Cerebrovascular Diseases Extra

Case Report

Cerebrovasc Dis Extra 2022;12:116–121
DOI: 10.1159/000525598

Received: February 23, 2022
Accepted: April 8, 2022
Published online: August 10, 2022

Subarachnoid and Intraventricular Hemorrhage in a Patient with a Pure Arterial Malformation and Two Associated Aneurysms in the Posterior Inferior Cerebellar Artery: A Case Report and Literature Review

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Keywords
Pure arterial malformation · Subarachnoid hemorrhage · Intraventricular hemorrhage

Abstract
Introduction: Pure arterial malformations (PAMs) are rare vascular abnormalities defined as dilated, tortuous arterial loops without any associated venous compartment. PAMs are thought to be benign developmental anomalies that can be safely managed conservatively. ***Methods:*** We present a case of life-threatening hemorrhage in a patient with a PAM associated with two aneurysms and review the literature describing hemorrhages associated with PAMs. ***Results:*** A 65-year-old female presented with subarachnoid and intraventricular hemorrhage. A digital subtraction angiography revealed a posterior inferior cerebellar artery PAM associated with two saccular aneurysms, which were subsequently microsurgically clipped. At the 1-year follow-up, the patient was neurologically intact. In our literature review, we identified 21 papers describing a total of 37 PAMs. Patients were predominantly female (64.9%) and their median age was 35 years. Almost half (48.6%) of PAMs were associated with aneurysms. In the group of PAMs that were not associated with an aneurysm, the intracranial hemorrhage rate was 15.8%, while in cases of coexisting PAM and aneurysm it was 44.4% ($p = 0.0789$). ***Conclusions:*** PAM natural history remains unknown, particularly in cases of coexistence with aneurysms. Patients so affected require careful observation. The description of PAMs as benign vascular malformations should be revised. Surgical management of hemorrhagic PAMs coexisting with aneurysms is possible and should be considered.

Introduction

Pure arterial malformations (PAMs) are rare vascular abnormalities defined as dilated, tortuous arterial loops (or a mass of arterial loops) without any associated venous compartment [1, 2]. PAMs are typically described as benign developmental anomalies that can be safely managed conservatively, with no risk of intracranial hemorrhage [2, 3]. Here, we present a case of life-threatening subarachnoid and intraventricular hemorrhage in a patient with a posterior inferior cerebellar artery (PICA) PAM associated with two aneurysms. Additionally, we review the literature describing hemorrhages associated with PAMs, with special emphasis on PAMs in conjunction with cerebral aneurysms.

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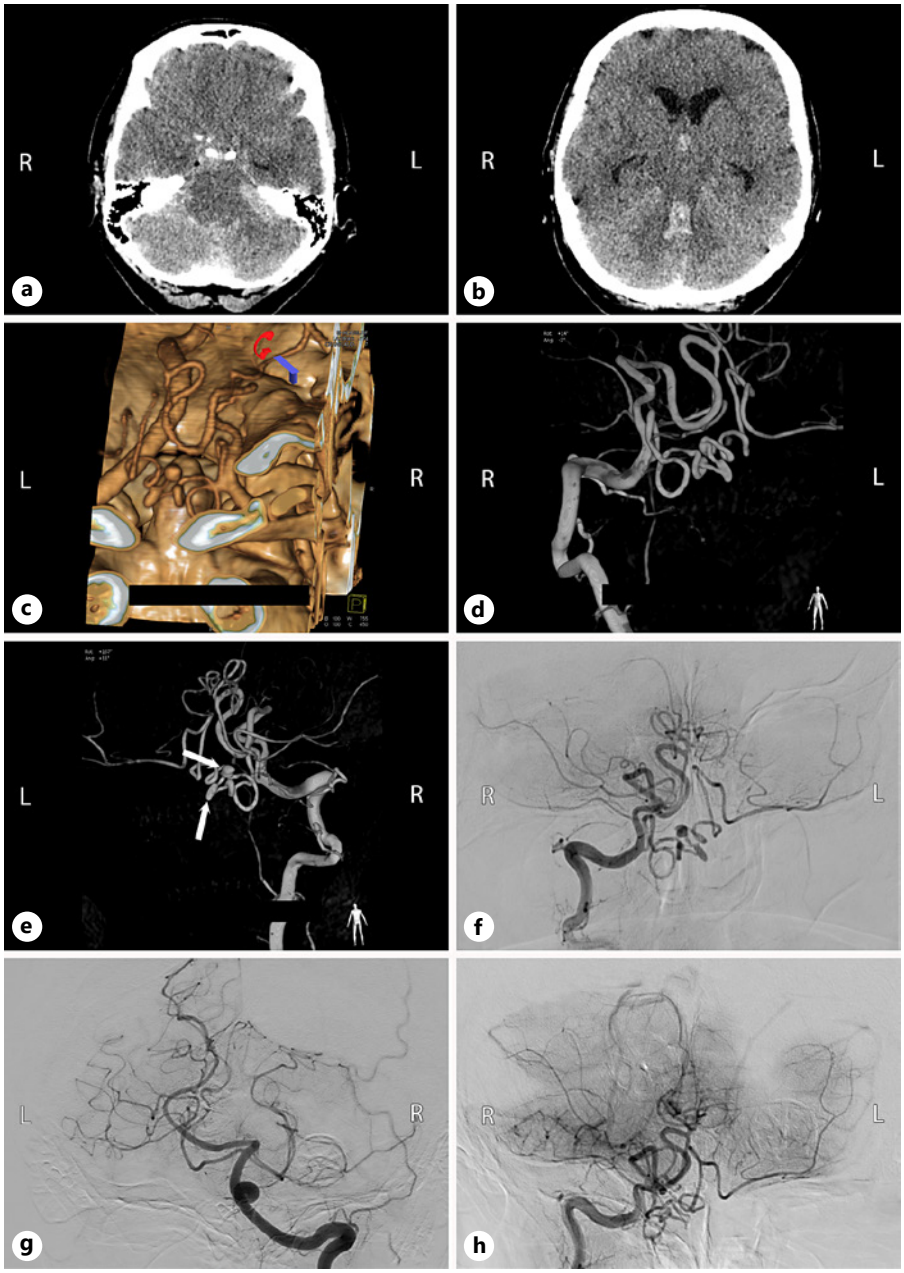

Fig. 1. Images of described patient. A non-enhanced head CT shows subarachnoid (**a**) and intraventricular (**b**) hemorrhage. A CTA (**c**) shows a vascular malformation with characteristics similar to PAM. **d–f** DSA reveals right PICA PAM associated with 2 aneurysms (arrows). **g**, **h** A 1-year follow-up image shows a stable PAM, no aneurysms, and an anatomical variant of the left PICA originating from the right vertebral artery. CT, computed tomography; CTA, computed tomography angiography; DSA, digital subtraction angiography; L, left side; PAM, pure arterial malformation; PICA, posterior inferior cerebellar artery; R, right side.

Results

A 65-year-old woman was admitted to our department after a sudden and severe headache a few days earlier. At admission, she was conscious, dozy, opened her eyes upon request, and whispered with basic verbal contact (Glasgow Coma Scale [GCS] 14, World Federation of Neurological Surgeons [WFNS] grade II), with no other neurological deficits. A non-enhanced brain computed tomography (CT) scan revealed diffuse and thick subarachnoid and intraventricular hemorrhage (Fig. 1a, b). A CT angiography (CTA) study raised suspicion of a PICA aneurysm (Fig. 1c). The patient consequently underwent cerebral digital subtraction angiography (DSA), which revealed a PICA PAM associated with two saccular aneurysms (Fig. 1d–f). Additionally, DSA uncovered an anatomical variant of the left PICA originating from the right vertebral artery (VA), below the right PICA that was a terminal branch of the right VA. Due to the presence and location of the aneurysms, the patient was scheduled

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Table 1. Literature review of PAM cases published after 1995 [1–21]

Author, year	Cases, *n*	Age, sex	Presentation	Intracranial hemorrhage	PAM location	Aneurysm	Aneurysm location	Treatment
Doran et al., 1995 [4]	1	14 F	Probable partial complex seizures	No	bilat ACAs	No	N/A	None
Vanslambrouk et al., 2000 [5]	1	5 M	Minimal right hemiparesis	No	L PCA	No	N/A	None
Uchino et al., 2003 [6]	1	35 F	Sudden, severe H/A	No	R SCA	No	N/A	None
Beringer and Alenghat, 2004 [7]	1	49 M	Intermittent frontal H/A	No	bilat pericallosal	No	N/A	None
McLaughlin et al., 2013 [1]	1	54 F	Acute episode of dizziness	No	L PComA, P2	Yes	L PComA	None
Lanzino et al., 2014 [8]	1	10 F	Short-lasting, left-sided H/A	No	L PComA/PCA	Yes	L PComA/PCA	Coil embo of the pseudoaneurysmal component
McLaughlin et al., 2014 [9]	1	8 F	Isolated H/A	No	L ICA C6, M1 MCA	Yes	L ICA C6	None
Feliciano et al., 2014 [10]	1	42 M	Severe and sudden H/A, left-sided weakness	Yes, right basal ganglia	R MCA	Yes	R small medial lenticulostriate	None
Sako et al., 2016 [11]	1	35 M	Vertigo	No	L dist PICA	No	N/A	None
Silva et al., 2017 [12]	1	42 F	Worst H/A of life	Yes (SAH)	L PICA, L VA	Yes	L PICA	Resection of the aneurysm, in situ end-to-end anastomosis
Sorenson et al., 2018 [3]	1	17 F	Migraines with aura	No	R PICA	No	N/A	None
Brinjiki et al., 2018 [2]	12	10 F, 19 F, 27 F, 25 F, 25 F, 34 F, 38 F, 11 M, 17 M, 47 F, 35 F, 20 F	Multiple	No	multiple	Yes, 4/12	multiple	None
Rosalind et al., 2018 [13]	1	45 F	SAH	Yes (SAH)	PCA	Yes	PCA	Clipping
Munich et al., 2019 [14]	1	37 F	H/A, blurry vision, partial L CN3 palsy	Yes	P1 PCA	Yes	PCA	Surg – clipping
Yue et al., 2019 [15]	1	45 M	H/A, dizziness, gait instability, bilateral papilledema	No	R ACA	Yes	ACA	Surg
Li et al., 2020 [16]	1	77 M	Sudden-onset H/A, nausea, confusion	Yes (SAH)	L VA	Yes	L AICA	Surg – trapping
Liu et al., 2020 [17]	3	36 F, 24 F, 53 M	H/A, occasional dizziness, left limb numbness	1 out of 3	L PComA, R ICA, L PComA	1 out of 3	L PComA (+moya moya syndrome on that side)	Sten + coil
Chua et al., 2021 [18]	1	38 M	Progressive H/A, nausea	yes (SAH)	R PICA	No	N/A	Onyx embo
Yao et al., 2021 [19]	2	51 M, 49 M	Severe H/A (both)	Yes	L PICA, L VA	Yes, in both cases		Surg
Iwaki et al., 2021 [20]	1	15 M	Narrowing of the visual field	No	Rt PComA, PCA	No	N/A	Surgical – clipping PAM
Lu et al., 2021 [21]	2	43 F, 53 F	Intermittent syncope; H/A	1 out of 2	L ICA, R P1 PCA	No	N/A	Bypass; bypass
Present case, 2022	1	65 F	Sudden and severe H/A	Yes	R PICA	Yes	R PICA	Surg – clipping

ACA, anterior cerebral artery; AICA, anterior inferior cerebellar artery; CN3, oculomotor nerve; bilat, bilateral; dist, distal; embo, embolization; H/A, headache; ICA, internal carotid artery; L, left; MCA, middle cerebral artery; N/A, not applicable; PAM, pure arterial malformation; PICA, posterior inferior cerebellar artery; PCA, posterior cerebral artery; PComA, posterior communicating artery; R, right; SAH, subarachnoid hemorrhage; SCA, superior cerebellar artery; surg, surgical; VA, vertebral artery.

to undergo surgery. While awaiting the operation, the patient suddenly deteriorated: she was unconscious with abnormal extension after stimulation (4 GCS, WFNS grade V). The patient was intubated, and brain CT revealed acute hydrocephalus. An urgent external ventricular drainage (EVD) brought clinical improvement of the neurological status. The patient was operated on the following day.

The patient underwent a midline suboccipital craniotomy with C1 laminectomy. The cisterna magna was filled with solid blood clots. Due to the abnormal anatomical variant discovered in the DSA, microsurgical dissection with clot removal was performed from the right side. The right PICA was visualized below the right cerebellar tonsil, just above a loop of the left PICA. Subsequent dissection revealed a tortuous, segmentally dilated course of the PICA up to the tonsillomedullary segment, confirming the PAM. Along the course of the malformation, there were two saccular aneurysms, a finding that was endorsed by intraoperative indocyanine green (ICG) videoangiography. The more distal aneurysm had the appearance of a previous rupture. After dissection, the necks of the aneurysms were ligated with two hockey-stick Yasargil microclips, respectively. Another ICG videoangiography confirmed appropriate flow in the PICA up to its cortical segment and obliteration of the aneurysms. Remaining blood clots were removed from the cisterna magna and subsequently from the IV ventricle, achieving outflow of the cerebrospinal fluid.

During the postoperative period, the EVD was removed and the patient continued to improve neurologically. She was subsequently transferred to the neurology department for neurological rehabilitation. At 1-year follow-up, the patient was neurologically intact and imaging showed a stable PAM and no aneurysms (Fig. 1g, h).

Discussion

Pure Arterial Malformations

PAMs were first described by McLaughlin et al. [1] in 2013. Their most commonly hypothesized etiology is an arterial dysplasia resulting from a congenital defect. Unlike aneurysms or arteriovenous malformations, with which PAMs are commonly mistaken on noninvasive arteriograms, PAMs are believed to have a benign nature [2]. Specifically, PAMs are not believed to cause neurological deficits or intracranial hemorrhages. In opposition to this popular belief, there is a growing literature describing intracranial hemorrhages associated with or caused by PAMs (Table 1). Some of these reports describe surgical or endovascular treatment [14–16, 18, 20]. Irresistibly, these give rise to this question: how can hemorrhages associated with PAMs be explained?

Hemorrhages Associated with Pure Arterial Malformations

One possible explanation is that intracranial hemorrhages associated with PAMs are, in fact, caused by a different, coexisting entity. Indeed, some PAMs described in the literature are accompanied by aneurysms, as presented herein (Table 1) [14–16, 19]. PAM hemodynamics may promote the formation of aneurysms by establishing a sequence of cause (hemodynamic aneurysm formation) and effect (intracranial hemorrhage). Correspondingly, Xia et al. [22] have advocated for close clinical and radiological follow-up with DSAs and MRIs, as in some of the PAMs there may be aneurysm formation. A prototypical example of the radiological and clinical evolution of a PAM to form an aneurysm was described by Yue et al. [15].

Alternatively, PAMs would need to be recognized as malformations that do not have a benign nature and may indeed cause intracranial hemorrhage. In that spirit, Chua et al. [18] described a "ruptured PAM" that was treated with Onyx.

Long-Term Follow-Up

In either scenario, in the future more careful observation of patients diagnosed with PAMs should be considered by clinicians and researchers, particularly when the PAM coexists with an aneurysm. To better understand the relationship of these entities, reports of long-term observations are necessary.

Indications for Treatment

As of now, what remains certain about PAMs is that these malformations are poorly understood and require thorough studies. The dogma of the benign nature of PAMs should be further questioned. On that account, we believe that treatment should be considered for PAMs associated with intracranial aneurysms (IAs) due to their unknown natural history – specifically the risk of rupture of IAs – and the growing number of reports of subarachnoid hemorrhage (SAH). As elaborated further in the text, the risk of intracranial hemorrhage in case of coexistence may be as high as 44.4%. Microsurgery is a reasonable option in treating these cases, as endovascular access through tortuous vessels is, by virtue of the definition of PAM, significantly restricted. Moreover, associated IAs

often have wide necks that further impede successful embolization. Furthermore, regardless of the coexistence of IAs, we believe that all hemorrhagic and symptomatic PAMs require treatment. Proximal occlusion of PAMs, combined with a bypass, is an encouraging, hypothetically permanent, method of treatment [23].

Diagnostic Criteria

There also is a need for clear, unequivocal criteria for diagnosing PAMs. Since their introduction, there have been published discussions in which one research team claimed to have reported a PAM, while another argued that the reported malformation was not a PAM, and vice-versa. Lanterna et al. [24], in their letter to the editor, reported a PAM case, to which McLaughlin et al. [9] responded that PAM diagnosis could not be definitively established in the described patient. Similarly, Brinjikji and Lanzino responded to Lai and Patel's [25] 2 cases, stating that they do not "believe that the lesions described in the letter were pure arterial malformations but, rather, acutely ruptured dissecting aneurysms." Additionally, Jia et al. [28] refused to diagnose PAMs (as suggested to them by Brinjikji and Lanzino [26]), in place of segmental dolichoectasia of the internal carotid artery.

McLaughlin et al. [9], in their response to a letter to the editor, suggested establishing PAM diagnosis via (1) DSA with a 6-s frame and (2) 3D angiogram, with which we fully agree [24]. What is more, a helpful guide was published recently by Oushy et al. [27] Consequently, a report by Sako et al. [11] on diagnosing PAM without DSA should be treated as an exception or casuistry.

Literature Review

We performed a literature review of PAM cases published after 1995 and included articles with unambiguous PAM diagnosis (e.g., availability of a high-quality imaging). A rationale for doing so was that some cases (particularly these published prior to the formal introduction of PAM as a distinct entity in 2013 [1]) presented different types of intracranial arterial vasculopathies than PAMs (for instance dilatative arteriopathies vel dolichoectasias, arterial dissections, or developmental arterial anomalies vel arterial vascular dysplasia) or the diagnostic imaging was not good enough to confirm a diagnosis of PAM.

In our literature review, including our case, we identified 21 papers describing in total 37 PAMs, with female sex predominance (64.9%) and a median age of 35 years (Table 1). Several authors before have already presented literature reviews of PAMs, with similar demographic findings [15, 17, 20, 21]. Almost one half (48.6%, 18/37) of PAMs were associated with aneurysms, 21 in total (1 case with 2 aneurysms, 1 with 3). In the group of PAMs that were not associated with an aneurysm, there were only 3 reports of intracranial hemorrhage (15.8%, 3/19), while in case of coexistence, intracranial hemorrhage incidence was 44.4% (8/18). The association between presence of an aneurysm and intracranial hemorrhage was determined with Fisher's exact test and not considered to be statistically significant, with $p = 0.0789$. The total incidence of intracranial hemorrhages was 29.7% (11/37). Of patients presenting with an intracranial hemorrhage, 72.7% (8/11) also had an aneurysm.

The published cases considered in our literature review reflect a reporting bias due to the fact that researchers are more likely to describe unusual cases. Additionally, PAMs coexisting with an intracranial hemorrhage, regardless of their association, are more likely to be discovered than are asymptomatic cases.

Conclusions

PAMs are rare intracranial vascular malformations that may be solitary or associated with aneurysms. PAM natural history remains unknown, particularly in cases of coexistence with aneurysms. Such patients require careful observation. Additionally, there are a growing number of reports of hemorrhagic cases. For that reason, the characterization of PAMs as benign vascular malformations should be revised. Surgical management of hemorrhagic cases of PAMs coexisting with aneurysms is possible and should be considered.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Due to the retrospective nature of the study, the ethics approval was not required in this case report. The study was conducted according to the Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This study was not supported by any funding sources.

Author Contributions

Katarzyna Wójtowicz: conceptualization, methodology, and literature review supervision, Łukasz Przepiórka: manuscript preparation, literature review preparation, and project administration, Przemysław Kunert: project supervision, literature review edition, manuscript review, and final approval, Andrzej Marchel: case description, manuscript review, and final approval. All the authors have read and agreed for publication of the current version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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