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Case Report

Diffuse idiopathic intracranial fusiform aneurysm development. Case report and literature review

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Abstract

Background: Fusiform intracranial aneurysms (FIAs) are uncommon lesions representing less than 15% of all intracranial aneurysms in most large series. Their etiology has been linked to a variety of causes including atherosclerosis, fibromuscular dysplasia, cystic medial necrosis, connective tissue disease, hypertension, diabetes, hyperlipidemia, infection, cardiac myxoma, oral contraceptive use, vasculitis, and lymphoproliferative disorders. The finding of numerous lesions in a single patient is distinctly uncommon.

Case Description: We describe the unique case of a 47-year-old female who developed multiple FIAs over a 6-year period without an obvious underlying pathology. The patient's medical history was significant for obesity, migraine headaches, insomnia, breast cancer, and chronic skin rash. Various diagnoses were explored including infectious etiologies, autoimmune vasculopathies, malignancy-related causes, connective tissue disorders, and underlying genetic conditions. However, all investigations, including aneurysm wall and skin biopsies were negative or deemed noncontributory toward making a definitive diagnosis.

Conclusion: We report an unusual case of a patient with a normal cerebral angiogram developing numerous, FIAs without obvious underlying etiology over a 6-year period. Close clinical and radiological follow-up is recommended in this case because the natural history of the disease is unclear at this point. The literature regarding potential causes of multiple fusiform intracranial aneuryms is reviewed.

Key Words: Aneurysm, fusiform, idiopathic

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INTRODUCTION

Fusiform intracranial aneurysms (FIAs) are uncommon lesions representing less than 15% of all intracranial aneurysms in most large series.[5,12] Their etiology has been linked to a variety of causes including atherosclerosis, fibromuscular dysplasia, cystic medial necrosis, connective tissue disease, hypertension, diabetes, hyperlipidemia, infection, cardiac myxoma,

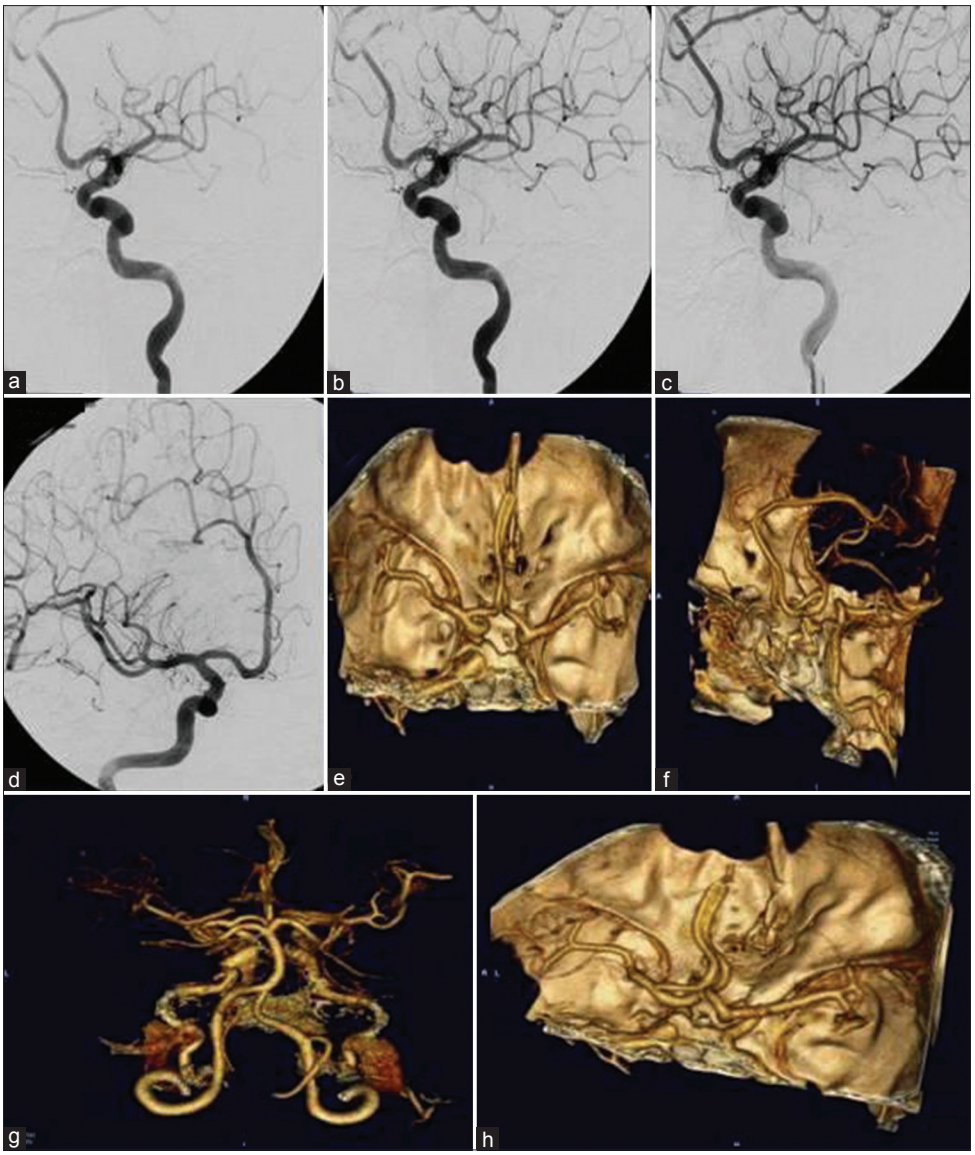

Figure 1: (a-h) Multiple views of a four vessels cerebral angiogram and 3D reconstructions taken 6 years prior to presentation, demonstrating no intracranial aneurysm or significant vascular lesion

and oral contraceptive use.[5,6,12] Multiple lesions are very rare, and may be related to a variety of autosomal dominant syndromes, vasculitis, myxoma, and lymphoproliferative disorders.[1,3,4,6-9,13] Due to selection and referral bias in most series, it is difficult to estimate with accuracy the true incidence of this rare finding.

We describe the unique case of a 47-year-old female who developed multiple FIAs over a 6-year period without an obvious underlying pathology. The patient's medical history was significant for obesity, migraines, insomnia, breast cancer, and chronic skin rash. Various diagnoses were explored including: Infectious etiologies, autoimmune vasculopathy, malignancy-related possibilities, connective tissue disorders, and genetic diseases. However, all investigations, including aneurysm wall and skin biopsies were negative or deemed noncontributory toward making a definitive diagnosis.

CASE REPORT

A 47-year-old female developed confusion, headaches, and questionable seizure like activity. These symptoms prompted an emergency department visit at which time a computed tomography (CT) scan was performed and reported as unremarkable. She was left with a persistent dull headache and generalized weakness. Three weeks later, she developed a new episode of severe headache associated with photophobia, meningismus, nausea, vomiting, and dizziness. Her primary care physician ordered a magnetic resonance imaging (MRI), which showed scattered subarachnoid hemorrhage (SAH)

located principally within the territory of the right middle cerebral artery (MCA).

The patient was promptly admitted to a hospital facility and underwent a computed tomography angiography (CTA), which demonstrated multiple elongated intracranial vascular abnormalities. These lesions involved both hemispheres including the anterior and posterior circulation. Of interest, 6 years prior to admission, she had presented with similar symptoms including the acute onset of severe headache. She had undergone a CT scan, which was reportedly negative, and a lumber puncture, which had demonstrated an elevated red blood cell count. This prompted a cerebral angiogram, which demonstrated normal intracranial vasculature without evidence of an aneurysm or other abnormality [Figure 1].

Past medical history was significant for migraine headaches, hypothyroidism, obesity (status postgastric bypass), and a diagnosis of breast cancer 4 years earlier with lumpectomy and radiation therapy. Family history was explored fully and was noncontributory in this case. In particular, there was no family history of aneurysm, stroke, connective tissue disorder, or other identified genetic issue condition within the family.

The patient was transferred to our facility and underwent catheter angiography, which revealed at least 20 fusiform aneurysms involving bilateral middle, anterior, and posterior cerebral arteries [Figure 2]. The largest aneurysm involved a right M2-M3 posterior division branch and had a roughly 5 mm saccular component, which was felt to have been the most likely source of the SAH.

The differential diagnosis for the dramatic development of multiple FIAs included hyper-IgE-related syndromes, autoimmune-inflammatory or malignancy-induced vasculopathy, connective tissue disease, genetic abnormalities affecting collagen production and structure as well as cardiac myxoma. The patient underwent numerous investigations including MRI [Figure 3], and testing for/of human immunodeficiency virus (HIV), dobutamine stress echocardiogram, Epstein–Barr virus, erythrocyte sedimentation rate, syphilis, C-reactive protein, antinuclear antibodies, antineutrophil cytoplasmic antibody, complement and immunoglobulins testing, skin biopsy, transthoracic and transesophageal echocardiograms. All examinations were unremarkable.

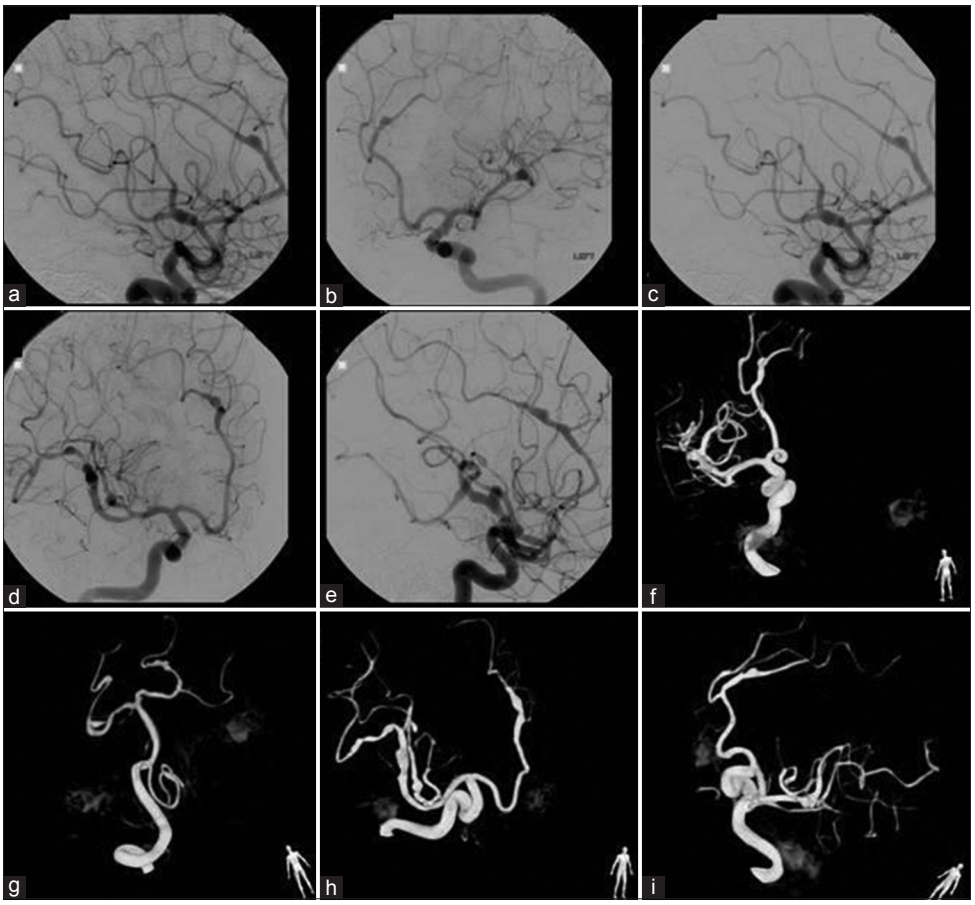

Figure 2: (a-e) Admission angiographic views of the left and right internal carotid arteries demonstrating multiple fusiform aneurysms involving the anterior and posterior divisions of both MCA M2-M3 segments.; (f-i) 3D reconstructions showing multiple fusiform aneurysms affecting all major intracranial arteries

The multiple investigations undertaken in the present case are detailed in Table 1.

The patient underwent microsurgical exploration through an extended right-sided pterional approach with wide splitting of the Sylvian fissure. The saccular component of the large right MCA branch aneurysm was confirmed as the source of bleeding and was clipped successfully [Figure 4]. Multiple nearby fusiform lesions were wrapped and/or clipped, and a fusiform aneurysm of the anterior temporal artery was clipped allowing us to biopsy the "clipped" portion of the aneurysmal wall. Intraoperatively, most of the lesions were white and thickened in appearance, clearly larger than the angiographic appearance due to wall thickening and

Table 1: Investigations performed in patient with multiple fusiform intracranial aneurysms

Investigation	
Blood work	Human immunodeficiency virus (HIV), Epstein-Barr virus, erythrocyte sedimentation rate, syphilis, C-reactive protein, antinuclear antibodies, antineutrophil cytoplasmic antibody, complement and immunoglobulins testing
Cardiac evaluation	Dobutamine stress echocardiogram, transthoracic and transesophageal echocardiograms
Radiological imaging	CT, MRI, MRA, Catheter angiogram
Biopsy	Skin biopsy, direct biopsy of aneurysm wall

CT: Computed tomography, MRI: Magnetic resonance imaging, MRA: Magnetic resonance angiography

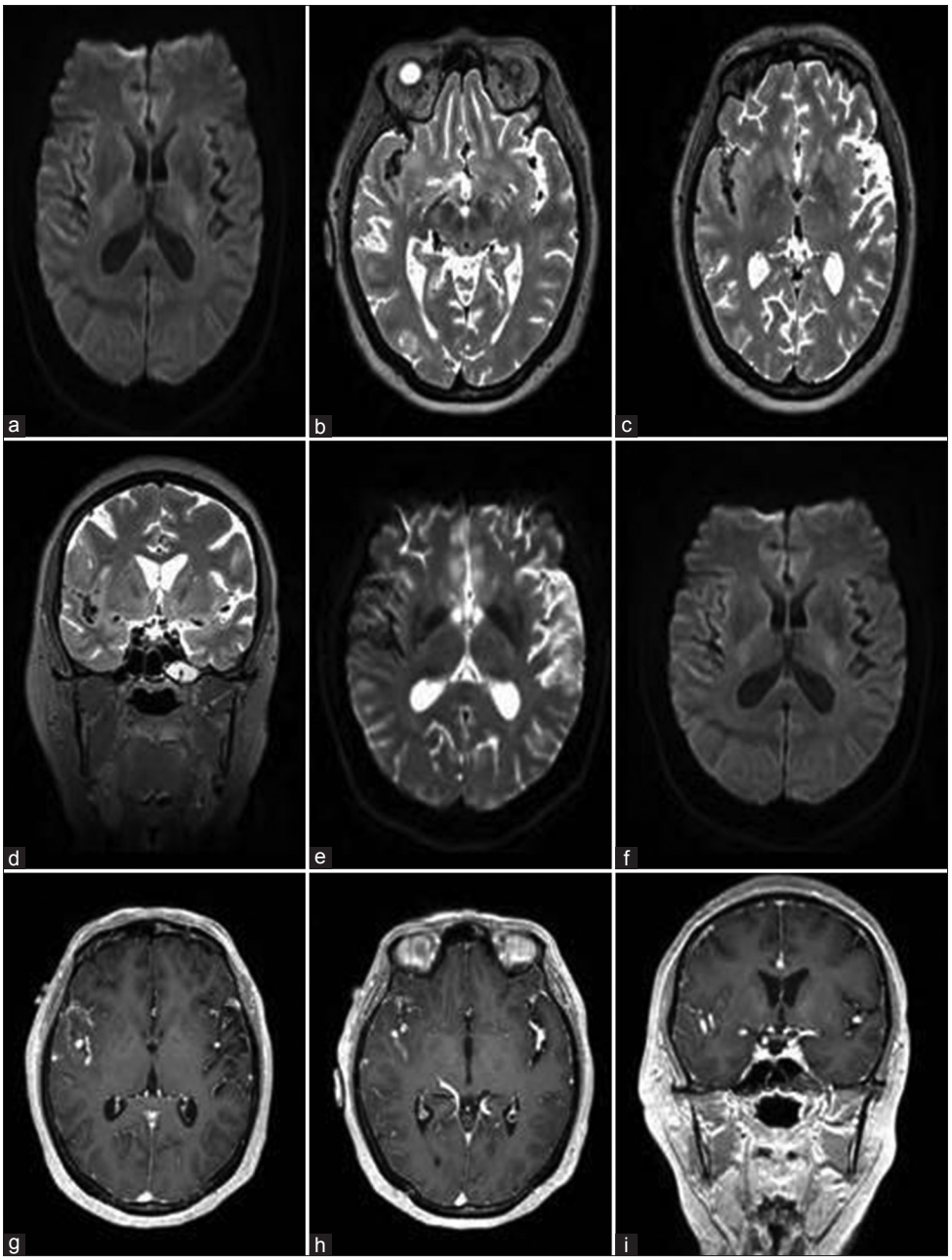

Figure 3: (a-i) Multiple MRI images, T1 and T2, confirming multiple fusiform aneurysm dilatations involving the anterior circulation. Of interest, there is no evidence of ischemic injury on the diffusion-weighted imaging

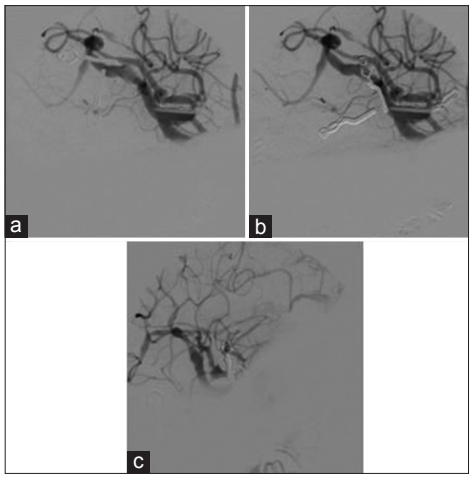

Figure 4: Intraoperative angiography following surgical clippings of the right MCA posterior division (saccular component) and the fusiform dilatation of the anterior temporal artery; showing complete obliteration of the aneurysm without evidence of parent artery compromise

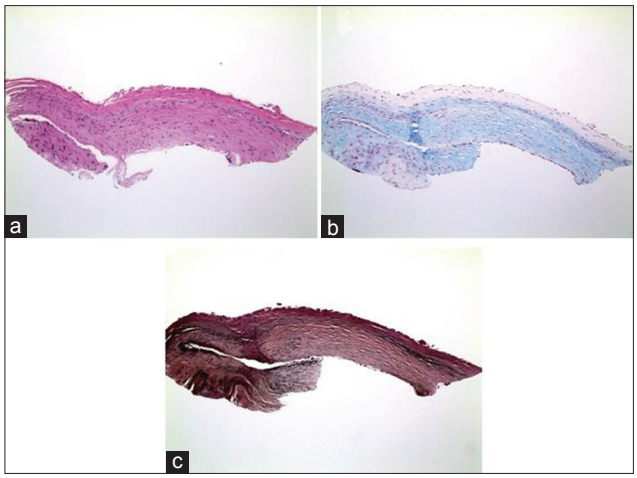

Figure 5: (a) Hematoxylin and eosin. Original magnification ×100. Significant inflammation is absent. Well-developed distinction between intima, media and adventitia is not apparent. (b) Alcian blue (pH 2.5) Original magnification ×100. Alcian blue highlights acid mucosubstances and acetic mucins. Small amounts of staining are normal in blood vessel walls but increases in early lesions of atherosclerosis. The illustrated sample is essentially normal or mildly increased. (c) Verhoeff van Giesen elastic stain. Original magnification ×100. Note that no distinctive internal elastic lamina is visible within the sample

possible internal thrombosis. There were no intraoperative complications, and the patient awoke from surgery without neurological deficit. The biopsy demonstrated nonspecific intimal hyperplasia and all histological biomarkers were negative [Figure 5].

A literature search was performed using both PubMed and Medline search engines. The following word combinations were explored: "intracranial aneurysm", "fusiform", "diffuse", and "idiopathic aneurysm formation".

DISCUSSION

Multiple FIAs are exceedingly rare lesions. Possible etiologies suggested in previously reported cases have included Carney's syndrome, cardiac myxoma, viral infection (mostly due to Epstein–Barr and varicella-zoster), as well as a lymphocytic vasculitis reaction in x-linked lymphoproliferative syndrome.[1-4,6-11,13] Previously reported cases of multiple FIAs and associated medical conditions are detailed in Table 2.

We have previously described a patient with numerous FIAs related to a cardiac myxoma.[6] In these cases, several possible mechanisms have been suggested including: Tumor cells infiltrating cerebral vessels via vasa vasorum with subsequent destruction of the vessel wall, vascular occlusion by tumor material with subsequent scarring and pseudoaneurysm formation, or direct invasion of the tumor cells through the arterial wall.[2] In the case of infectious diseases, the typical pathological findings are medial fibrosis with loss of the muscularis layer associated with destruction of internal elastic lamina and intimal hyperplasia.[1] In our case, the only significant histological finding was intimal hyperplasia, which is a common observation in patients with saccular intracranial aneurysms.

In the case of x-linked lymphoproliferative syndrome (Duncan's syndrome), the immune system is unable to properly combat infection by viral agents such as Epstein–Barr. The characteristic intracranial manifestation is a diffuse necrotizing vasculitis affecting the major arteries, primarily in the vertebrobasilar circulation.[4,7,13] While we initially considered infectious disease a potential cause, all investigations were unremarkable.

Because of a previous history of skin lesions in our patient, a possible diagnosis of autosomal dominant hyper IgE syndrome (AD-HIES) was entertained. This is a primary immune deficiency characterized by the classic triad of recurrent skin boils, cyst-forming pneumonias, and extreme elevations of serum IgE. Vascular abnormalities associated with this syndrome can include tortuosity and aneurysmal dilatation of mid-sized intracranial arteries, with SAH as an infrequent clinical sequela. Other recognized manifestations are eczema, mucocutaneous candidiasis, and several connective tissue and skeletal abnormalities. Both the actual disease and a variant disease-causing mutation were excluded in our patient. A variant of sex-linked lymphocytic necrotizing vasculitis was excluded as well.

CONCLUSION

We report an unusual case of numerous, diffuse FIAs without obvious underlying etiology. The fact that the

Table 2: Previously reported syndromes and diseases associated with fusiform intracranial aneurysm development

Author (year)	Age/sex	Syndromes/diseases	Clinical presentation	Outcome/prognosis
Loeffel *et al.* (1985)	8 years, M	XLP or Duncan disease	EBV infectious mononucleosis	Autopsy revealed necrotizing vasculitis and multiple cerebral aneurysms
Murakami *et al.* (1998)	10 years, F	None	Chronic EBV, VAHS	Death due to respiratory failure. Autopsy confirmed large vessel vasculitis
Dutz *et al.* (2001)	13 months, M	XLP	VAHS, chorioretinitis, bronchiectasis, mononeuritis and respiratory failure	Death at 12 years due to respiratory failure. Autopsy confirmed polyarteritis nodosa
Jean *et al.* (2001)	32 years, F	Left atrial myxoma	Multiple fusiform myxomatous cerebral aneurysms	One of the aneurysm was resected. Patient's condition stable at 8-year follow-up
Ake *et al.* (2006)	29 years, F	AIDS	HIV-associated cerebral aneurysmal arteriopathy	Death as a result of massive SAH
Daugherty *et al.* (2006)	14 years, F	Common variable immunodeficiency with T-cell dysfunction	Varicella angiitis, internal carotid, basilar, and posterior cerebral artery fusiform aneurysms	CT angiogram at 6 months demonstrated stable aneurysms. No ischemic episodes after discharge
Weeks *et al.* (2006)	7 years, M	XLP	EBV encephalitis, CNS lymphoproliferative disease, and lymphoma	Death
Sedat *et al.* (2007)	50 years, F	Left atrial myxoma	Fusiform aneurysms middle, anterior, and posterior cerebral arteries	Asymptomatic at 1-year follow-up
Ryou *et al.* (2008)	27 years, F	Carney complex (triad of myxoma, mucocutaneous pigmentation, and endocrine overactivity)	Multiple fusiform myxomatous cerebral aneurysms	Asymptomatic and stable aneurysms, 10 years follow-up period
Jaworska *et al.* (2012)	55 years, M	Chronic heart failure, chronic kidney disease, and hypertension	Multiple fusiform mirror-image aneurysms	Patient transferred to other hospital
Santillan *et al.* (2012)	68 years, F	Left atrial myxoma	Fusiform dilatation bilateral anterior and middle cerebral arteries	Annual follow-up magnetic resonance angiography stable

XLP: X linked lymphoproliferative syndrome, EBV: Epstein-Barr virus, VAHS: Virus associated hemophagocytic syndrome, SAH: Subarachnoid hemorrhage, CNS: Central nervous system

patient had a normal cerebral arteriogram just 6 years earlier further adds to the unusual nature of the case. Close clinical and radiological follow-up is recommended in this case because the natural history of the disease is unclear at this point in time.

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