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BRIEF COMMUNICATION

Cerebellar vermis: a vulnerable location of remote brain haemorrhages after thrombolysis for ischaemic stroke

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Abstract Extra-ischaemic (remote) brain heamorrhages after thrombolysis for ischaemic stroke occur in less than 3 % of treated patients, but it worsens prognosis. Little attention has been paid to the location of the haematomas. Among 12 patients with remote brain haemorrhage after thrombolysis, we report three patients with haemorrhage in the cerebellar vermis (25 %), with poor outcome. Previous hypertensive vasculopathy is deemed to be the most plausible cause.

Keywords Thrombolysis · Remote brain haemorrhage

Introduction

Intravenous thrombolysis is regarded as the standard of care in ischaemic hyperacute stroke, but there is a non-negligible risk of brain haemorrhage in around 6 % of treated patients [1]. The haematoma may be located in the ischaemic area but in remote areas of the brain as well, which accounts in 1.3 % of treated patients in the NINDS study [1] and in 2 % of cases in the ECASS2 study [2]. Remote haemorrhages (or extra-ischaemia) make up 7–27.5 % of brain haemorrhages post-thrombolysis [2, 3]. The reason for remote brain haematomas (RBH) is poorly understood, although some factors have been incriminated such as increased permeability of brain barrier and the action of proteases and free radicals along with the direct effect of r-TPA [2, 3],

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The purpose of this study is to share our experience in remote brain haemorrhages post-thrombolysis in terms of location and possible predictors of outcome in comparison with the haemorrhages in the area of infarction.

Patients and methods

Between 2005 and 2015, we treated 560 patients with r-TPA for ischaemic stroke according to international standardised protocol [4]. Informed signed consent was obtained prior to inclusion. Every patient underwent one or more brain CT after thrombolysis to monitor for possible haemorrhage. We compared RBH and non-RBH cases in terms of vascular risk factors, leukoaraiosis, age, sex, NIHSS score at admission, and hospital mortality.

Statistical analysis was based on χ^2 test for qualitative or dichotomous variables and the *t* test for quantitative variables.

Results

Symptomatic brain haemorrhage seen on brain CT, with mass effect, occurred in 31 (5.5 %) and asymptomatic in 20 patients. We found a total of 15 remote haemorrhages, of which 12 were symptomatic (2.1 % of patients; 38.7 % of haematomas); and 3 asymptomatic. In three patients the haematoma was located in the cerebellar vermis and it was fatal in two of them (Fig. 1); the other patient was severely disabled. In the remaining patients, the haemorrhage was lobar. In Table 1 we report the variables analysed in two groups: non-remote and remote haemorrhages. We included both symptomatic and asymptomatic cases. We found a 50 % mortality in the group of remote haemorrhages

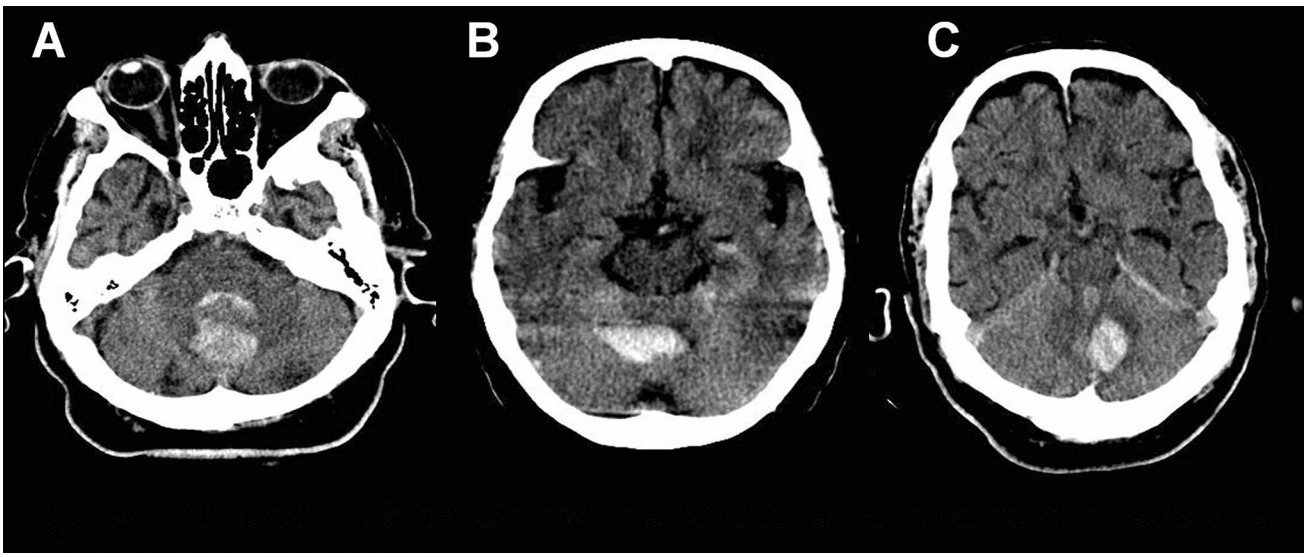

Fig. 1 Brain CT of the three patients with remote brain haemorrhage in the cerebellar vermis

Table 1 Variable comparisons between patients with non-remote and remote brain haematomas

Variable	Non-remote BH ($n = 36$)	Remote BH ($n = 15$)	Significance p value
Median age (years) and range	73.5 (66–81)	72.5 (64.5–79)	0.530 t test
Male sex	22 (61.1 %)	9 (64.3 %)	0.8 X^2 test
Hypertension	25 (69.4 %)	6 (42.9 %)	0.08 X^2 test
Atrial fibrillation	10 (27.8 %)	3 (21.4 %)	0.734 X^2 test
Tobacco habit	3 (8.3 %)	3 (21.4 %)	0.331 X^2 test
Leukoaraiosis	9 (25 %)	6 (42.9 %)	0.216 X^2 test
Median and range NIHSS score	17 (11–21)	12.5 (6–17))	0.071 t test
Previous stroke	3 (8.3 %)	1 (7.1 %)	1 X^2 test
Diabetes M	5 (13.9 %)	2 (14.3 %)	1 X^2 test
Hyperlipidemia	10 (27.8 %)	4 (28.6 %)	1 X^2 test
Mortality	8 (22.2 %)	7 (50 %)	0.054 X^2 test

In this table, we included both asymptomatic and symptomatic haemorrhages

BH brain haemorrhage

compared with 22.2 % in the group of non-remote haematomas; such a difference was clinically relevant and almost statistically significant (X^2 test, $p = 0.054$). We did not find any association between RBH and vascular risk factors, age, sex, NIHSS score and leukoaraiosis, but the sample was too small to draw definitive conclusions. Coagulopathies were discarded given that it was part of the protocol for thrombolysis.

Discussion

The incidence of extra-ischaemic haemorrhages in our series was similar to the ones of NINDS and ECASS2 studies, with 25 % being of cerebellar location.

Most post-fibrinolysis haematomas occur in the area of infarction because of damaged brain tissue, loss of haemostatic control and late repermeabilization, whereas remote haemorrhages tend to occur in pre-existing brain pathologies and/or coagulopathies [5].

Amyloid angiopathy has been associated with remote brain haemorrhages [6, 7]. In a retrospective recently published study with 992 patients undergoing thrombolysis for ischaemic stroke, and on whom MRI was performed, the presence of remote haematomas (2.6 %) was related with the presence of lobar microbleeds and multiple infarcts [8]. In our series, 25 % of RBH occurred in the cerebellum, a location atypical for bleeding caused by this angiopathy. We do not know the mechanism for which the cerebellar vermis arises as a vulnerable location of remote

haematomas, with gloomy outcome. In the remaining 75 % of patients, RBH were lobar in consistency with the amyloid hypothesis. Advanced age, history of previous stroke, and leukoaraiosis are other predisposing factors [9]. Extensive leukoaraiosis, which is considered a surrogate marker of small vessel disease, has been strongly associated with RBH but not with haemorrhages in the ischaemic area [10]. It could be also suggested that remote bleeding could be caused by simultaneous infarction in the corresponding areas in addition to the symptomatic infarction, and non-visualised on computed tomography at admittance, but the mass effect and the lack of infarction on a posterior brain CT are against this hypothesis.

With regard to the location of RBH, most of the RBH in our series (75 %) are lobar, as it was in the Finnish series of 63 RBH (out of 2485 thrombolysed patients) [10]. In this series, the authors found 8 cases of RBH in the cerebellum (12.7 %) and concluded that the cerebellar location of RBH is associated with hypertensive vasculopathy.

In conclusion, the occurrence of extra-ischaemic haemorrhage in the cerebellar vermis is worthy of attention. Although histopathology was not available in any of the patients, the most plausible cause is a pre-existing vasculopathy associated with hypertension.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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