Spontaneous disappearance of brain arteriovenous malformation: a case series.

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Spontaneous disappearance of brain arteriovenous malformation: a case series.

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Running Title

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Abstract

Objective: Brain arteriovenous malformation (BAVM) is defined as abnormal communication between cerebral of arteries and veins, without capillaries. Clinically, it may involve intracranial hemorrhage or seizures. Complete spontaneous resolution, known as BAVM disappearance, has been reported in rare cases.
Methods: We retrospectively collated all cases of BAVM in Lille University Hospital, from 2005 to 2018, and identified all cases of spontaneous BAVM disappearance on angiography (nidus and early venous drainage).
Results: There were 4 cases of spontaneous BAVM disappearance, in 3,573 patients: i.e., prevalence of 0.1%. Sex ratio was 2:2; ages ranged from 14 to 46 years; nidus size was generally small (< 20mm); 3 of the 4 patients had superficial venous drainage. Revelation of BAVM was by hemorrhage in 3 cases and by seizure in 1. There were no cases of recanalization at 1 year's follow-up.
Conclusion: Spontaneous BAVM disappearance is rare. Associated factors include small nidus, superficial venous drainage and hemorrhage.

Résumé

Objectifs: Les malformations artério veineuses (MAV) cérébrales correspondent à la communication anormale entre veines et artères cérébrales, sans réseau capillaire. Elles peuvent se manifester cliniquement, par un tableau d'hémorragie intracrânienne, ou par de l'épilepsie. Il a déjà été reporté de rares cas de disparition spontanée de MAV en angiographie.
Méthodes: Tous les cas de MAV cérébrales prises en charge dans notre service de neurochirurgie du centre hospitalier universitaire de Lille entre 2005 et 2018 ont été colligées, et nous avons identifié parmi eux toutes les disparitions spontanées des MAV, définie par la disparition complète de la MAV (nidus et drainage veineux précoce), à l'angiographie.
Résultats: Quatre cas de disparition spontanée de MAV ont été retrouvés parmi une cohorte de 3573 patients, correspondant à une prévalence de 0,1%. Le sex ratio était de 2:2, les âges de 14 à 46 ans, la taille des nidus était en général petite (< 20mm), le drainage veineux était superficiel pour 3 patients sur 4. La MAV était révélée par un saignement dans 3 cas, et par une comitialité dans un cas. Aucun cas de recanalisation n'a été noté après un an de suivi.
Conclusion: La disparition spontanée de MAV cérébrale est un phénomène rare. Les facteurs qui y sont associés pourrait inclure un nidus de petite taille, un drainage veineux superficiel, des MAV ayant saigné.

1. Abbreviations

ASA: American Society of Anesthesiologists
BAVM: Brain Arteriovenous Malformation
CT: Computerized Tomography
MRI: Magnetic Resonance Imagery
LGK: Leksell Gamma Knife

2. Introduction

Patients with Brain arterio venous malformation (BAVM) harbor risks of intracranial hemmorhage, neurologic deficit, seizure and headache. Prevalence of asymptomatic BAVM on brain MRI is around 0.05% {7} and their risk of bleeding is still disputed. Some authors reported a risk of 1.5% per year in patients with unruptured BAVM and 4.8 % per year in patients with ruptured BAVM {3}. Previously ruptured BAVMs, deep location, exclusive deep venous drainage and associated aneurysms are the main risk factors of bleeding according to many authors.{3,7,8,11}.

Spontaneous complete occlusion of BAVM is a very rare phenomenon, defined by complete disappearance of nidus and early venous drainage, on angiography. There is no data about follow-up length and modality. The frequency of this phenomenon is supposed to range between 0.1 and 1.3 %{7,8}. There are only few observations in literature, with about 70 cases reported ever since 1955. The causes are debated and mostly reported to hemodynamic alterations of various origins.

Our study aimed to analyze all cases of patients with spontaneous BAVM disappearance recorded in our center. We indeed noticed some similarities in our cohort, such as small nidus size, superficial venous drainage, hemorrhage, that we esteemed interesting to report and consider in the future, while discussing treatment of such kind of patients.

3. Patients and Methods

3.1. Study design

We studied medical records of all cases of patients with ruptured and unruptured BAVM (n= 3573) undergoing regular follow up in our institution from 2005 to 2018, in order to identify those who experienced spontaneous regression of their BAVM . This cohort includes patients referred from other hospitals to our institution for Leksell Gamma Knife radiosurgery treatment. Patients included or their representant gave their consent to take part to this study

3.2. *Clinical presentation*

Age at diagnosis, medical history, ASA score {1} and neurological symptoms were recorded in each patient. The functional outcome was evaluated with the modified Rankin scale 1 year after BAVM occlusion.

3.3. *Radiological data*

Initial brain CT scan, MRI and conventional angiography were performed to detect any hemorrhage and to evaluate the nidus location, its size, the feeding arteries, the venous drainage and the presence of intranidal or perinidal aneurysm. The Spetzler and Martin score was noted for each patient {24}. These radiological examinations were repeated 6 months and 1 year after BAVM disapperance.

All patients gave their consent to that study, which met the acceptance criteria for our ethic committee.

4. **Results**

4.1. *Population*

Among all patients, four experienced spontaneous BAVM disappearance, among 3573 patients, corresponding to a prevalence of 0,1%. In these 4 patients (2 males and 2 females), the age at diagnosis was between 14 and 46 years old. Ruptured BAVM was noted in 3 patients and unruptured BAVM was noted in 1 patient with episodes of seizure (**Table 1**).

4.1.1. First patient

First patient was a 38 years-old man, whose BAVM was diagnosed after right fronto parietal hematoma revealed by brutal onset of hemiplegia. Nidus was small, with few feeding arteries coming from middle and anterior cerebral arteries and superficial drainage in superior sagittal sinus. Leksell gamma knife radiosurgery treatment was planned for this patient, 8 months after surgery, but angiography revealed complete disappearance of the BAVM, confirmed by 1 year later angiography.

4.1.2. Second patient

Second case was a 14 years-old boy who presented with brutal left hemianopsia, due to right occipital hematoma. Angiography revealed a small nidus, with feeding artery coming from right posterior cerebral artery (4 mm diameter) and drainage in superior sagittal sinus through a 2 mm diameter vein. 2 months post hemorrhage arteriography revealed slight reduction in nidus size, and angiography performed before Leksell gamma knife radiosurgery, 6 months after bleeding, demonstrated complete resolution.

4.1.3. Third patient

In our third patient, a 35 years-old female, BAVM was diagnosed because of seizures. Feeding arteries came from left middle cerebral artery, leading to a small nidus, draining in left Rosenthal vein. Treatment planned was also Leksell gamma knife radiosurgery, delayed because of pregnancy. 36 months after diagnosis, arteriography revealed complete BAVM disappearance, that was confirmed on delayed angiography, 7 years later.

4.1.4. Fourth patient

Last case was a 46 years-old woman, who was transferred for left parietal hematoma, revealed by confusion. Nidus was small (16 mm), with one feeding coming from left cerebral posterior artery (1mm diameter), and superficial drainage in superior sagittal sinus through a 0.5mm wide vein. Follow up revealed spontaneous disappearance of the BAVM, on 18 months post bleeding angiography.

The three adults underwent a delayed control angiography, more than one year after the BAVM disappearance (18,21 and 84 months), but the follow up for the child was not performed in our center, and unfortunately we have no follow-up data about him.

4.2. *Treatment discussion*

All cases were discussed in multidisciplinary neurovascular meeting, including vascular neurosurgeons, neurosurgeons committed to Leksell Gamma Knife (LGK) radiosurgery, interventional neuroradiologists and neurologists. In cases 1, 2 and 3, LGK stereotactic radiosurgery was planned because of small nidus size located in eloquent zone, and BAVMs disappearance was noticed during angiography performed immediately before treatment. For case 4, surgery was decided, and neuronavigation preoperative MRI featured BAVM disappearance as depicted in **Figure 1**, which was confirmed by angiography.

4.3. *Noteworthy characteristics of these four BAVMS*

Focusing on the BAVMs characteristics in these four cases, we noted that a small nidus was present in all cases, feeding arteries originated from both anterior and posterior circulation, and drainage veins were superficial in 3 cases. Period of disappearance ranged from 6 months to 3 years. BAVM regression was confirmed by delayed angiography (**Table 2**). We draw these hypotheses: cases 1, 2 and 4 had small nidus, superficial drainage and ICH. So these cases include all factors reported in literature: a hemorrhage leading to hemodynamic changes, mass effect and vasospasm. All these factors lead to vessel obliteration and potential BAVM disappearance. Case 3 is different, because seizure revealed BAVM that remained unruptured. Then, disappearance was quite longer than in other cases (36 months), venous drainage was deep and unique and it is noteworthy that this patient treatment was delayed because of a pregnancy. From this fact and because the BAVM was not similar to the three other cases, we propose the hypothesis that hormonal factors may be implied.

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5. Discussion

These four cases of BAVM spontaneous disappearance happened for small BAVMs with a single feeding artery or unique draining vein, after episode of hemorrhage or in situations of hormonal imbibition.

5.1. *Epidemiology of BAVM disappearance*

Spontaneous disappearance of BAVMs is a very rare phenomenon. Only few cases have been reported. In his review of literature, Buis {4} reported an incidence of 0.3%. In other studies, the incidence was ranging from 0.8 %{9} to 20% {10}. Patel {23} reviewed 18 cases in their center, Adulrauf {2} and Lee{16} both reported 4 cases per center, corresponding respectively to incidences of 1.3%, 0.8 and 0.5%. Buis {4} reported that mean age at diagnosis of BAVM regression was 37 years, clinical presentation was ICH in only 57%. In this study, the median nidus diameter was 2 cm, with a single feeding artery in 46 % and a single draining vein in 59%. The mean timespan between diagnosis and disappearance was 54 months and in three cases a recanalization was observed.

Even if patients from other centers were referred to our institution for radiosurgery, the prevalence in our cohort reaches 0.1%, with a balanced sex ratio, young age at time of diagnosis including one pediatric case (25%). Clinical presentation was ICH in 75%. We observed 100% of small nidus (from 2 to 16mm), with a single feeding artery in 75 %, and a

single draining vein in 75%, and 75% of superficial venous drainage. The mean timespan between diagnosis and disappearance was 14 months and no case of recanalization was noted, even after long follow up and control angiography.

5.2.*Associated factors with BAVM disappearance*

Many factors are reported as associated factors with BAVM regression: small nidus size {6}, single feeding artery {17,19,21}, few draining veins {9,12,21,22}. In our series, small nidus appears the most significant associated factor with BAVM disappearance. Nevertheless, single feeding artery, superficial venous drainage and hemorrhage were present in 3 patients (75%). In the litterature, hypothesis is laid that the number of arteries is not related with disappearance, but only with nidus size. For veins, it is also supposed that a single draining vein is a factor for BAVM disappearance, as the thrombosis of this single vein could lead to the disappearance of the BAVM. Then, thrombosis could be caused either by compression due to the hematoma, or by a state of hypercoaguability in some patients

A recent paper about spontaneous diasapperance of spinal arteriovenous malformations also reports angiography procedure as a significant contributing factor, because of prothrombotic properties of contrast agents {9}.

From our four cases, we draw these hypotheses: cases 1, 2 and 4 had small nidus, superficial drainage and ICH. So these cases gather all factors reported in literature: a hemorrhage leading to hemodynamic changes, mass effect and vasospasm. All these factors lead to vessel obliteration and potential BAVM disappearance. Case 3 is different, because seizure revealed BAVM that remained unruptured. Then, disappearance was quite longer than in other cases (36 months), venous drainage was deep and unique and it is interesting to notice that this patient treatment was delayed because of a pregnancy. From this fact and because the BAVM was not similar to the three other cases, we propose the hypothesis that hormonal factors could be implied.

It has been reported that the use of oral contraceptive drugs can be responsible for spontaneous cerebral vein thrombosis or spontaneous thrombosis of a BAVM draining vein {13,14,15}. In case of cerebral thromboembolism it has been shown that the risk increases with oestrogene rates {14} It is known that pregnancy leads to hormonal changes, oestrogen rates increase and therefore hypercoagulability, that could have lead in this case to the thrombosis of the draining vein. In case of haemmoraghe, BAVMs disappear faster, thanks to mass effect.

5.3. *Long term follow-up needed*

Finally, in our cohort, we reported no case of recanalization. It is recommended to keep following patients, because some cases of delayed recanalization are reported, up to 39 months after BAVM disappearance {5,18,20}. Matano et al. {16} also suggest that spontaneous disappearance of BAVMs does not exist and correspond to angiographically occult arteriovenous malformations, no longer detected on angiography but still remnant.
So these patients should be followed up and not considered as definitely cured.

6. Conclusion

BAVM spontaneous regression does exist, but it is a rare event. Only small BAVM, with few feeding arteries and few draining veins are concerned. When BAVM is revealed by bleeding, it is easy to understand that hemodynamic changes can lead to the BAVM thrombosis. On the opposite, mechanisms of thrombosis in unruptured BAVMs remain unclear, but hormonal changes seem to be mainly implied. Finally, although we do not report any case of recanalization, it has been reported in previous papers, so that it is still recommended to keep a long term follow up for these patients, at least by MRI with appropriate vascular sequences.

Human and animal rights

The author declare that the work described has not involved experimentation on human or animals.

Informed Consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Disclosure of interest

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Figure legends

Table 1. Patients characteristics
mRS: modified Rankin Score

Table 2. Brain Arteriovenous Malformation characteristics
PCA : Posterior Cerebral Artery, ACA : Anterior Cerebral Artery, MCA : Middle Cerebral Artery.
SPM Score: Spetzler and Martin Score

Figure 1. Case 4 angiography.A : May 2016. 16 mm nidus, feeding artery : Cerebral Posterior Artery, superficial drainage. B November 2017 : no nidus left

A. Angiography featuring small nidus, feeding through Posterior Cerebral Artery and superficial drainage.
B. Angiography showing BAVM disappearance.

Spontaneous disappearance of brain arterioveinous malformations : a retrospective cohort study.

Tables and Figures

Table 1. Patients characteristics

Case	Gender	Age at diagnosis	Medical history	Rupture	Clinical feature	mRS after BAVM disappearance
1	Male	38	Cirrhosis	+	Hemiplegia	3
2	Male	14	0	+	Headache and left hemianopsy	1
3	Female	35	0	-	Seizure	1
4	Female	46	0	+	confusion	0

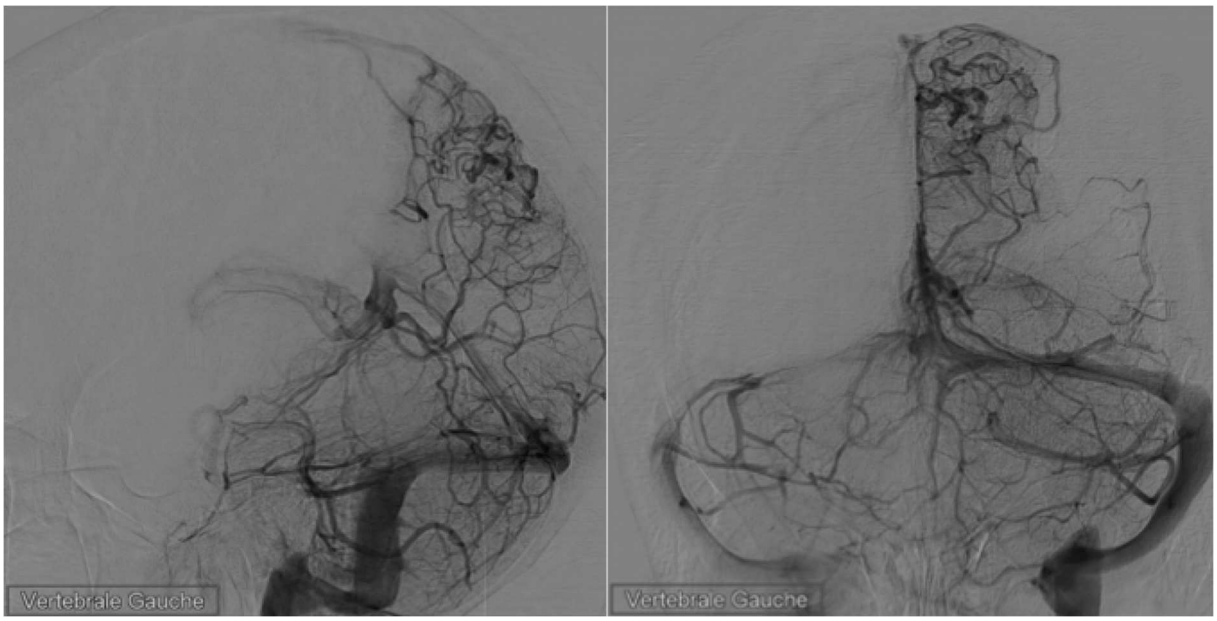
mRS: modified Rankin Score

Table 2. Brain Arterioveinous Malformation characteristics.

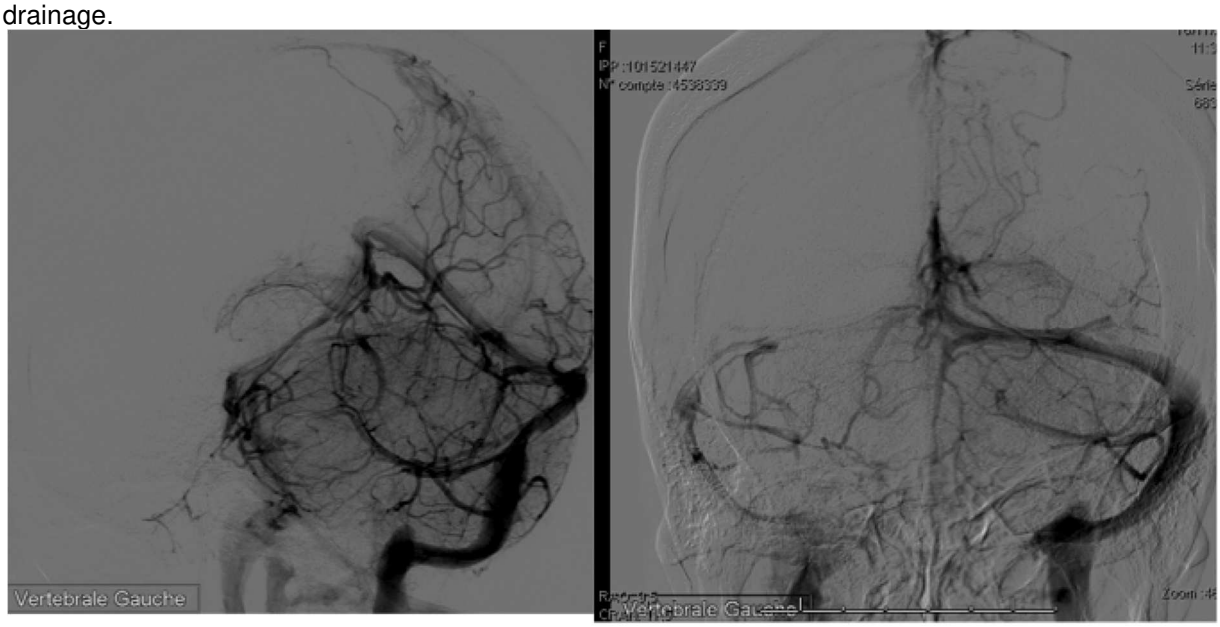
Case	Nidus size	Feedind arteries	Draining veins : number and location	Associated aneurysm	Eloquent zone	SPM score	Time to disappear (months)	Angiographic follow up (months)	Follw up (months)
1	6 mm	Right MCA and ACA	Superficial 1 vein	+	+ right motor zone	2	8	12	21
2	2 mm	Right PCA	Superficial 1 vein	-	+ right occipital lobe	2	6	6	12
3	2 mm	Left MCA	Deep 1 vein	-	+ left temporal posterior lobe	3	36	84	84
4	16 mm	Left PCA	Superficial 2 veins	-	+ left occipital lobe	2	6	18	18

PCA : Posterior Cerebral Artery, ACA : Anterior Cerebral Artery, MCA : Middle Cerebral Artery. SPM Score: Spetzler and Martin Score

Figure 1. Case 4 angiography.A : May 2016. 16 mm nidus, feeding artery : Cerebral Posterior Artery, superficial drainage. B November 2017 : no nidus left



A. Angiography featuring small nidus, feeding through Posterior Cerebral Artery and superficial drainage.



B. Angiography showing BVAM disappearance.