as well as the expansion of the time window for intravenous thrombolysis to 4½ hours may potentially increase the burden of sICH [1, 2].

We present the first case of tsICH aggressively treated with a documented favourable long-term outcome. Despite global unfavourable prognosis of tsICH and the frequently nihilistic attitude to this dramatic condition, our report should be reason enough to at least consider aggressive treatment in selected cases and on an individual basis. We think that the treatment should be evaluated on individual basis in patients that meet criteria for craniotomy in malig-

nant MCA stroke or for acute ICH treatment. Prospective studies addressing outcome and treatment of tsICH are needed.

References

- 1 Derex L, Nighoghossian N. Intracerebral haemorrhage after thrombolysis for acute ischaemic stroke: an update. *J Neurol Neurosurg Psychiatry*. 2008;79:1093–9.
- 2 Strbian D, Sairanen T, Meretoja, et al. Patient outcomes from symptomatic intracerebral hemorrhage after stroke thrombolysis. *Neurology*. 2011;77:341–8.
- 3 Goldstein JN, Marrero M, Masrur S, et al. Management of thrombolysis-associated symptomatic intracerebral hemorrhage. *Arch Neurol*. 2010;67:965–9.
- 4 Morgenstern LB, Hemphill JC, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage. A Guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2010;41:2108–29.
- 5 Vahedi K, Hofmeijer J, Juettler E, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol*. 2007;6:215–22.