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CASE REPORT - VASCULAR NEUROSURGERY - ANEURYSM

Fatal intracranial aneurysm rupture after thrombolytic treatment for ischemic stroke: a case report and literature review

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Abstract

Intravenous thrombolysis is a proven treatment of acute ischemic stroke. Its complications include intracranial hemorrhage; the risk may be increased in the presence of an unruptured aneurysm. We present a case report of a patient who suffered fatal subarachnoid hemorrhage after thrombolysis from a known aneurysm. A history of recent previously inexperienced headaches was revealed retrospectively, suggestive of sentinel bleedings. A similar patient was identified in the literature; we thus propose that this history should be excluded in patients harboring an aneurysm considered for thrombolytic treatment.

Keywords Aneurysm · Stroke · Subarachnoid hemorrhage · Thrombolysis · Outcome

Introduction

Administration of intravenous tissue plasminogen activator (tPA) is a proven treatment of acute ischemic stroke [7, 17]. However, its use is not without risks and can lead to potentially serious complications including intracranial hemorrhage. The rate of hemorrhage varies between 2 and 7% [22] depending on definition and patient population. Increased risk may be associated with advanced age, hypertension, anticoagulant use, large infarction volume, or underlying vascular pathology, such as unruptured intracranial aneurysm (UIA). Previously published guidelines list the presence of UIA as an exclusion criterion for intravenous tPA administration [3]. A revised statement considers this treatment reasonable even in the presence of UIAs smaller than 10 mm (class IIa, level of evidence C—limited data) [17].

Since stroke and UIAs share to some extent similar underlying risk factors, higher prevalence of UIAs among stroke victims is not surprising. Despite recent studies and guidelines suggesting that thrombolytic treatment in the presence of UIA is safe [2, 4, 5, 14, 17, 28], case reports of severe subarachnoid hemorrhage (SAH) following intravenous tPA administration are well recognized in the stroke literature [8, 18, 21].

The purposes of this study are to present a case report of fatal aneurysm rupture immediately following intravenous tPA treatment and to analyze similar patients from the literature with the aim of identifying specific factors that could precipitate aneurysm rupture.

Case report

A 70-year-old man presented with wake-up stroke with expressive aphasia and right-sided weakness. The initial computed tomography (CT) (Fig. 1a) showed no apparent ischemia or hemorrhage; CT angiography (CTA) (Fig. 1b) revealed a 3-mm large aneurysm of the C7 segment of the internal carotid artery and no major vessel occlusion. Intravenous administration of tPA (Actilyse®) was started; in total, 70 mg was planned and a bolus of 7 mg was administered after door-to-needle time of 35 min. Following administration of approximately half the planned amount, the patient suddenly lost consciousness with a Glasgow Coma Scale of 3. Emergent CT showed massive SAH (Fig. 1c). At this time, the patient exhibited clinical signs of brain death which was later

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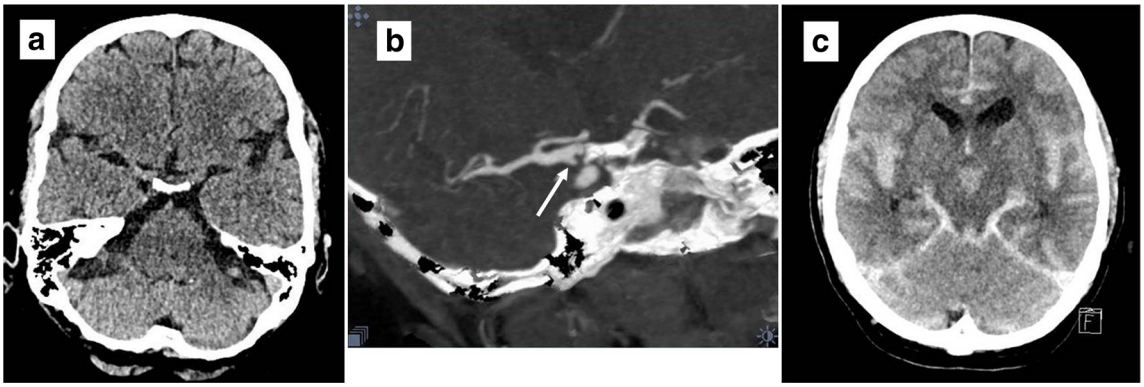

Fig. 1 **a** Initial CT showing no signs of subarachnoid hemorrhage on non-contrast CT scan at the level of the aneurysm. **b** Aneurysm of the internal carotid artery (arrow). **c** Massive subarachnoid hemorrhage after thrombolysis

confirmed by brainstem evoked potentials and formal angiography. Subsequent interview with the patient's family revealed a history of severe, previously unknown, headaches during the preceding week suggestive of repeated sentinel bleeding.

A literature review identified seven relevant articles describing additional eight patients similar to ours (Table 1) [8, 11, 13, 18, 21, 24, 27]. In addition, one patient experienced SAH after being treated with tPA for myocardial infarction [12]. Pretreatment CTA or formal angiography was performed in six patients (including ours), and in two cases, the aneurysm was distal to the occluded segment and could not be diagnosed on initial vessel imaging [13, 27]. The aneurysm was known in two patients at the start of thrombolytic treatment (present case and Shi et al. [24]), suspected in one [21], and initially missed and found in retrospect in another (a distal lenticulostriate artery aneurysm) [24]. Two aneurysms ruptured after direct intraarterial lysis of the occluded (and parent) artery [13, 21], and the remaining aneurysms ruptured after intravenous tPA administration. Following rupture of the aneurysm, six patients (as well as the patient treated for myocardial infarction) died as a direct consequence of SAH, one patient achieved good recovery without neurological deficit [27], and two patients were left severely disabled [11, 24]. The only common factor contributing to rupture we were able to identify among the reported patients is a history of recent, previously inexperienced, headaches in the presented case and the one reported by Rammos et al. [18].

Discussion

The prevalence of UIAs in the general population is approximately 2–3% [20, 26], but higher in the stroke population [2, 5, 14]; values of nearly 10% have been reported [4, 5, 14]; thus, the proportion of stroke patients harboring UIAs is by no means negligible. Furthermore, availability and widespread use of CTA in the diagnostic work-up of acute ischemic stroke will undoubtedly lead to increased detection of UIAs among stroke patients in the near future. As a consequence, stroke physicians should be aware of possible risks associated with this condition and its influence on treatment complications and patient outcomes.

Several studies have shown that the presence of an UIA in patients undergoing tPA treatment does not negatively influence rates of intracranial hemorrhage, in-hospital mortality, and both discharge and 3-month mRS scores [1, 2, 4–6, 10, 14, 15, 23, 25, 28]. Thus, the presence of an UIA (smaller than 10 mm) is no longer considered a contraindication for tPA administration [17]. Given this growing body of literature concerning safety of tPA administration in the presence of an UIA, stroke physicians no longer hesitate to treat an acute condition (stroke) which can have profound negative impact on the patient's life rather than worry about an unspecified risk of rupture of (probably) chronic aneurysm. At the moment of presentation, stroke is the condition responsible for the immediate patient's status and as such, its treatment has absolute priority and is justified. Likewise, neurosurgeons do not hesitate to administer induced hypertension in the treatment of delayed ischemic neurological deficit after SAH even in the presence of another unruptured (and unsecured) aneurysm [9, 16, 19]. Similar to stroke, the risk of adverse outcome due to vasospasm-induced delayed ischemic neurological deficit is too high and the risk of rupture of an additional aneurysm at best rare.

Even though aneurysm rupture following thrombolysis is rare; its consequences are nearly always disastrous. We identified eight additional patients similar to the one reported in our case report; of these, only one achieved favorable recovery, six died and two were left severely disabled (88.9% rate of unfavorable outcome). We were unable to identify common factors that could contribute to rupture apart from history of recent sentinel headaches in our patient and the one reported by Rammos et al. [18]. In both of these cases, the history was established retrospectively and, due to aphasia, could not have been revealed during admission and before thrombolysis administration. On the other hand, the aneurysm that was diagnosed before tPA was started and had this history of recent thunderclap headaches been known, we would probably

Table 1 Summary of cases of aneurysm rupture after thrombolysis reported in the literature. (*F* female, *M* male, *IU* international units, *NR* not reported, *tPA* tissue plasminogen activator, *IA* intraarterial, *IV* intravenous, *ME* mechanical embolectomy, *CE* coil embolization, *SAH* subarachnoid hemorrhage, *MCA* middle cerebral artery, *ACOM* anterior communicating artery, *PCOM* posterior communicating artery, *PICA* posterior inferior cerebellar artery, *ICA* internal carotid artery, *LSA* lenticulostriate artery, *mRS* modified Rankin Scale)

Author	Age, gender	Symptoms	Initial angiography	Treatment	Endovascular procedure	Aneurysm	Size	Rupture timing	Outcome	Remark
Matsumaru 1998 [13]	52, F	Left hemiparesis	Right ICA occlusion, aneurysm not visible	300,000 IU of urokinase IA	IA lysis	Right MCA	NR	Periprocedural	Death	Multiple ruptures
Ritter 2003 [21]	72, M	Right hemiparesis	Left MCA occlusion, aneurysm suspected	2 × 5 mg tPA IA	IA lysis	Left MCA	15 mm	Periprocedural	Death	
Rammos 2012 [18]	51, F	Right hemiparesis + aphasia	Not done	IV, dose NR	ME + CE after SAH	ACOM	7 mm	Not specified	Death	Recent sentinel headache retrospectively
Haji 2014 [8]	71, M	Right hemiparesis + aphasia	Not done	90 mg tPA IV	–	PCOM; PICA	6 mm; 8.5 mm	5 h	Death	
Zaldivar-Jolissaint 2015 [27]	71, F	Left hemiparesis	Right MCA occlusion, aneurysm not visible	0.9 mg/kg tPA IV	Only angiography	Right MCA	6 mm	24 h	No deficit	Uneventful clipping, rupture confirmed
Kim 2017 [11]	51, M	Right hemiparesis + aphasia	Not done	0.9 mg/kg tPA IV	–	Right MCA	3 mm	2 h	mRS 5	Aneurysm clipped, mRS due to both stroke and SAH
Shi 2019 [24]	"Elderly", NR	Left hemiplegia	No major vessel occlusion, aneurysm visible	IV tPA, dose NR	–	Right MCA /LSA	5 mm	2 h	Death	
	"Middle-aged", M	Right hemiplegia	No major vessel occlusion, aneurysm missed	IV tPA, dose NR	–	Left distal LSA	2 mm	1.5 h	Bed-ridden	Aneurysm visible in retrospect
Present case	70, M	Right hemiparesis + aphasia	No major vessel occlusion, aneurysm visible	35 mg tPA IV	–	Right ICA	3 mm	20 min	Death	Recent sentinel headache retrospectively

consider direct endovascular procedure or conservative therapy. Excluding history of recent SAH headaches could be part of pretreatment work-up in stroke patients harboring an UIA before tPA is started. This information can be obtained from the patient or immediate family with relative ease, however should not cause significant delay in starting tPA administration. We are aware that such a generalization based on only two reported patients is a little daring, but the grievous outcome after aneurysm rupture likely justifies this simple measure.

Conclusions

Although the presence of an UIA smaller than 10 mm is not considered a contraindication for thrombolytic treatment in acute ischemic stroke, every effort should be made to exclude recent sentinel bleed when an UIA is diagnosed during initial diagnostic work-up. When the patient is unable to provide this information, the immediate family should be contacted if possible. These measures must not cause significant delay of thrombolytic therapy. If recent aneurysm rupture is suspected, other treatment options should be contemplated instead of intravenous thrombolysis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval For this type of study, formal consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study.

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