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Case report

Progressive regression of intracranial arteriovenous malformations after Onyx embolization

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ABSTRACT

Progressive regression of cerebral arteriovenous malformations (AVMs) is a rare phenomenon that may occur spontaneously or after previous surgical or endovascular incomplete obliteration. We present two cases of AVMs occluded partially with Onyx followed by the unexpected cure of the lesions with the angiographic evidences as well as multiannual follow-up.

1. Introduction

Arteriovenous malformations (AVMs) are complex and heterogeneous anomalies with a risk of hemorrhage up to 4% per year [1,2]. In order to prevent cerebral bleeding or rebleeding and associated neurological consequences a treatment of cerebral AVMs is not infrequently attempted. The decision as to whether to treat an AVM is often controversial [3], since every form of AVM therapy harbors a certain risk of complications. The intervention options for patients with AVMs include surgical resection, radiosurgery and endovascular technique as a single method or in combinations [4,5]. It is commonly acknowledged, that only complete AVM nidus obliteration provides a protection from bleeding from this vascular lesion [1].

Moreover, there are studies suggesting that partial occlusion of an AVM may potentially increase the risk of hemorrhage, although, the literature data are incoherent in this respect [1,2,6]. In any case, every residual AVM after partial obliteration has still a capability to bleed, therefore, it is advocated to eliminate this AVM remnant if only further interventional management is feasible [2,7]. When a conservative approach is applied, what may be rarely justified, an option exists to perform a series of angiograms in order to determine if spontaneous AVM regression has come about

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[7,8]. Actually, the exact natural history of AVM remnants is unpredictable due to the rarity of this phenomenon and a small amount of data in the literature [7,8]. As far as endovascular treatment is concerned, there are only few reports in the literature of spontaneous thrombosis of AVM after partial embolization [8,9]. In the current study we present another two cases of spontaneous regression of AVMs after partial Onyx agent (ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide) embolization with the angiographic evidences and multiannual follow-up.

2. Case reports

2.1. *Case 1*

A fifty-two-year-old male had complained of swelling and thickening of the lower eyelid of the right eye for 6 months. Neurological examination did not reveal any neurological deficits but changes on the eyelid without localized edema of the eyelid. A CT angiography showed an AVM in the right perirolandic area (Fig. 1). Selective angiograms of the right ICA, and right MCA and ACA confirmed a 29-mm sized AVM with a vein draining into the superior sagittal sinus (Fig. 2A). After determining the appropriate position of the microcatheter Ultraflow (ev3, Irvine, California, USA) tip, embolization of the AVM nidus was performed with 3 ml of Onyx 18 (ev3, Irvine, CA), under fluoroscopic guidance followed by short angiograms to better visualize surrounding vascular anatomy. Immediate post-embolization angiogram depicted subtotal occlusion of the lesion (Fig. 2B). During the procedure heparinized saline was continuously infused into the arterial line. The post-embolization course was unremarkable and the patient was discharged home uneventfully. Control angiogram performed 8 months later depicted spontaneous thrombosis of the residual AVM what resulted in complete occlusion of the AVM (Fig. 2C). Subsequent control angiography was performed 24 months after treatment and no recanalization was presented. The patient remained neurologically intact for the entire follow-up period.

2.2. *Case 2*

A forty-three-year-old male had complained of cerebellar symptoms including horizontal nystagmus and positive Romberg's test for 2 years. CT angiography showed an infratentorial AVM in the right cerebellar hemisphere (Fig. 3). Selective angiograms of the right VA, and right SCA confirmed a 28-mm sized AVM with a vein draining into the vein of Galen (Fig. 4A). Embolization of the AVM nidus was performed with 4.5 ml of Onyx. A clinically irrelevant reflux of embolic material into posterior inferior cerebellar artery was noted and resulted in partial occlusion of this vessel. Immediately 20 mg of abciximab was injected locally with

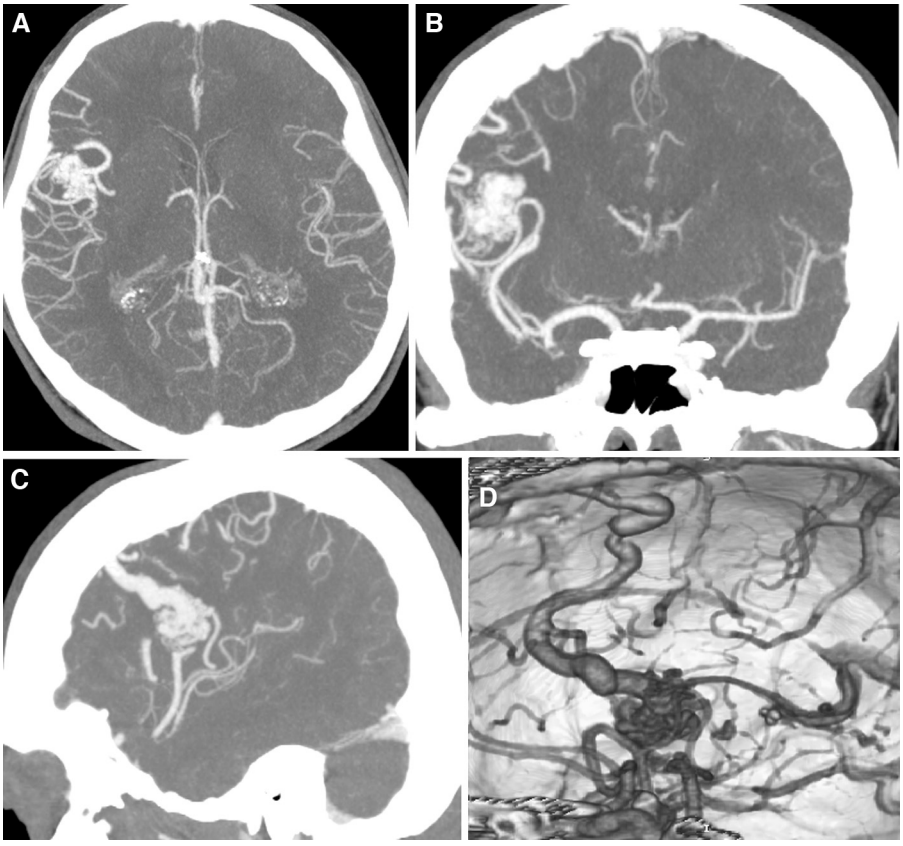

Fig. 1 – Preoperative images. Axial (A), coronal (B), and sagittal (C) CT angiograms showed a small (<3 cm) right perirolandic arteriovenous-malformation. On 3D volume-rendered CT reconstruction (D) one dilated vein draining into the superior sagittal sinus was presented (contralateral view).

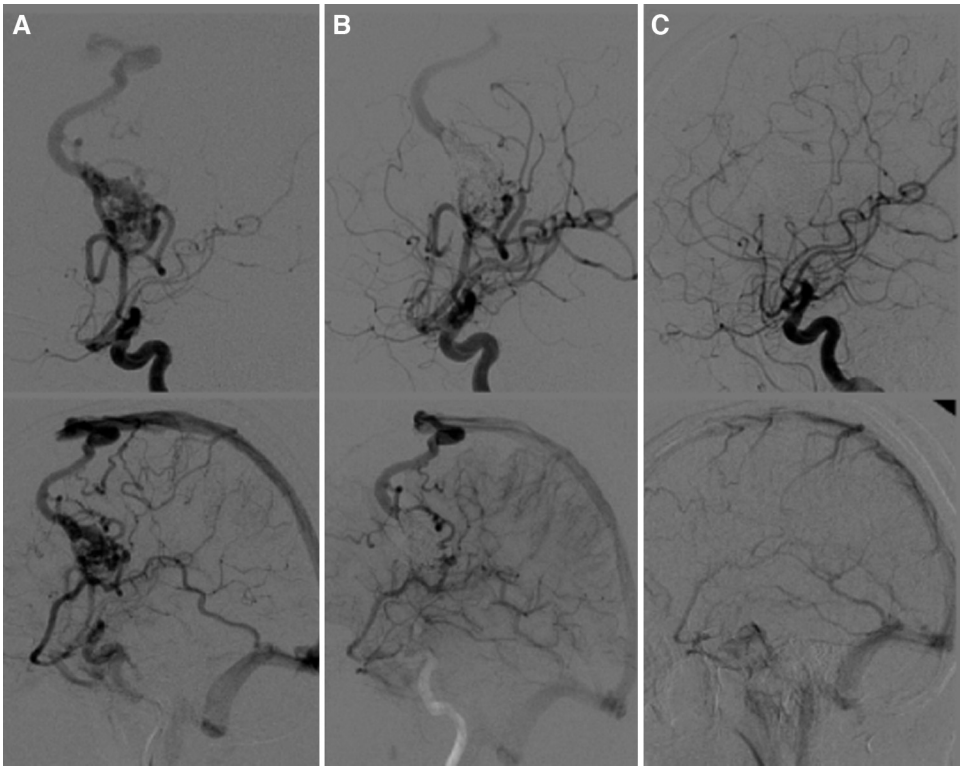

Fig. 2 – Right perirolandic arteriovenous-malformation. Lateral internal carotid angiograms. Arterial (upper row) and venous (lower row) phases. (A) Before treatment; (B) immediately after treatment; (C) 8 months after treatment. The malformation appeared subtotally occ1uded in a single session. The control follow-up angiogram showed a spontaneous obliteration of the residual AVM with no evidence of venous drainage. The control angiogram taken 16 months later (not shown) confirmed complete occlusion of the AVM.

good angiographic effect. Post-embolization angiogram depicted subtotal occlusion of the lesion (Fig. 4B). The patient was discharged from the hospital without any neurologic deficits. A second stage of embolization attempted one month later was failed due to lack of direct arterial access to the lesion. A control angiogram obtained 34 months after the initial endovascular treatment revealed total obliteration of the AVM (Fig. 4C). During the entire follow-up period the patient's clinical status remained unchanged and the cerebellar symptoms persisted.

3. Discussion

It is widely accepted that only total elimination of an AVM affords protection from hemorrhage [1]. The management strategy in case of a residual lesion after previous treatment is microsurgical excision of the remnant, radiosurgery or endovascular embolization [10]. Although a spontaneous AVM obliteration in a presumed mechanism of thrombosis is attainable [11], the rarity of this phenomenon with the reported rate of 0.7–0.8% [8,11,12] allows to take it into consideration only in exceptional cases, e.g. the lack of patient's consent for further interventional treatment.

As far as factors associated with progressive AVMs regression after embolization are concerned, the literature data are sparse and based merely on case-reports [9,13]. A greater number of reports have been devoted to the still exceptional and insufficiently understood phenomenon of spontaneous AVM thrombosis [11,12,14–17]. In this group the most important predictors for AVM regression are hemodynamic changes caused by intraparenchymal bleeding and small size of AVM with a single draining vein [11,12,14–17]. In case of intracerebral hematoma and associated brain edema the mass effect on the feeding arteries may diminish blood flow in the AVM what results in thrombosis in draining vessels [12,15,16,18]. It is hypothesized that arteriosclerosis, vasospasm secondary to bleeding, thromboembolism or systemic coagulation disorders may also promote the feeding artery occlusion [12]. Moreover, there are reports that kinking of feeding arteries and draining veins caused by organization and gliosis of clot is likely to alter the AVM hemodynamics, leading to slowing blood flow with subsequent thrombosis [14,16,19]. It is controversial, if the presence of a single arterial feeder plays a role in spontaneous AVM regression [14,16,17,20]. It is suggested that the occurrence of a single feeding artery is a feature of small AVMs that have a greater tendency toward regression than larger ones [16]. Owing to the fact that following occlusion of the feeding artery an AVM recruits arterial collaterals if the shunt remains patent, this factor is treated as of less significance [12]. According to Lee et al. the most important determinant contributing to spontaneous AVM regression is the venous thrombosis of dominant draining veins [12]. Abrupt venous thrombosis may lead to

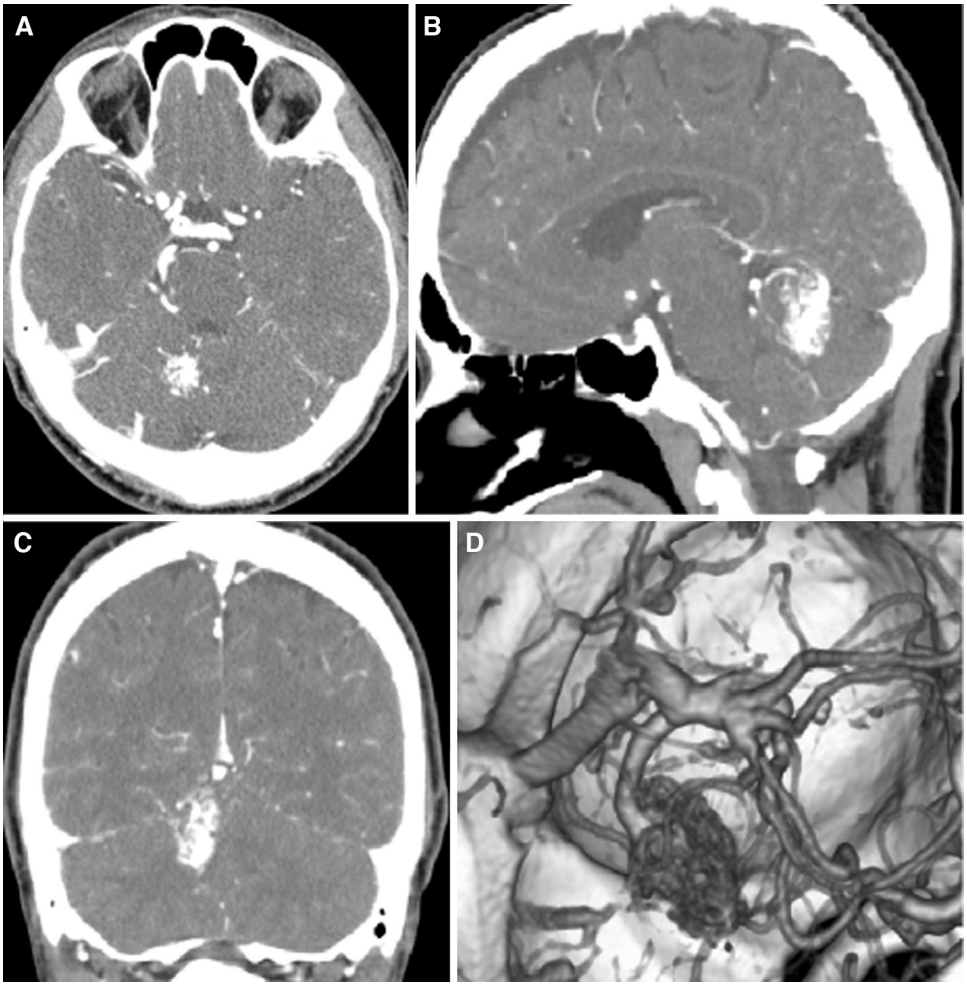

Fig. 3 – Preoperative images. Axial (A), sagittal (B), and coronal (C) CT angiograms showed a small (<3 cm) arteriovenous malformation of right cerebellar hemisphere. 3D volume-rendered CT (D) revealed a venous drainage through one dilated vein into the vein of Galen (anterolateral view).

intracranial hemorrhage, but as a result of gradual progressive venous thrombosis, the patient experiences small hemorrhages with coexisting neurological events, such as seizures or hemiparesis [12,16]. The often-mentioned angiographic feature of AVMs that underwent spontaneous thrombosis is the presence of a single draining vein [11,15–17]. Abdulrauf et al. suggests that the obstruction of a single draining vessel leads to complete venous outflow blockage with subsequent stasis of blood and AVM thrombosis [17]. The vein may be occluded as a result of external compression (hemorrhage, swelling), abnormality in the vein (clot embolus from the nidus or feeders) or may be associated with patient's factors (hypercoagulable state) [17]. There exist a hypothesis that obstruction of one single vein is more probable than obstruction of multiple draining veins, thus occlusion of a single vein is more likely to cause complete thrombosis of an AVM [16]. In the literature 73% spontaneously thrombosed AVMs had a solitary draining vein [12].

It is indicated that small size of an AVM is a factor associated with progressive regression of the lesion [11,12,14–17]. According to review of 68 cases of AVMs with spontaneous thrombosis a median nidus size was 2 cm [16]. However, based on literature data only 50% AVMs that spontaneously regressed were small [12]. It is also reported that superficially located AVMs are more prone to regress than deep AVMs [20]. Unfortunately, angiographic or anatomic features of AVMs that present in the lesions linked to spontaneous obliteration are also commonly observed in nonregressing AVMs [8], so up to date there is no any certain indicators that could imply the expectant treatment in case of a residual AVM.

In two cases described in the current study we decided to obliterate the AVM residuals in the second stage of endovascular curative management but it turned out that the lesions were no more apparent in the control angiograms. Both presented AVMs were superficially located, had small (<3 cm) nidus sizes and had a single draining vein, thus, they shared the above-mentioned angiographic features predisposing to spontaneous progressive AVMs regression. The phenomenon of the spontaneous thrombosis after endovascular treatment of AVM has been already reported and there exists a theory that isobutyl 2-cyanoacrylate (IBCA) as well as Onyx may trigger an active AVM thrombosis in a mechanism of hemodynamic alteration [9,13]. As far as the durability of occlusion is concerned, the majority of cases of spontaneously

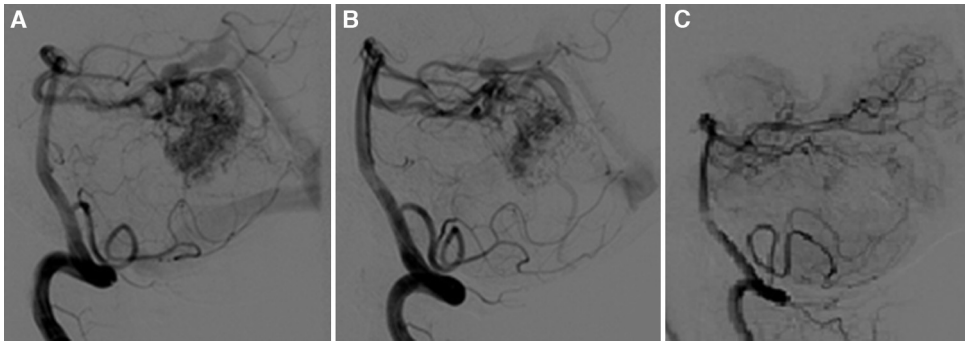

Fig. 4 – Arteriovenous malformation (AVM) of right cerebellar hemisphere. Lateral vertebral angiograms. (A) Before treatment; (B) immediately after treatment; (C) 34 months after treatment. The post-embolization angiogram depicted subtotal occlusion of the lesion. A second stage of embolization attempted one month later was failed due to lack of direct arterial access to the lesion. The control angiogram obtained 34 months post-embolization revealed total obliteration of the AVM.

thrombosing AVMs reported in the literature do not recur in the long term follow-up, but although rare, there are cases of confirmed AVMs recanalization [11] what implies the mandatory radiographic follow-up. To our knowledge, there is only one case about progressive AVM thrombosis after Onyx embolization [9], however, the long term durability of the complete AVM obliteration is unknown in that report. The long term angiographic follow-up screening of 24 and 34 months achieved in our patients is in favor of persistence of this phenomenon.

It is also worth mentioning, that angiography may be limited in revealing the entire AVM in the thrombosed lesions [15]. Matano et al. reported a case of spontaneous regression of cerebral AVM following intracerebral hemorrhage. Although preoperative angiography indicated spontaneous regression of the lesion, the AVM shunt remnant was confirmed by indocyanine green videoangiography during surgery in the patient [15]. Thus, there is still a possibility of a small arteriovenous shunt remnant in patients with completely thrombosed AVMs on angiography, what should be also taken into consideration.

4. Conclusions

Spontaneous thrombosis resulting in long-term angiographic obliteration of AVMs may occur after previous subtotal Onyx embolization. The embolic agent Onyx is likely to initiate the progressive thrombosis, although, further investigations are needed.

Conflict of interest

None declared.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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