Case Report

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Radiosurgical Treatment of a Patient with a Ruptured Arteriovenous Malformation Located in a Functionally Significant Area

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ABSTRACT Arteriovenous malformations (AVMs) of the brain are quite rare vascular pathologies, but they are life-threatening, due to the risk of intracerebral hemorrhage. Stereotactic radiosurgical treatment of patients with cerebral AVM is performed in cases where surgical removal is impossible or embolization with a stable occlusive effect cannot be performed. Currently, for the diagnosis of AVM, magnetic resonance imaging (MRI) is increasingly used because of its non-invasiveness and minimal risks. When a malformation is located in a functionally significant area, then a non-invasive technique is used to assess its interposition and mapping - functional magnetic resonance imaging.

We have presented the experience of radiosurgical treatment of a 43-year-old male patient with a ruptured AVM located in the left temporal lobe, near Wernicke's area. The patient underwent stereotactic radiosurgical treatment with Elekta Leksell Gamma Knife Perfection device, taking into account the location of the AVM in a functionally significant area, preoperative mapping was performed. After two years, according to MR angiography, the arterial component in the projection of the irradiated AVM was not visualized, which was confirmed by the data of cerebral angiography. Thus, a clinical example has demonstrated the high efficiency of MRI in the diagnosis and assessment of the results of the performed stereotactic radiosurgical treatment of AVMs.

Keywords: arteriovenous malformation; stereotactic radiosurgery; "Gamma Knife"; magnetic resonance imaging; MR angiography; functional magnetic resonance imaging, AVM rupture

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AVM — arteriovenous malformation
ACE — angiotensin converting enzyme
APTT — activated partial thromboplastin time
WI — weighted image
AI_r — RBC aggregation index at rest
AI_m — RBC aggregation index in motion
C — coefficient of neutrophil stimulation
C_{os} — coefficient of oxidative stress
CT — computed tomography
MDA — malondialdehyde
INR — international normalized ratio
NST-test — test for nitrosine tetrazolium
iNST — induced NST-test
MRI — magnetic resonance imaging
TAA — total antioxidant activity
LA — late stages of apoptosis
LPO — lipid peroxidation
EA — early stages of apoptosis
MCA — middle cerebral artery
MMWPs — medium molecular weight peptides
SRS — stereotactic radiosurgical treatment
TT — thrombin time
fMRI — functional magnetic resonance imaging
CAG — cerebral angiography
CIC L — large circulating immune complexes
CIC S — small circulating immune complexes
CIC M — medium circulating immune complexes
NOx — nitrite/nitrate nitric oxide

Arteriovenous malformations (AVMs) are congenital anomalies of cerebral vessels, which are a "glomus" of pathologically formed vessels bypassing the blood from the arterial vessels to veins without the participation of the capillary network. The incidence of AVM is 1.34 per 100 000 population [1]. Due to incompletely formed walls of bypassing vessels, as well as high pressure and flow velocity in the AVM structure, the risk of their rupture with subsequent intracranial hemorrhages increases. This risk is 1.2–4% per year, and with already ruptured AVMs, it reaches 6–18% per year [2, 3]. Disability after an AVM hemorrhage occurs in 58–81% of patients [4].

Today, there are several methods of treating patients with cerebral AVMs, which are preferred depending on the size, structure, location of the malformation and the patient's condition: microsurgical removal, endovascular embolization, stereotactic radiosurgery, and combined treatment.

Stereotactic radiosurgical treatment (SRS) of patients with cerebral AVMs is used in cases where surgical removal is impossible or embolization with a stable occlusive effect cannot be performed. Under the action of ionizing radiation in the walls of blood vessels, endothelial proliferation occurs, which leads to a gradual narrowing of the lumen of the vessel (obliteration). The obliteration is long and takes from 1 year (in 50% of patients) to 2 or 3 years (in 80% and 90% of patients, respectively) [5, 6]. The probability of AVM obliteration is 50–95% 5 years after a single radiosurgical treatment [7–11].

Various research methods are used to diagnose AVMs: cerebral angiography (CAG), computed tomography (CT), and magnetic resonance imaging (MRI). Previously, CAG of the brain was the most commonly used method in the diagnosis of vascular diseases. However, this method is not suitable for monitoring patients with AVM without rupture and can only be carried out in a hospital setting, where it is possible to manage adequately such risks as spontaneous bleeding, allergic reactions, nephrotoxicity, and thromboembolism [12]. The CT method does not provide 100% information about the structure of the AVM glomus; it is also quite difficult to determine the afferent (sensory) and efferent (motor) pathways of nerve fibers without the introduction of a contrast agent.

In this case, an important role in the diagnosis of AVMs is played by a non-invasive technique, magnetic resonance imaging. MRI data provide information both about the structure of the AVM and its size, and structural changes in the brain substance (perifocal edema, hemorrhage age, etc.). To assess the vascular structures during MRI, the introduction of a contrast agent is not always required, but if such a need arises to obtain additional data, then a contrast agent based on gadolinium (rare earth metal, paramagnetic) is used, which does not cause acute allergic reactions. Therefore, MRI and MR angiography are increasingly used in the diagnosis of AVMs, and more and more patients prefer this method because of its non-invasiveness and minimal risks.

If an AVM is anatomically located in a functionally significant area or closely adjacent to it, then a non-invasive technique, functional magnetic resonance imaging (fMRI), is used to map it for the purpose of accurate spatial assessment and preliminary analysis of its location in relation to closely located brain structures. This method is based on the registration of local changes in the level of oxygenation of venous blood in the brain when performing a certain task or at rest. The images obtained in this case are called BOLD -contrast (Blood Oxygen Level Dependent).

MRI is used not only when planning a radiosurgical operation and to obtain the true volume of a malformation, but also to assess the results of treatment. According to various authors, the sensitivity of MRI in assessing obliteration is quite high and is 73–86% according to L.D. Lunsford [13] and 78.1–80.6% according to O. Abdelaziz [14]. MRI can achieve 96% accuracy in assessing obliteration compared to 75% in CAG [13].

In the Radiosurgery Center Department of the N.V. Sklifosovsky Research Institute for Emergency Medicine, 53 MRI studies were performed to prepare patients for SRS from April 2016 to December 2019. At the first stage, in order to reduce the possible neurological deficit after the procedure, patients with AVMs in functionally significant areas underwent fMRI during preoperative preparation before the installation of a stereotaxic frame.

The observation below considers an example of the treatment of patient B. with AVM of the left temporal lobe.

Patient B., aged 43, was admitted to the neurosurgical department of the N.V. Sklifosovsky Research Institute for Emergency Medicine. Upon admission, he complained of loss of consciousness, generalized seizures with a frequency of 1 time per month. From the anamnesis it is known that a month before hospitalization in the city clinical hospital, AVM rupture of the left temporal lobe was diagnosed (AVM classification according to Spetzler-Martin — II). The general condition of the patient was satisfactory. The patient was conscious, Glasgow Coma Scale (GCS) score 15. There were no meningeal symptoms. Pupils OD=OS, photoreactions, corneal reflexes were preserved, alive. Nystagmus was not identified. The face was symmetrical, the tongue was in the midline. Paresis and sensitivity disorders were not detected. Coordinator tests were performed satisfactorily. The functions of the pelvic organs were not impaired. There was no aphasia.

To clarify the nature of the changes and verify the repeated AVM rupture, the patient underwent MRI using a GE Signa HDxT 3.0 T device (Table 1) according to the extended protocol. As can be seen from the Table, the MRI protocol included pulse sequences for visualization of the brain substance, assessment of blood vessels, and fMRI images for assessing the location of functionally significant areas.

Table 1

Advanced Magnetic Resonance Imaging Protocol

The name of the impulse sequences (IS)	IS Description	Indication of IS
Ax T2 FLAIR	FLAIR (Fluid Attenuated Inversion Recovery) in axial view	To assess the substance of the brain and search for pathological changes
Sag CUBE T1	3D -T1 -gradient sagittal echo (sequence for fast T1-weighted imaging, formed from two pulses of opposite polarity)	To obtain anatomical data
Ax SWI	Axial Gradient Echo (GRE)	High-contrast images sensitive to venous blood, hemorrhages, and iron accumulation
3D-TOF	Non-contrast 3D time-of-flight magnetic resonance angiography	Assessment of the structure of intracranial arteries
Ax T2*	T2* is a tissue parameter characterizing the decline in free induction in the axial projection	To get functional data

According to MRI, in the left temporal lobe, in the posterior sections of the superior temporal gyrus, a network of pathologically tortuous vessels was determined, which linear dimensions were 15x15x15 mm. The perifocal substance of the brain had signs of hemosiderosis (MR-signs of a previous hemorrhage). According to MR angiography of the intracranial arteries, arterial blood flow was determined in the tortuous vessels of the described formation and the draining vein (vessel diameter did not exceed 0.5 mm). Cortical branches of the left middle cerebral artery (MCA) approached the vascular glomus (Fig. 1, 2).

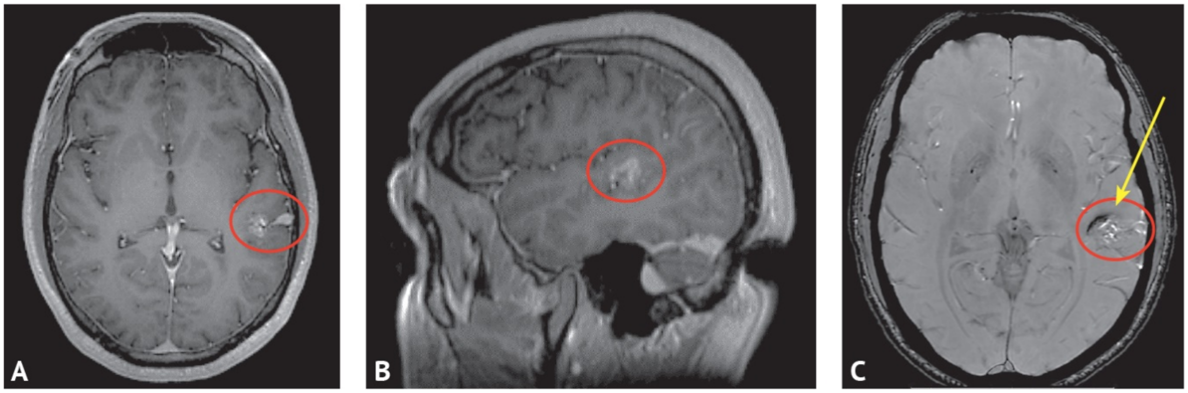

Fig. 1. Magnetic resonance imaging of the brain of patient B. before carrying out stereotactic radiosurgical treatment of arteriovenous malformation. A — Ax T1 with contrast enhancement, B — Sag T1 with contrast enhancement, C — SWI (susceptibility weighted imaging). In the left temporal lobe, arteriovenous malformation is determined (the contours are marked in red), linear dimensions up to 15x15x15 mm, according to SWI data with the presence of a previous hemorrhage (hypointense area along the anterior contour of the formation) (indicated by a yellow arrow)

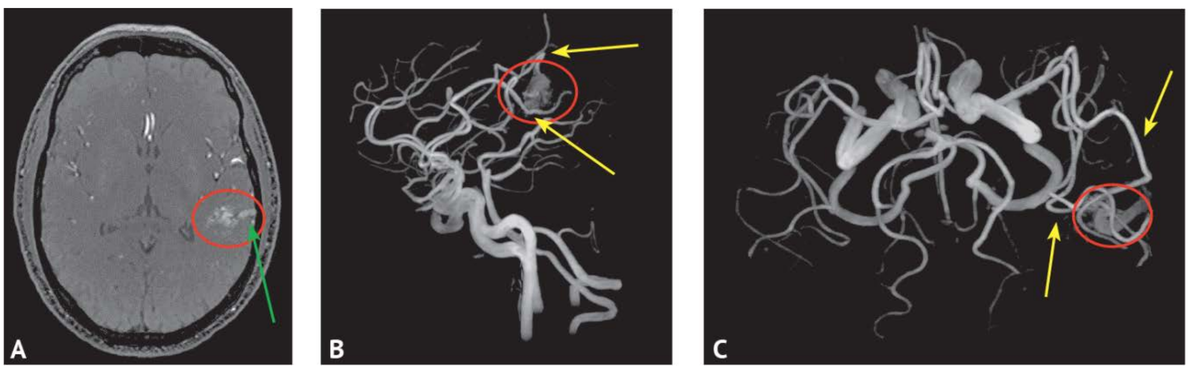

Fig. 2. Magnetic resonance imaging of the patient's brain prior to stereotactic radiosurgical treatment. A — Ax 3D-TOF, B — 3D reconstruction in the sagittal projection C — 3 D reconstruction in axial projection. In the tangle of pathological vessels in the left temporal lobe (arteriovenous malformation) (borders are marked in red), an MR signal characteristic of arterial blood flow is determined, a similar signal is detected in the draining vein, the diameter of arterial vessels does not exceed 0.5 mm, the diameter of the draining vein is up to 5.0 mm (green arrow). The cortical branches of the left middle cerebral artery approach the vascular glomus (indicated by yellow arrows)

Given that the AVM was located in close proximity to Wernicke's area, preoperative mapping was performed using a paradigm to visualize the cortical representation of the sensory center of speech. The paradigm had a block design and consisted of 8 periods of the active state of the patient and 8 periods of rest. The duration of each period was 24 seconds. For each period, 96 volumes were collected. The obtained data were post-processed using the BrainEx program (Nordic NeuroLab , Norway).

When functional MRI was performed using the speech audio paradigm in the left temporal lobe, the zone of signal enhancement was determined along the anterior contour of the mass formation — the localization corresponded to the sensory center of speech (Fig. 3).

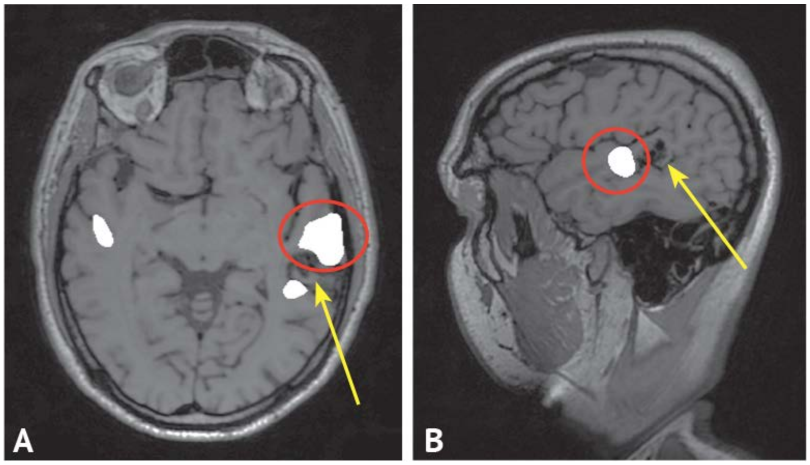

Fig. 3. Functional magnetic resonance imaging of the brain of patient B., performed before the stereotactic radiosurgery treatment. A — image in the axial plane, B — image in the sagittal plane. The sensory center of speech (the local area is white, the contours are circled in red) is located in the left temporal lobe, an arteriovenous malformation (marked with yellow arrows) attaches along the posterior contour

After MRI, the next stage of the patient with an AVM rupture was digital subtraction CAG using the SIEMENS Axiom Artis FC device, according to which two afferents from the left and an efferent with MCA were identified by superficial drainage into the left transverse sinus. The size of the racemose part was 15x15x15 mm (Fig. 4).

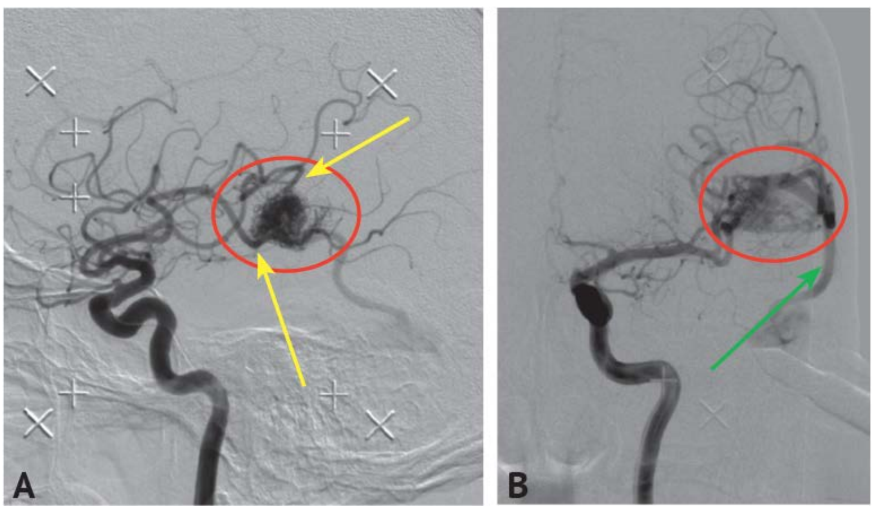

Fig. 4. Digital subtraction cerebral angiography. A — image in the sagittal plane, B — image in the coronal plane. Arteriovenous malformation of the left temporal lobe is visualized (borders are marked in red), 2 afferents from the left middle cerebral artery (yellow arrows) and 1 efferent with superficial drainage into the transverse sinus on the left (green arrow) are identified, the size of the racemose part is 15x15x15 mm

The AVM in the left temporal lobe had the following characteristics: it was located in a functionally significant area, it was in the acute period of hemorrhage, which was repeated (taking into account the anamnesis). According to the scale for determining the risk of surgical intervention (Spezler-Martin classification), this corresponded to II degree. Thus, the risk of recurrent hemorrhage and ischemic complications in the area of the cortical occipital branch of the left MCA was quite high. Due to the location of the AVM in a functionally significant area, microsurgical intervention would be associated with a high risk of disability. Therefore, the patient underwent SRS using the ELEKTA Leksell GammaKnife Perfexion machine (Fig. 5, 6). The duration of exposure was 138.5 minutes (Table 2).

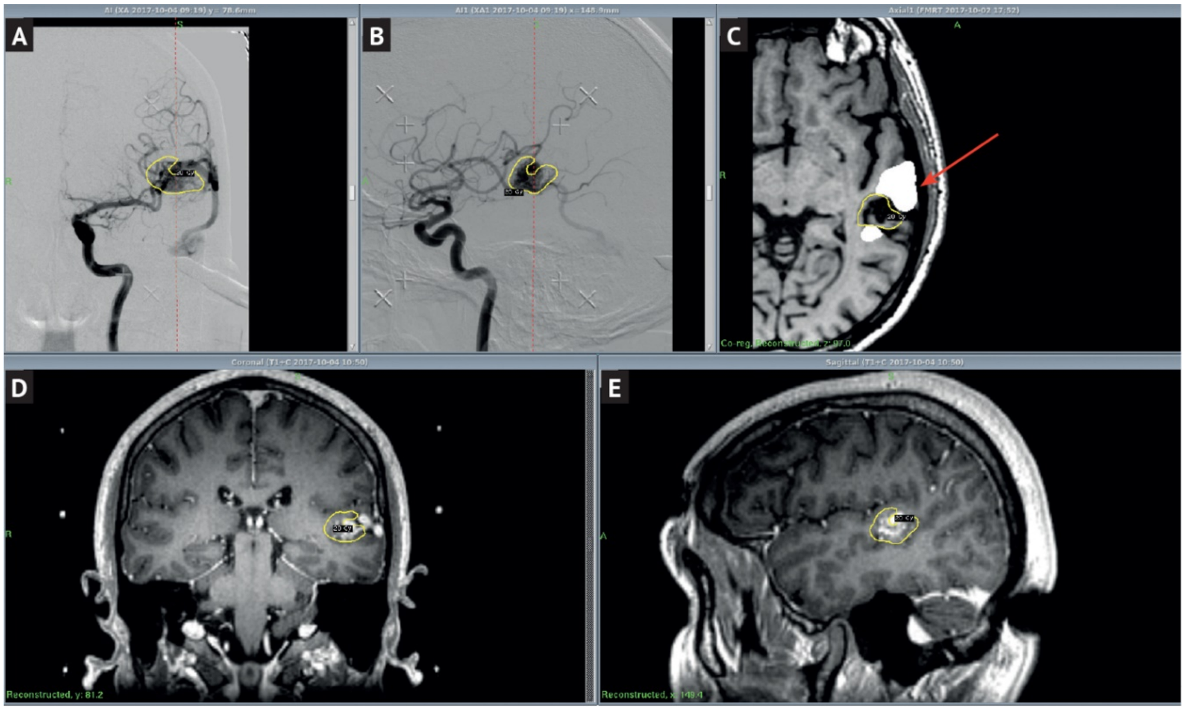

Fig. 5. Images of Leksell GammaPlan planning station 10.1. The yellow line shows the isodose distribution of the prescribed dose of 20 Gy. The red arrow shows the sensory center of speech (local area in white). Digital subtraction cerebral angiography: A — image in the coronal plane; B — image in the sagittal plane; C — image of functional magnetic resonance imaging in the axial plane; D — Cor T 1 with contrast enhancement; E — Sag T 1 with contrast enhancement

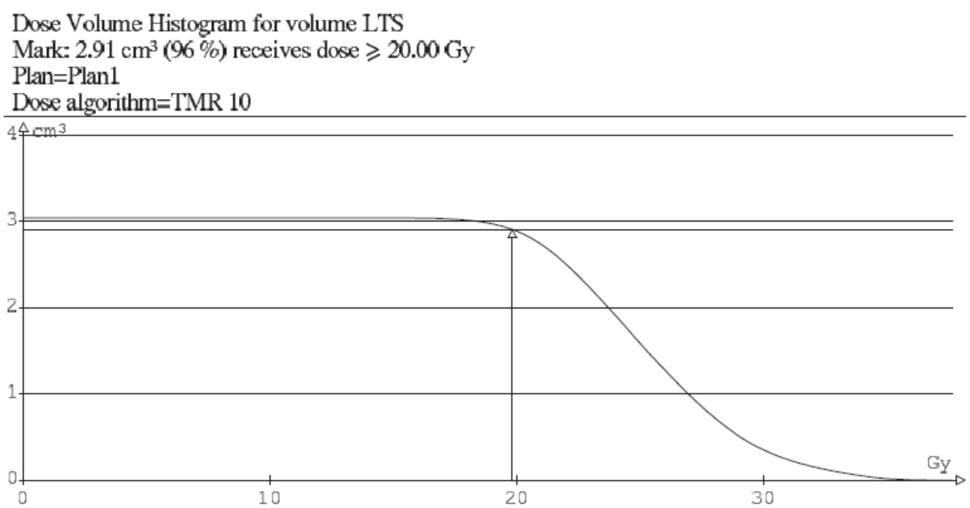

Fig. 6. The graph of dose dependence taking into account the volume of arteriovenous malformation (AVM). A dose of 20 Gy captures 96% of the AVM volume, taking into account a closely located functionally significant area

Table 2

The protocol of stereotactic radiosurgical treatment of patient B. with arterioveous malformation of the left temporal lobe. Prescribed Dose, Prescribed Isodose, and Maximum Dose (Gy) Values Used in Stereotactic Radiosurgery for Left Temporal Lobe Arteriovenous Malformation

Localization	Prescribed dose, Gy	Prescribed isodose, %	Dose max , Gy
Left temporal lobe	55	55	36.4

Over the next 2 years, the patient underwent examinations by a neurosurgeon at the Radiosurgery Center with the following frequency: the first visit was 6 months after radiosurgical treatment, then examination and consultation every 12 months. During this time, the patient continued to have generalized convulsive seizures, but their frequency decreased to 1 time in 3 months, and a positive effect of taking carbamazepine was revealed during the treatment. According to the data provided by MRI and CT studies, the racemose component of the AVM of the left temporal lobe decreased over time. After 2 years from the date of SRS, taking into account the accumulated data indicating a tendency to obliteration, it was decided to perform follow-up MRI and CAG for the final confirmation of AVM obliteration in this patient.

According to the results of the control MRI of the brain with intravenous contrast enhancement and non-contrast MR angiography of the intracranial arteries, it was revealed that in the place of the pathological network in the left temporal lobe, an area of hypointense signal on T1 WI (weighted image) was determined, which was much smaller than the previously described AVM. On the periphery of this area against the background of edema, diffuse accumulation of the contrast agent was determined, which corresponded to the manifestations of radiation necrosis (Fig. 7, 8). The convexital vein remained along the lateral contour, its diameter decreased to 2.0 mm (previously it was 5.0 mm). According to MR angiography, the arterial component in the projection of the irradiated AVM was not visualized, which was confirmed by the CAG results (Fig. 9).

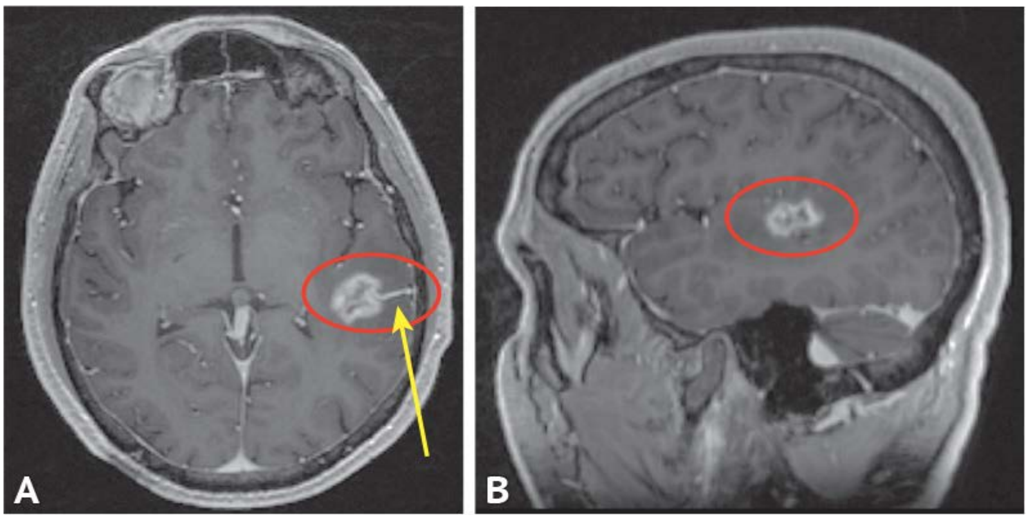

Fig. 7. Control magnetic resonance imaging of the patient's brain two years after stereotactic radiosurgical treatment. A — Ax T 1 with contrast enhancement, B — Sag T 1 with contrast enhancement. Along the periphery of irradiated arteriovenous malformation (borders are marked in red) in the left temporal lobe, an area of diffuse accumulation of a contrast agent is determined, which is characteristic of manifestations of radiation necrosis. On the lateral contour of the formation, a convexital vein is visualized, reduced in diameter to 2.0 mm (indicated by a yellow arrow)

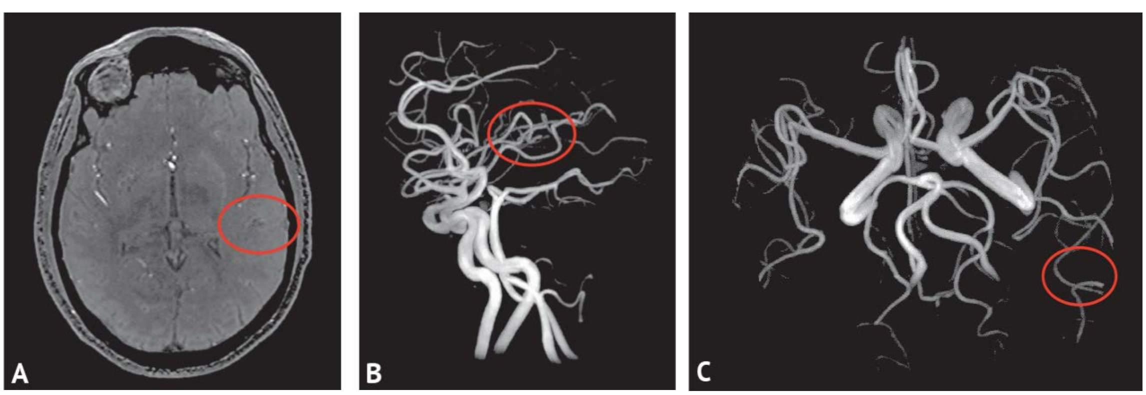

Fig. 8. Control image of magnetic resonance imaging of the patient's brain 2 years after stereotactic radiosurgical treatment. A — Ax 3D-TOF , B — 3D reconstruction in the sagittal projection, C — 3 D reconstruction in the axial projection. No arterial blood flow was detected in the projection of the irradiated AVM (borders are marked in red)

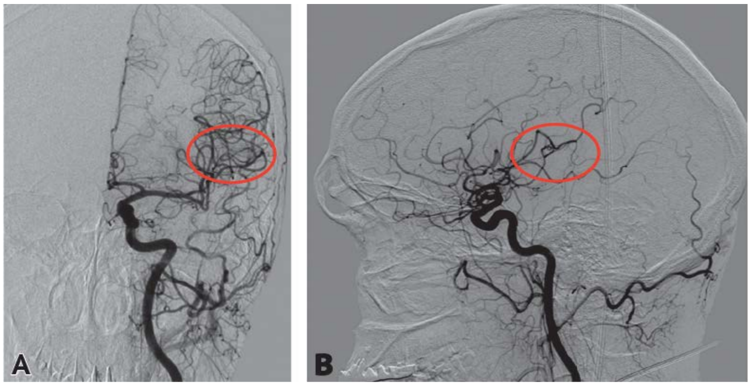

Fig. 9. Digital subtraction cerebral angiography. A — image in the coronal plane, B — image in the sagittal plane. The previously described arteriovenous malformation (borders in red) with afferents from the left middle cerebral artery of the cerebral artery is not visualized. Two years after stereotactic radiosurgical treatment

CONCLUSION

This observation proves the effectiveness of MRI in diagnosing and evaluating the results of stereotaxic radiosurgical treatment of arteriovenous malformations of the brain using the ELEKTA Leksell GammaKnife Perfexion apparatus in the acute period of hemorrhage. This non-invasive technique is highly informative, the absence of radiation exposure and acute allergic reactions after the introduction of a contrast agent, which reduces the risk of possible complications and the number of studies conducted for the patient for subsequent treatment.

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