Endovascular Treatment of Acute Thrombosis of Cerebral Veins and Sinuses

SERGEY BORISOVICH YAKOVLEV, ALEKSEI VASILIEVICH BOCHAROV,
KETEVAN MIKELADZE, SERGEY SURENOVICH GASPARIAN,
NATALIA KONSTANTINOVNA SEROVA, ALEXANDER ROMANOVICH SHAKHNOVICH

Neurosurgery Institute, Russian Academy of Medical Sciences; Moscow, Russian Federation

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SUMMARY – *Acute thrombosis of cerebral veins and sinuses (ATCVS) is a multifactorial disease with grave consequences. Because of its rare occurrence there are no proven treatment guidelines. Sixteen patients with ATCVS were treated. The final diagnosis was confirmed by digital subtraction angiography. Sinus catheterization was performed via transfemoral venous access. Treatment included mechanical manipulation of thrombi and thrombolytic therapy. A regression of clinical symptoms with a concomitant decrease of intracranial hypertension was achieved in all patients. Long-term results were studied in eight patients: none presented clinical signs of intracranial hypertension. Endovascular transvenous recanalization is an effective treatment for acute thrombosis of cerebral veins and sinuses. Along with the local thrombolysis, significant potential in the treatment of this complex pathology lies in the transvenous endovascular techniques of mechanical thrombus extraction, especially in patients with intracranial hemorrhage for whom the use of thrombolytic agents is restricted.*

Introduction

The first description of cerebral venous and sinus thrombosis is attributed to the French doctor Ribes, who in 1825 discovered the thrombosis of the superior sagittal sinus and cerebral veins at autopsy in a man who had suffered severe headaches and seizures for six months¹. Up until the second half of the 20th century, thrombosis of cerebral veins and sinuses was usually found at autopsy². In the early 1950s, the introduction of venography made it possible to diagnose thrombosis with greater accuracy and differentiate it from idiopathic intracranial hypertension³. The British gynecologist Stansfield is credited with the implementation of anticoagulant heparin in the treatment of cerebral venous and sinus thrombosis in 1942^{2,4}.

The incidence of thrombosis of cerebral veins and sinuses is 1000 times lower than that of arterial strokes⁵, and it is generally a disease of young adults and children⁶. According to the literature^{7,8}, ATCVS is observed in three to

four cases per one million population; 75% of these patients are women of reproductive age (20 to 35 years) who also have various congenital coagulopathies. Unilateral infarctions are extremely rare⁹. The incidence of thrombosis in children is up to seven cases per one million population. Every eighth patient subsequently develops severe disability. Mortality varies from 10% to 50%. However, with the timely implementation of appropriate treatment, recovery occurs in more than 80% of patients^{6,10-14}.

The clinical symptoms of ATCVS vary widely and the course of disease is highly individual for each patient. The determining factors are: location and spread of the process, patient's age, degree of development of venous collaterals of the brain, as well as the primary cause of blood clots in the venous system of the brain. The following symptoms are most frequent: severe headaches, intracranial hypertension, paresis and paralysis of cranial nerves, seizures, motor and sensory disturbances in the extremities, and impaired consciousness to varying degrees. The underlying pathogenetic

mechanism of the disease is the difficulty of venous outflow from the brain tissue caused by an obstruction of a major drainage pathway. This factor leads to the development of venous intracranial hypertension, cerebral edema, and as a consequence, CSF hypertension. The ventricles of the brain usually stay at normal size, or become slit-like. In the most severe cases, ischemic and/or hemorrhagic lesions may develop in the brain tissue.

The rare occurrence of ATCVS and little experience in treating this disease do not allow for a statistically valid study that would evaluate the effectiveness of a method of treatment. Hence, there are no proven treatment guidelines. However, according to a retrospective review, the mortality rate for patients treated with either IV heparin or local thrombolytics was 13% compared with 48% in untreated patients¹² and local thrombolysis has better follow-up results in severe cases¹⁵.

Materials and Methods

During the period from 2005 to 2012, the N.N. Burdenko Neurosurgery Institute examined and treated 16 patients with ATCVS: four males, 12 female, aged from six to 51 years. Disease duration from the first symptoms was 4-27 days (Table 1).

Etiological risk factors were: oral contraceptives – three patients, pregnancy – one, pregnancy with associated thrombophilia – one, hormone replacement therapy for endocrine disorders – two, thrombophilia – one, chemotherapy for blood disorders – two, anemia – one, antiphospholipid syndrome – one, direct surgery of parasagittal meningioma – one. In three cases the cause could not be established. All patients were admitted with emergency indications (Table 1). After treatment, all patients were consulted by a hematologist and had a full work-up to identify blood clotting disorders. Thus, in some patients etiologic factors were verified retrospectively.

Primary diagnosis was established on the basis of CT, MR venography, and transcranial Doppler. The rate of blood flow in the straight sinus ranged from 40 to 120 cm/s¹⁶. The final diagnosis was confirmed by digital subtraction angiography, which was done during local endovascular therapy. Sinus catheterization was performed via transfemoral venous access. After puncture of the femoral vein, an introducer 6F was installed in the femoral vein.

Guide catheter 6F was installed in the internal jugular vein, in some cases it was inserted in the sigmoid or transverse sinuses. For sinus catheterization Excelsior SL-10 (Boston Scientific) or Prowler 14 (Codman) microcatheters were used. With the help of a microguidewire the catheter was threaded through the thrombus and superselective sinusography was performed. Next, the tip of the microcatheter was placed directly into the thrombi, and before administration of drugs, the thrombi were mechanically manipulated with a micro guidewire. The following thrombolytic agents were used: actilyse (rtPA), prourokinase, and urokinase. Throughout the procedure, heparin was administered at a dose of 5,000 units/hour (on average 7500 units were given per procedure). After the procedure, introducers were sutured to the skin of the thigh, and were removed the next day. Hemostasis was carried out in most cases by local compression of soft tissues in the puncture site. In two cases the femoral artery puncture sites were sealed with suturing devices.

After endovascular treatment the patients received heparin 5000U four times a day or Clexane (enoxoparin) 40-80 mg/day during two weeks, monitoring coagulation, then Plavix (clopidogrel) 300 mg/day during two weeks with the transition to Aspirin 75 mg/day for one year.

Results and Discussion

Clinical symptoms in patients with ATCVS are shown in Table 1. In addition to a pronounced cephalgic syndrome, all patients had various degrees of papilledema. Severe cerebral and intracranial hypertension symptoms with the confirmed diagnosis of ATCVS according to CT or MR angiography was considered an indication for endovascular intervention. Most of the interventions were performed on an emergency basis on the day of the admission.

According to cerebral contrast angiography, isolated total or partial thrombosis of the superior sagittal sinus (SSS) was established in five patients. The combination of SSS and the involvement of one of the lateral or transverse sinuses was found in seven patients, an isolated occlusion of the lateral sinus (LS) – in one patient, SSS and both LS – in 2 patients, occlusion of the SSS, LS and straight sinus – in one patient. The involvement of the lateral sinus was observed more frequently on the right side (seven patients) than the left (two patients). By means of angiography, the localization and

Table 1 Summary of patients with acute thrombosis of cerebral sinuses and veins treated with endovascular intervention.

<i>Number</i>	<i>Age</i>	<i>Sex</i>	<i>Etiology</i>	<i>Days from onset to admission</i>	<i>Clinical picture</i>	<i>Localization</i>	<i>Changes in brain</i>
1	27	F	Hormone replacement therapy ES	9	HD, right VI nerve paresis, left hemiparesis, mild cerebellar symptoms, a single episode of seizure, PE	SSS, STRS, right TS	Locus of hemorrhagic infiltration in the right parietal lobe
2	66	F	Hormone replacement therapy ST	15	HD, PE with hemorrhage, a sharp decrease in visual acuity	SSS, right PS, right IJV	–
3	55	M	ChT		HD, PE, paresis of the left VI nerve, ataxia	The front third of the SSS	–
4	30	M	Thrombophilia	4	HD, nausea, vomiting, mild hearing loss	SSS, bilateral LS	–
5	37	F	Thrombophilia, pregnancy	9	HD, severe PE with hemorrhage	Right LS	–
6	26	F	OC	10	HD, severe PE with bleeding, bilateral paresis of VI nerves, right hemiparesis	SSS, right SRTS	–
7	36	M	APLS	9	HD, nausea, vomiting, mild hearing loss, severe PE, nystagmus	SSS, right LS	–
8	37	M	Not identified	7	HD, developing PE	SSS, left STRS	–
9	22	F	Pregnancy	8	HD, vomiting, PE, nystagmus, bilateral paresis of VI nerves.	SSS	–
10	33	F	OC	6	HD, vomiting, PE	SSS, Bilateral LS	–
11	31	F	OC	14	HD, dizziness, PE	SSS, left LS	–
12	15	F	ChT	4	HA, seizure, left hemiparesis	SSS	–
13	18	F	Not identified	10	HD, bilateral paresis of VI nerves, right hemiparesis	Front and middle third of the SSS	–
14	51	F	Surgery of parasagittal meningioma	14	HD, PE	Middle and posterior parts of SSS	–
15	40	F	Not identified	27	HD, vomiting, PE, bilateral paresis of VI nerves	Partial thrombosis of SSS, thrombosis of right LS	–
16	14	F	Anemia	3	HD, vomiting, PE, ataxia, right hemihypesthesia	SSS, right LS	–

Abbreviations: APLS – antiphospholipid syndrome, OC – oral contraceptives, ChT – chemotherapy for acute leukemia, ES – estrogen, HD – headaches, IJV – internal jugular vein, LS – lateral sinus, PE – papilledema, SSS – superior sagittal sinus, ST – corticosteroids, STRS – straight sinus, TS – transverse sinus.

Table 2 Treatment and outcome in patients with acute thrombosis of cerebral sinuses and veins.

Number	Age	Sex	Type of treatment	The dosage of drugs	Outcome according to angiography	Dynamics of clinical symptoms	Long-term results
1	27	F	LT+ST: Actilyse	25 mg locally, and 25 mg IV	Partial recanalization	Improvement, regression of PE on the 12 th day	
2	66	F	LT+ST, Actilyse	30 mg locally, and 25 mg IV	Partial recanalization	Unchanged	
3	55	M	LT: Actilyse / Heparin	2 mg /5,000 units locally	Complete recanalization	Improvement, regression of PE on the 5 th day	
4	30	M	LT+ST: Actilyse twice	20 mg locally, and 80 mg IV	Partial recanalization, rethrombosis in 2 days	Improvement	Recovery (15 months)
5	37	F	LT+ST: Actilyse	30 mg locally, and 60 mg IV	Complete recanalization	Improvement	Recovery (15 months)
6	26	F	LT+ST: Actilyse	50 mg locally, and 50 mg IV	Complete recanalization	Improvement	Recovery (3 years)
7	36	M	LT+ST: Prourokinase	1 million units locally; 6 million units IV on the 2 nd day	Partial recanalization, rethrombosis. Complete recanalization on the 5 th day	Improvement	Recovery (2 years)
8	37	M	LT+ST: Actilyse	50 mg locally, and 50 mg IV	Complete recanalization	Improvement, regression of PE on the 7 th day.	Recovery (1 year)
9	22	F	LT+ST: Prourokinase	1 million units locally, and 1 million units IV	Partial recanalization	Improvement, reduction of PE on the 7 th day.	
10	33	F	LT+ST: Urokinase	800 thousand units locally, and 1 million units IV	Complete recanalization	Improvement, regression of PE on the 8 th day	Recovery (2 years)
11	31	F	LT+ST: Actilyse	50 mg locally, and 50 mg IV	Partial recanalization	Improvement, reduction of PE on the 7 th day.	Recovery (9 months)
12	15	F	LT+ST: Actilyse	12 mg locally, and 6 mg IV	Partial recanalization	Improvement	
13	18	F	LT+ST: Actilyse, stent thrombus extraction	30 mg locally, and 20 mg IV	Complete recanalization	Improvement	
14	51	F	Stent thrombus extraction, LT: Actilyse	50 mg locally	Partial recanalization	Improvement, regression PE on the 10 th day.	
15	40	F	Stent thrombus extraction, LT+ST: Actilyse, balloon dilatation of SSS	40 mg locally, and 50 mg IV	Partial recanalization	Improvement, regression PE on the 1,5 month.	Recovery (11 months)
16	14	F	Stent thrombus extraction, ST	40 mg IV	Partial recanalization	Improvement	

Abbreviations: LT – local thrombolysis, PE – papilledema, ST – systemic thrombolysis, IV – intravenous.

Figure 1 18-year-old female. Acute thrombosis of front and middle third of the SSS (zones of occlusion in sinuses shown with arrows). Local transvenous thrombolysis with actilyse. Mechanical thrombus extraction with a stent. Complete recanalization. A) MR venography. B) Venous phase of cerebral angiography. C) Selective sinusography through a microcatheter placed in anterior parts of the sinus. D) Partial recanalization of sinus after injecting 35 mg of Urokinase during 1 hour. E) Venous phase of cerebral angiography shows full recanalization after mechanical thrombus extraction with a stent. F) Image of thrombi removed by stent.

extent of thrombosis were identified and the extent of the venous outflow from the cranial cavity was calculated by measuring the transit time of contrast material, ranging from 16 to 26 seconds (normal – 12 seconds). Particularly high numbers were typical for SSS thrombosis and for the cases of a combination of thrombosis of SSS and LS. The cases of these localizations were characterized by the maximal involvement of alternative outflow routes from the cranial cavity by anastomoses between the superficial veins of the brain and the cavernous sinus, as well as between the superficial veins and deep veins through anastomoses in the white matter of the brain. In the SSS thrombosis, the role of anastomoses between superficial veins and veins of the scalp through the diploic veins was very important.

Local thrombolytic therapy was performed in 15 patients, in four cases mechanical thrombus extraction with a stent was performed. In one case mechanical thrombus extraction with a

stent was performed after failed local and systemic thrombolysis (Table 2, obs. no. 13; Figure 1). In another case mechanical thrombus extraction with a stent was performed after systemic thrombolysis (Table 2, obs. no. 13, Figure 2). According to the control angiography immediately after thrombolysis, complete or partial recanalization of the sinuses was achieved in all patients. Rethrombosis occurred in two patients two days after the procedure. One of them required a second procedure, the other had a single intravenous administration of the maximal therapeutic dose of a thrombolytic drug. In both cases complete recanalization was achieved.

Immediately after the intervention, patients reported a significant reduction or disappearance of the cephalgic syndrome. Most of the time the existing focal symptoms tended to regress on the next day. Ultimately, all patients achieved regression of clinical symptoms with a simultaneous decrease of intracranial

Figure 2 14-year-old female. Acute thrombosis of SSS, right LS. Mechanical thrombus extraction with a stent. Partial recanalization. A) Venous phase of cerebral angiography. B) Selective sinusography through a microcatheter placed in the anterior parts of the sinus; C) Partial recanalization of the sinus venous phase after mechanical thrombus extraction with a stent.

hypertension, confirmed by the decrease of papilledema. Normalization of the cerebral venous circulation manifested in the reduction of blood flow velocity in the straight sinus to normal numbers in three to 14 days, according to the transcranial Doppler data.

Long-term results were studied in eight patients in the period from one to five years. In all cases, no clinical signs of intracranial hypertension were found. According to CT and MR angiography, complete recanalization of the sinuses persisted.

The search for new methods of rapid reca-

nalization in cases of ATCVS led to attempts to use mechanical thrombus extraction, which allows a decrease in the doses of thrombolytic anticoagulant drugs, and, consequently reduces the risk of bleeding complications¹⁷.

The method of mechanical thrombus extraction is very promising because sinus recanalization is achieved in a shorter time, although there is a possibility of migration of fragments to the right chambers of the heart and further to the pulmonary artery.

For thrombus extraction, balloon catheters and other devices for breaking down blood

Table 3 Methods and devices for mechanical thrombus extraction.

<i>Type of thrombus extraction</i>	<i>Device</i>	<i>Mechanism of action</i>	<i>Benefits</i>	<i>Limitations</i>	<i>Possible complications</i>
Balloon	Balloon catheter, Fogarty HyperForm	Removal of large fragments of a thrombus	Ability to create channels within a thrombus	Partial hooking of blood clot	Pulmonary embolism
Reolitic	AngioJet	Gradual destruction of the clot with a pulsating jet of saline, aspiration	Aspiration with devices	Difficult navigation due to catheter rigidity, possibility of perforation of venous collectors	Blood loss, hemodilution
By aspiration	Penumbra System	Gradual destruction of the thrombus, aspiration	Adequate distal navigation, rapid destruction of the thrombus, Aspiration with devices		
Mechanical	Stent Solitaire AB	Fragmentation of the thrombus, removal by parts	Easy navigation of sinuses, reliable hooking of blood clot	Manual aspiration from guide catheter	Pulmonary embolism unlikely

clots were traditionally used. The advantages and disadvantages of different methods of mechanical thrombus extraction are listed in Table 3. In our series of observations, due to the fact that local thrombolysis was ineffective, one case of successful mechanical thrombus extraction of the superior sagittal sinus by means of a stent was performed. To the best of our knowledge, there are no reports in the literature on the use of stents for thrombus extraction. In our opinion, usage of the Penumbra system, a device used for arterial thrombus extraction, is very promising. This device has a soft catheter allowing distal catheterization and at the same time it has an option for aspiration. Successful use of this device for recanalization in the cases of ATCVS, as reflected in the individual publications in recent years^{18-20,22} allows us to suggest wider use of this safe and effective method of mechanical thrombus extraction in the near future.

Conclusion

Endovascular transvenous recanalization is a highly effective treatment for acute thrombosis of cerebral veins and sinuses restoring the venous hemodynamics of the brain and normalizing intracranial pressure in the shortest possible time, thereby preventing the serious consequences of the disease.

Indications for endovascular local thrombolysis in acute thrombosis of cerebral veins and sinuses are severe cerebral and/or focal neurological symptoms in combination with intracranial hypertension.

Along with local thrombolysis, a significant potential in treatment of this complex pathology lies in the transvenous endovascular techniques of mechanical thrombus extraction, especially in patients with intracranial hemorrhage, for whom the use of thrombolytic agents is restricted.

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Ketevan Mikeladze, MD
 Neurosurgeon, IV Department, Room 622
 N.N. Burdenko Neurosurgery Institute of Russian
 Academy of Medical Sciences
 4th Tverskaya Yamskaya 16
 Moscow, 125047 Russian Federation
 Tel.: 7-499-251-6583
 Fax: 7 495-995-3106
 E-mail: kmikeladze@gmail.com