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Case Report

Spontaneous regression of a thrombosed cerebral arteriovenous malformation in a patient with a prothrombotic state associated with multiple myeloma: A case report and literature review

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ABSTRACT

Background: Cerebral arteriovenous malformations (AVMs) are pathologic communications between veins and arteries of the brain vasculature. Its spontaneous regression is rare, and many factors have been described in the effort to explain this phenomenon, including a hypercoagulable state.

Case Description: We present the case of a spontaneous unruptured AVM regression in a patient where thrombosis of the malformation was found, probably due to a prothrombotic state associated with multiple myeloma (MM).

Conclusion: We aim to contribute to the study of this rare phenomenon, presenting the relationship between a hypercoagulable state caused by MM and the spontaneous AVM regression that has not been previously reported.

Keywords: Cerebral arteriovenous malformation, Multiple myeloma, Prothrombotic state, Spontaneous regression, Vascular neurosurgery

INTRODUCTION

Spontaneous and complete regression of a cerebral arteriovenous malformation (AVM) is an infrequent but well-recognized event, with an estimated prevalence of 0.5–1.3%.[1,7,17] In 70% of such cases, the cerebral AVM occludes after symptomatic intracerebral or subarachnoid hemorrhage by compression of the afferent and efferent vessels by the presence of bleeding.[1,12,16] On the other hand, spontaneous regression of an unruptured cerebral AVM is an even rarer and poorly understood phenomenon, being AVM spontaneous thrombosis the postulated mechanism.[1,14,17]

CASE REPORT

A 49-year-old male was diagnosed in May 2014 with a spontaneous deep venous thrombosis (DVT). Then, treatment with apixaban at a dose of 5 mg twice daily was initiated, suspended

3 months later due to an episode of gastrointestinal bleeding. In September 2014, after a severe headache, an MRI was performed showing a right occipital AVM Spetzler-Martin grade II. Its afferent vessel was the posterior cerebral artery and venous drainage through the right transverse and straight sinus. In November 2014, he was diagnosed with multiple myeloma (MM) IgG kappa, ISS III, and IIIB Durie-Salmon. He received chemotherapy based on 15 cycles of 28 days each with thalidomide 100 mg/day, cyclophosphamide 50 mg/day, dexamethasone 20 mg weekly (ThaCyDex), and one dose of 4 mg zoledronic acid. Evolution was favorable with complete remission in the following months and protocol for autologous bone marrow transplant was started.

In September 2015, the patient had partial seizures with visual hallucinations, clonic movements of the left limbs, cephalic and eye left version, and secondary generalization. A neurological examination documented left homonymous hemianopia. Nonenhanced head CT scan showed a hyperdense serpentigenous trace in the right parieto-occipital region, with a hypodensity adjacent to this area and without evidence of hemorrhage. An MRI was performed 4 days later and found the same serpentigenous paths shown in the CT scan [Figure 1]. A cerebral angiography 20 days postevent, the AVM was no longer observed [Figure 2]. When discharged from the hospital, the patient did not have any additional neurological deficit.

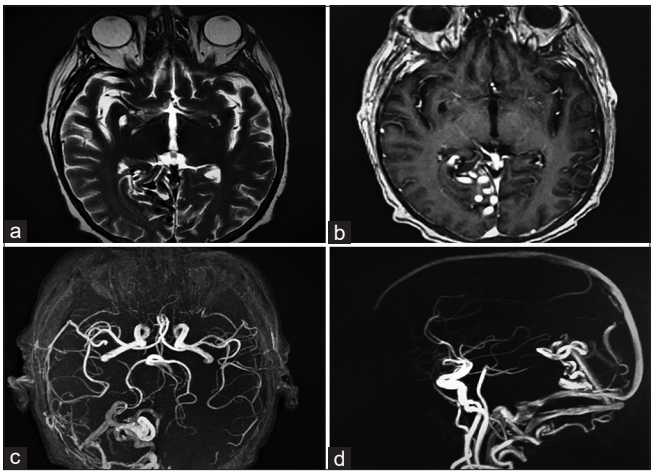

Figure 1: MRI where we observed a serpentigenous path of the arteriovenous malformation at the parieto-occipital region. (a) Axial T2-weighted sequence. (b) Axial T2-FLAIR sequence. (c) Axial 3D TOF. (d) Sagittal 3D TOF.

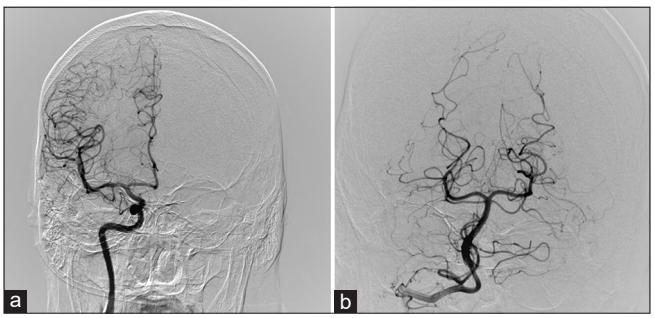

Figure 2: Cerebral angiography 20 days postevent showing arteriovenous malformation (AVM) regression. (a) Right internal carotid artery angiogram. (b) Posterior circulation angiogram, without any evidence of AVM.

DISCUSSION

The case report illustrates the spontaneous and complete thrombosis of an unruptured cerebral AVM due to a prothrombotic state in a patient with MM. This association is not reported. Multiple theories have been proposed to explain the spontaneous regression of unruptured cerebral AVMs. The main factors postulated include the presence of intravascular turbulence and tortuous venous drainage, single drainage vein and/or single afferent artery, superficial location, small and medium size, and a probable hypercoagulable state.[1,2,7,14,15,17,18]

We carried out a literature review of cases of unruptured cerebral AVMs, which showed spontaneous regression without evidence of bleeding or intervention of any kind before obliteration.[1,2,5-7,9-12,14-19] We found a total of 16 patients, including the present case, with angiographically documented spontaneous regression [Table 1]. Clinical presentation was seizures in 68.7% and headache in 25%; only one patient was asymptomatic and discovered incidentally. The minimum and maximum age at diagnosis were 14 and 67 years, respectively, with a higher incidence in males (75%) than females (25%). Supratentorial was the prevalent location. AVMs <3 cm represented 62.5%, between 3 and 6 cm were 31.2%, and only one large malformation was found. A unique afferent artery was present in 31.2% and unique venous drainage in 37.5% of the patients. The most common feeding artery was the middle cerebral artery with 62.5%, and the superior sagittal sinus drainage was prevalent with 43.7%. Only one patient had a simultaneous appearance of a low-grade glioma adjacent to a malformation. It is noteworthy that afferent and vascular efference data were incomplete due to the lack of reported data. As shown in the table, only 3 cases (18.7%), including our case, have well-documented evidence that thrombosis of the unruptured AVMs has occurred.

Abdulrauf *et al.* had a 56-year-old patient with an occipital cerebral AVM that suffered thrombosis and later surgical excised with histological confirmation.[1] Sawlani *et al.* had a 44-year-old patient with a parieto-occipital cerebral AVM with an MRI that proved thrombosis.[18]

In the present case, it is evident that the patient carried a prothrombotic state associated with MM; indeed, he had a DVT and was receiving apixaban when he developed

Table 1: Literature review of unruptured cerebral AVM cases showing spontaneous regression.

Literature reports	Age/gender	CP	Lobe/side	Size	AF	UAF	VD	UVD
Lee *et al*., 2002[7]	36/M	Headache	Parietal/NA	M	MCA, ACA	(−)	SSS, SS	(−)
Patel *et al*., 2001[17]	42/M	Seizures	Parietal/Right	M	NA	(+)	NA	(+)
Abdulrauf *et al*., 1999[1]	56/F	Headache	Occipital/right	M	MCA	(+)	NA	(+)
Pasqualin *et al*., 1985[16]	41/M	Seizures	Frontal/left	L	ACA, MCA	(−)	SSS	NA
Omojola *et al*., 1982[12]	15/F	Seizures	Parietal/right	S	AChA	(+)	V. Galen	(+)
Panciani *et al*., 2008[14]	65/M	Headache	Cerebellar/left	S	PiCA, SCA	(−)	Petrous sinus	(−)
Cao *et al*., 2015[2]	31/M	Headache	Parietal/left	S	ACA	(−)	NA	NA
Pascual *et al*., 2007[15]	65/M	Headache	Occipital/right	S	PCA, CEA	(−)	SSS	(+)
Sawlani *et al*., 2004[18]	44/M	Seizures	Occipital/right	S	MCA, PCA	(−)	SSS	(−)
Nehls and Pittman, 1982[11]	59/M	Headache	Parietal/right	S	MCA	(+)	SSS	(+)
Megison *et al*., 1989[10]	25/M	Seizures	Temporal/left	S	MCA	(+)	V. Labbè	(+)
Marconi *et al*., 1993[9]	42/M	Seizures	Frontal/left	M	MCA, ACA	(−)	NA	NA
Hamada and Yonekawa, 1994[5]	14/F	Asymptomatic	Thalamus/left	M	PChA	(−)	SSV	(+)
Krapf *et al*., 2001[6]	62/M	Seizures	Parietal/right	S	MCA	(−)	SSS	(−)
Schwartz *et al*., 2002[19]	67/M	Seizures	Parietal/right	S	ACA, MCA	(−)	NA	NA
Present case, 2021	49/M	Seizures	Occipital/left	S	ACP	NA	ST, SR	NA

M: Male, F: Female, CP: Clinical presentation, AF: Arterial feeder, UAF: Unique arterial feeder, VD: Venous drainage, UVD: Unique venous drainage, AChA: Anterior choroidal artery, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, PCA: Posterior cerebral artery, CEA: Carotid external artery, PiCA: Posteroinferior cerebellar artery, SuCA: Superior cerebellar artery, SSS: Superior sagittal sinus, SS: Straight sinus: IPS: Inferior petrosal sinus, SSV: Superficial Sylvian veins, S: Small, M: Medium, L: Large, NA: Information not available

the neurological disorder. MM is an oncologic pathology associated with venous and arterial thrombosis, especially in extremities and, in rare cases, pulmonary and cerebral thrombosis.[3] There is an increased risk in patients with monoclonal gammopathy IgG or IgA and patients treated with immunomodulators. Furthermore, using thalidomide or lenalidomide induces thrombosis in 2–4%, it increases up to 12–26% with the use of dexamethasone (higher with high doses) increases up to 16–34% in multiple therapies.[3] Lenz and Saver reported a 74-year-old woman diagnosed with MM of 11 years of evolution in treatment with thalidomide 50 mg/day who developed thrombosis of the left internal jugular vein, internal cerebral veins, and straight sinus associated with bilateral thalamic venous infarcts.[8] Ortín *et al*. described a 45-year-old diagnosed with MM, treated with multiple chemotherapies including thalidomide, who had a stroke involving the intracranial internal carotid artery.[13] Eudo *et al*. reported an 83-year-old diagnosed with IgG kappa MM, treated initially with prednisolone and thalidomide, and then switched to lenalidomide and dexamethasone. A brain CT demonstrated thrombosis of the left sigmoid sinus and the left internal jugular vein.[4]

CONCLUSION

The relevance of this paper relies on the relationship we describe between the prothrombotic state in a patient with MM and the spontaneous regression of a thrombosed AVM. With this, we hope to contribute to the study of the pathophysiology that can explain this phenomenon in a more precise manner. More studies are needed on the subject, but as far as we are aware, we are the first to expose this relationship between a prothrombotic state, like the one seen in MM, and the spontaneous regression of an AVM, contributing to the understanding of these uncommon but interesting phenomena.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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