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Local intraarterial fibrinolysis in acute vertebrobasilar occlusion

Technical developments and recent results

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Summary. Local intraarterial fibrinolytic therapy (LIF) in patients with acute vertebrobasilar occlusion (AVBO) is a rational and if successful a life saving treatment. The recent progress in this field is determined by the use of microcatheters for superselective basilar artery catheterisation and a "short time, highdose" regimen using 750.000 IU Urokinase in not more than two h. Two out of 7 patients died and 1 did not improve to a better than a locked-in-state. Four patients however survived with excellent outcome.

Key words: Fibrinolysis - Urokinase - Basilar stroke

Acute vertebrobasilar occlusion (AVBO) is usually a life-threatening disease leading to death or major disability [1-4, 9]. The usefulness of local intraarterial fibrinolysis (LIF) in comparison with other managements of AVBO has been demonstrated [8].

Further experience regarding patient selection, management organisation and new developments concerning the neuroradiological approach may improve the results. We reviewed the data of our pilot study in regard to type and dose of fibrinolytic drugs and the technical aspects of drug administration during LIF [13]. The results significantly influenced our protocol when starting again with LIF in the University Hospital Eppendorf Hamburg. The guidelines of the recent protocol and the results after 12 months of experience are to be reported.

Patients and methods

Organisation

LIF is performed in our hospital in close cooperation between the departments of Neurology and Neuroradiology. An intensive care unit is run by the neurologists and a frequent and if necesary emergency consulting service is provided for the internal medicine wards. Neuroradiology runs two angiographic (DSA) rooms and is capable of performing emergency angiography at any time. Basic clinical data, for instance age, history, preexisting diseases, neurological state and state of consciousness, are set out on an info-sheet which is immediately sent to Neuroradiology after the patient has been seen by a neurologist. Most of the patients have impaired consciousness and some have swallowing difficulties. We usually intubate the patients who show a progression of stroke, until definite admission to angiography. CT which is necessary to rule out intracerebral hemorrhage is done while hematological data are evaluated in the emergency laboratory. The decision for angiography is made primarily on the basis of the clinical findings and the team is already alerted at this point. The indication for LIF then only depends on the angiographic findings (Table 1) if general contraindications against fibrinolytic drugs have been ruled out and if the laboratory data, such as blood cell and thrombocyte count, partial thromboplastin-time (PTT), and fibrinogen are normal.

Table 1. Local intraarterial fibrinolytic therapy clinical and angiological criteria

Contraindication	Questionable	Indication
Deep coma more than 6 h decerebration - rigidity	Deep coma less than 6 h with tetraparesis	Basilar territory stroke in progress incomplete deficit of brainstem - function, regardless the onset of sympt.
or	and/or	and
Nicely collateralized e.g. chronic occlusion	Atherothrombotic midbasilar occlusion	Basilar embolism Acute bilateral intracranial vertebrobasilar occlusion

Table 2. Basic data

Case	1 T.M.	2 O.M.	3 T.H.	4 S.B.	5 M.H.	6 G.J.	7.C.W.
Age	56	42	60	47	61	48	71
Delay of treatment after first symptom	8 h	48 h	12 h	16 h	6 h	5 h	4 h
Angiography: Atheroma$^+$ Thrombus/Embolus	ATH	ATH/E	ATH/E	E	E	E	E
* Somnolence ** Sopor *** Coma	*(*)	**(*)	**	***	*	*(*)	**
* Hemiparesis ** Tetraparesis *** Decerebration rigidity	*	**	**	***	*	*	*
Urokinase: Dose up to 2 h	500.000	650.000	250.000	500.000	700.000	700.000	500.000
Initial improvement	*	-	*	-	*	**	*
Final outcome	Death (Fig. 1)	Death	Recovery	Locked in syn.	Recovery (Fig. 2)	Recovery (Fig. 3)	Recovery (Fig. 4)

Angiographic approach

After a 5-French sheath-set has been placed in the groin, diagnostic angiography is performed using a 5-French soft-tip catheter (Schneider). A 45 degree oblique or p.a. projection of the vertebro-basilar territory after an injection at the orifice of the vertebral artery is usually - if DSA is employed - sufficient to show the important angiologic findings e.g., bilateral intracranial vertebral or basilar artery occlusion. While the materials for LIF are prepared we usually expose a left and right lateral projection of the carotid territory in order to demonstrate the collateral supply to the very top of the basilar artery and the postereor cerebral arteries.

Using a microcatheter which is guided by a steerable microwire (Tracker, Target-Therapeutics) coaxially with the 5-French-catheter it is now possible to come close to the site of the occlusion. In case of basilar embolism the thrombotic material is often only partially adherent to the wall of the basilar artery. Thus it is possible to place the catheter in the very tiny slit between thrombus and arterial wall. In intracranial vertebral artery thrombosis the catheter tip has to be placed distal to the PICA origin. DSA-roadmapping is helpful for proper placement of the catheter. After the catheter's placement has been confirmed, Urokinase infusion is immediately started: 500.000 IU in the first hour, 250.000 IU in the second hour. Angiographic controls are taken each 30 min. The treatment is finished definitely after recanalisation or after 2 h. Only if it had been impossible to place the catheter properly would we have decided to infuse 70 mg of recombinent tissue plasminogene activator (rt-PA) intravenously over a period of 90 min. This did not occur in our series. After the catheters have been removed the patient is taken to the intensive care unit. Heparinization is not started until PTT is shown to be twice the normal value or less.

Results

During the last 12 months the diagnosis of AVBO has been established in 10 patients. Table 2 shows the basic data concerning 7 patients who have been treated with LIF. In one patient (case 4) however treatment was undertaken although she did not meet the inclusion criteria (Table 1). This young female had a left subclavian artery thrombus removed with a Fogarty-catheter. The stroke in progression occuring afterwards was not estimated appropiately as for an embolic basilar stroke until coma and tetraplegia were completed after at least 12 h of observation. After admission to our hospital the LIF-treatment was started 16 h from the onset of symptoms. Although the patient survived in a locked-in-state, we do not consider this result as a success. However, we are strongly convinced that earlier treatment would have caused a better outcome. This conviction is supported by four other patients (No. 3, 5-7) in this group, who have been treated earlier with favourable results and a better clinical state at the beginning. From the clinical point of view it is remarkable that in all these 6 patients the clinical symptomatology started with a slight hemiparesis and dysarthria. One patient experienced acute hearing loss (No. 7). Somnolence occurred with the progression of the neurological signs. The clinical diagnosis was only possible due to careful observation and repeated neurological examination, which revealed only minor cranial nerve disfunction in the early stages. Signs contralateral to the hemiparetic side or central oculomotor disturbances were not regularly found at the beginning.

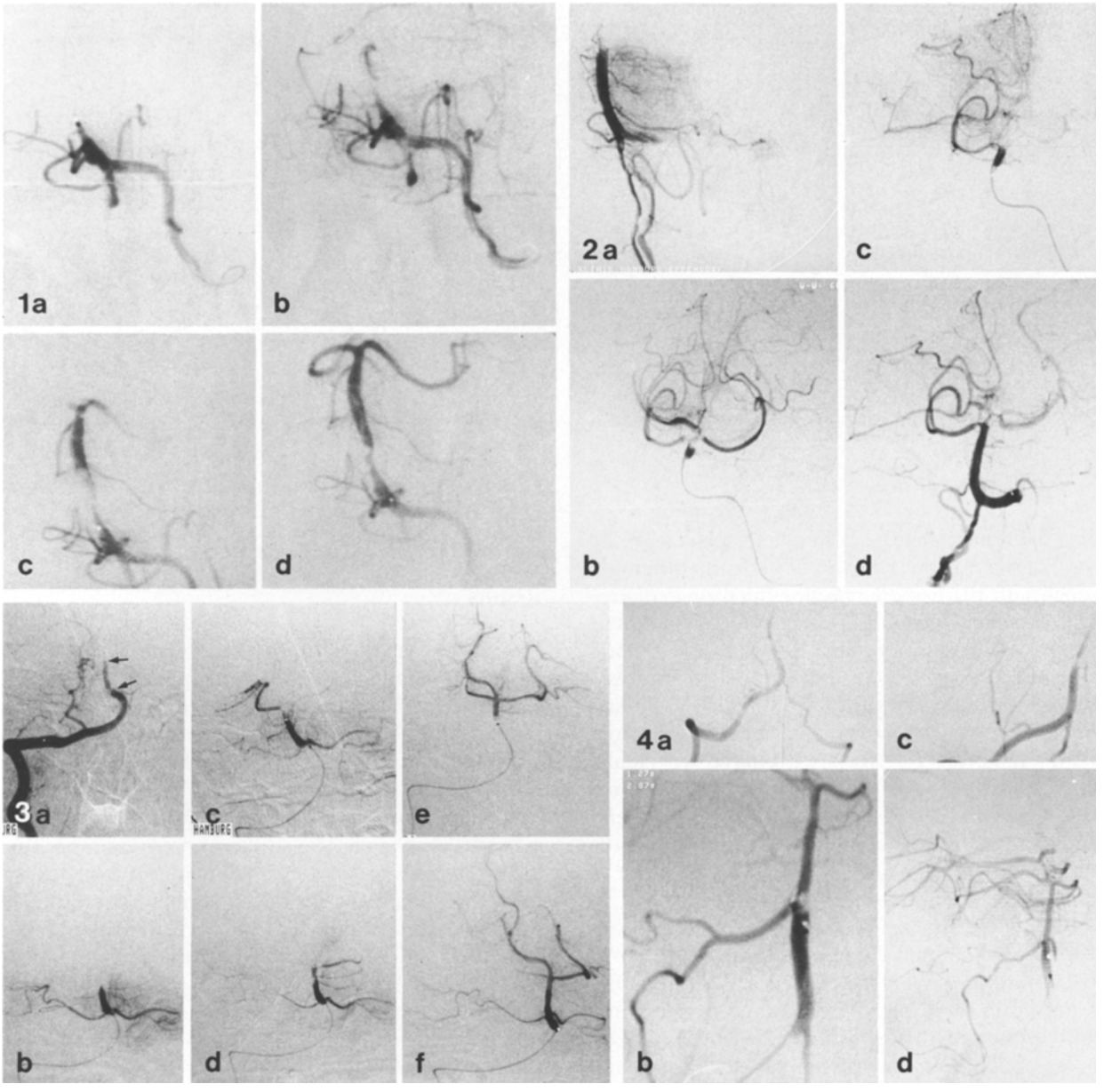

Fig. 1a–d. Atherothrombolic midbasilar occlusion. Oblique projection **(a):** microcatheter at the occluison point, **b, c** progressing recanalisation reveals a large thrombus. **d** Final control demonstrates a residual arteriosclerotic stenosis (case 1)

Fig. 2a–d. Top of the basilar embolism **(a). b, c** progressing recanalisation. **d** Final control angiogram (case 5)

Fig. 3a–f. Basilar embolism, with emboli *(arrows)* at the top and within the midbasilar artery **(a). b** Superselective angiogram distal to the midbasilar embolus. **c–e** progressing recanalisation. **f** Final control angiogram (case 6)

Fig. 4a–d. Midbasilar embolism at the level of the AICA *(arrow)*. **a** P.a. view; **b** oblique view; **c** superselective angiogram; **d** final control angiogram (case 7)

In one patient a mid-basilar occlusion was found at angiography. In this case (No. 1) initially good recovery was observed after LIF, in so far as the patient showed spontaneous limb movements again after initial tetraparesis. However 36 h after LIF the patient deteriorated again and finally died, though repeated angiography showed no re-occlusion (Fig. 1). Only minor lesions were found on CCT, not sufficient to explain the clinical state. Since autopsy was refused we have no explanation for this course.

In both cases 2 and 3 bilateral intracranial vertebral occlusion was the inital angiological finding. However, only one patient (No. 3) survived after re-

canalisation. In this case severe somnolence and oculomotor impairment at the beginning indicated a secondary embolism to the top of the basilar artery. Moreover, a superior cerebellar artery territory infarction on later CCT and an improving ataxia made this secondary embolic event very probable. Although these were obviously small emboli venishing concomitantly with the recanalisation of the vertebral artery in the one patient (No. 3), in the other (No. 2) a very large secondary embolus was found at the top of the basilar artery after recanalisation of the vertebral artery. Primary top of the basilar emboli however may be treated successfully as in cases 5 and 6 (Figs. 2, 3).

In all patients with primary or secondary basilar embolism small paramedian superior cerebellar artery infarcts were seen on control CCT. In one of these infarcts secondary hemorrhage, 1 cm in diameter, occurred afterwards under Heparin-treatment without clinical deterioration.

Discussion

As Archer and Horenstein [1] have demonstrated, the natural course of AVBO almost always leads to a lethal outcome confirming the experience of Kubik and Adams [9], our own study [2] showed that only one third of these fell into a hopeless state at the very beginning of their disease. The other patients initially exhibited extended basilar strokes which usually progressed slowly to the endpoint of coma, decerebrate rigidity and death. Progression of stroke was observed even in basilar embolism. Recently Fisher [8] described several cases of basilar stroke-in-progression, which all started with a hemiparesis only and over hours deteriorated to complete brainstem death. Heparin was in our cases not helpful in order to stop stroke progression.

Fibrinolytic drugs, however, showed remarkable effects concerning vascular recanalisation and also clinical improvement [2, 8, 14]. The feared complication of intracerebral hemorrhage [6, 7] did not occur except in those patients who already had visible infarcts on CCT. The prognosis of AVBO with LIF is determined by angiological and clinical criteria. The experience is reflected by our in/exclusion criteria (Table 1) which are derived from our pilot study [2]. Due to the clinically progressive character of the disease the outcome depends strongly on how much of the brainstem function has been already lost, regardless how much time elapsed until the instigation of therapy. This experience is confirmed by the cases presented in this report concerning the angiological aspects as well as the clinical findings. Thus we do not set up time limits for treatment, but limits determined by the clinical state prior to LIF. Recently Möbius et al. [11] reported on 14 patients who had been treated with LIF for AVBO. Following the same guidelines for treatment as proposed in this report 10 patients survived in their group. In all the six cases which are presented in this report and in the report of Möbius et al. [11] a progressive hemiparesis very often is the first and most obvious symptom although additional brainstem signs may be found by means of a sophisticated neurological examination. Hemiparesis with impaired consciousness, dysarthria, often vertigo and a clinically progressive course therefore are important and valuable hints as for basilar stroke. Emergency angiography is then necessary in order to confirm an appropriate angiological finding for LIF-treatment. A hesitating and expectant attitude is hazardous in this situation. A review of our data in 43 patients treated with LIF [2, 13] has shown that Urokinase treatment performed with maximally 250.000 IU in the first and 125.000 IU in each of the following 4 h may lead to recanalisation. However in several cases we suspected that we would have succeeded with better clinical results if a shorter recanalisation time could have been achieved. Formerly the calculation of the UK-doses being applied locally had not been easy since it had not been possible to place the catheter exactly at the site of the lesion in each case, but more proximal, below vascular branches.

By using Tracker-microcatheters we are now able to place the catheter tip at the lesion site in any case. By increasing the dose up to 500.000 IU in the first and 250.000 IU in the second hour, recanalisation could be achieved in our recent cases in 2 h or less. No complications occurred. We do not suggest continuing the treatment for more than two hours, since we learned from our former experience [13], that in the case of Urokinase the risk of hemorrhage is increased by a longer treatment period rather than by a higher dose.

The possible advantages of recombinant tissue plasminogene activator - a new fibrinolytic drug - have been discussed recently [5].

As far as we know the results of some ongoing studies on the usefulness of iv-infusion of rtPA in embolic carotid strokes are not yet convincing. However, in one case of basilar embolism successful treatment using i.v. rtPA has been reported [10]. We presently feel it not to be wise to hastily abandon our LIF regimen, which obviously provides good results, as long as the superiority of i.v. rtPA is not definitely documented.

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