Cerebral Aneurysms due to Cardiac Myxoma

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ABSTRACT

Cerebral aneurysms due to cardiac myxoma has been sporadically reported; however, the clinical features of this entity has not been fully elucidated. This meta-analysis was conducted to determine the reported clinical features and outcomes of this condition. It revealed a predominance of cardiac myxoma-related multiple fusiform aneurysms of the middle cerebral artery. The cerebral aneurysms developed at a mean of 53 months after cardiac myxoma resection. Left atrial myoxma was the most common causing cerebral aneurysm than a myxoma arising from any other sites of the heart. Most patients with myxoma-related cerebral aneurysms were under follow-up, conservative, or surgical treatments. Patients' outcomes were promising, with 69.4% (34/49) patients being stable. The overall mortality rate was 4.1% (2/49), and long-term survival seemed to be satisfactory. Cardiac myxoma resection cannot avoid the occurrence of cerebral aneurysm; therefore, cerebroimaging monitoring is recommended even after cardiac myxoma resection.

Key Words: *Intracranial aneurysm, Heart neoplasms, Endovascular procedures.*

INTRODUCTION

Cerebral embolism of cardiac myxoma is a rare cause of cerebral infarction, intracranial hemorrhage, intra-parenchymal metastases and intracranial aneurysmal formation.[1] Cerebral aneurysms are late complications of cardiac myxoma and can cause typical neurological manifestations.[2] The incidence of myxoma-related cerebral aneurysms was reported to be 2-29%.[3] Tamuleviciute *et al*. reviewed two separate databases of atrial myxoma and cerebral aneurysms, and found only one patient developed atrial myxoma-related intracranial aneurysms, accounting for 0.04% (1/2246) patients with atrial myxoma and 0.03% (1/3045) patients with intracranial aneurysms.[4] Sabolek *et al*. summarised the information of 34 patients with myxoma-related cerebral aneurysm;[5] 97% patients had an onset symptom of emboli, implying a relation between myxoma emboli and risk of cerebral aneurysmal formation.

Cerebral aneurysms are usually fusiform, multiple, and located at distal bifurcations of cerebral vessels.[6] The mechanism of myxoma-related cerebral aneurysms is considered a result of disrupted myxoma emboli and consequent vessel wall weakening.[7] Because the disruption of myxoma emboli to cerebral vessels is a slow course, neurological symptoms often present and cerebral aneurysms are found until several years after cardiac myxoma resection.[8]

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Due to rarity of the disorder, clinical features, particularly management policies and patients' prognosis remain unknown. This review was conducted to describe the clinical features and outcomes of this entity.

METHODOLOGY

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement guidelines were followed in this meta-analysis.[9] Articles published between 2000-2017 were systematically searched in the PubMed, Highwire Press, and the Cochrane Library databases. The MeSH terms and keywords used to identify articles included cardiac/atrial/left atrial/biatrial/ventricular myxoma and cerebral/anterior cerebral artery (ACA)/middle cerebral artery (MCA)/posterior cerebral artery (PCA)/posterior inferior cerebellar artery (PICA) aneurysm. Bibliographic references were tracked for completeness of literature retrieval.

All studies, abstracts and citations were carefully reviewed. Full texts of articles, likely to fulfill eligibility criteria, were obtained and assessed. Inclusion criteria were studies including patients with cardiac myxoma who had developed cerebral aneurysms due to cardiac myxoma. Sixty-one articles were found related to the topic and keywords in the literature search; and 50 articles, which met the inclusion and exclusion criteria during preliminary assessment, were included in the review. The exclusion criteria were irrelevant design (n=3), editorials or review article with no patient information (n=2), cerebral aneurysms caused by cardiac myxosarcoma or other etiologies (n=3), cardiac myxoma induced intracranial and visceral arterial embolization (n=1), cerebral cavernous malformations (n=1), and non-aneurysmal hemorrhage (n=1).

The data independently extracted from each study were study population, demographics, clinical features of cardiac myxomas and cerebral aneurysms, comorbidities, treatment, follow-up length and patients' outcomes.

Quantitative data were presented as mean ±standard deviation and were compared by independent sample t-test. The categorical variables expressed by frequency with percentage n (%), and were compared by Fisher's exact test. The statistical analyses were made by using SPSS software version 22.0 and p <0.05 was considered statistically significant.

RESULTS

A total of 50 reports,[1-5,7,10-53] were collected with 63 patients recruited into this study. There were 44 (72.1%) females and 17 (27.9%) males, with a female gender predominance (χ^2=23.9, p<0.001) (In 2 patients, gender was unknown). Patients were at the age of 43.8 ±17.1 years (n=62). There was no significant difference between the male and female patients (42.7 ±17.9 years *versus* 44.1 ±16.4 years, p=0.778).

In 58 patients, 127 presenting symptoms were described. Headache was the most common symptom accounting for 14.9% (19/127), followed by weakness (9.4%, 12/127), vision disturbance (7.9%, 10/127) and dizziness (7.1%, 9/127).

In 12 patients, the onset symptoms were sudden or acute; while in another 12 patients, the onset time was 8.4 ±13.4 months (range, 1 hour-3 years; median, 18 days, n=12).

The arising sites of the cardiac myxomas were the left atrium (63.5%, 40/63), atria (unspecified) (20.6%, 13/63), heart (unspecified) (11.1%, 7/63), biatria (1.6%, 1/63), left atrium and left ventricle (1.6%, 1/63), and left ventricle (1.6%, 1/63). Left atrial myxoma was the most common, causing cerebral aneurysm, than a myxoma arising from any other sites of the heart (χ^2=132.5, p<0.001).

The singularity or multiplicity of the cardiac myxomas was described in 49 patients, while it was not described for this purpose in 14 cases. The cardiac myxomas were solitary in 47 (95.9%) and multiple in two (4.3%) patients. The maximal dimensions of cardiac myxomas were 44.9 ±13.9 mm (n=20). Cardiac myxomas in 4 (6.3%) patients were recurrent.

Twenty (31.7%) patients had cerebral hemorrhages with four microhemorrhages and three subarachnoid hemorrhages. The obvious cerebral hemorrhages usually represented cerebral aneurysmal ruptures. Twenty-four (38.1%) patients had signs of brain infarctions: acute infarctions in 19 (79.2%); old infarctions in three (12.5%); and both acute and old infarctions in two (8.3%) patients.

The aneurysmal arteries were described in 46 patients, the MCA branches were the most commonly affected (Table I). The shapes of aneurysms were described in 50 patients, and most of the aneurysms were fusiform-shaped (Table II). In 55 (87.3%) patients, the singularity/multiplicity was described: solitary in 11 (20%) patients; and multiple in 44 (80%) patients. In 14 (22.2%) patients, the size of the aneurysm was reported, and it was 6.1 ±3.2 mm (n=14).

Table I: Cerebral arteries with aneurysmal formation in 46 patients.

Cerebral artery with aneurysmal formation	n (%)
Middle cerebral artery	39 (84.7)
Anterior cerebral artery	16 (34.8)
Posterior cerebral artery	15 (32.6)
Internal carotid artery	7 (15.2)
Posterior inferior cerebellar artery	5 (10.9)
Basilar artery	2 (4.3)
Superior cerebellar arteries	2 (4.3)
Vertebral artery	2 (4.3)
Vertebrobasilar artery	2 (4.3)

Table II: Shapes of aneurysms in 50 patients.

Shapes of aneurysm	n (%)
Fusiform	32 (64)
Saccular	6 (12)
Oncotic	4 (8)
Fusiform/saccular	2 (4)
Berry	1 (2)
Lobulated	1 (2)
Microaneurysms	1 (2)
Oncotic / serpentine	1 (2)
Serpentine	1 (2)
Wide-necked	1 (2)

Six (9.5%) patients had pathological evidence of cerebral artery myxomas. Three each (50%) by biopsy and surgical resection.

False positivity of medical imaging was noted in six (9.5%) patients: four (66.7%) were evaluated by computed tomography, and one each (16.7%) by magnetic resonance imaging, and cerebral angiography.

The pre- and post-operative plasma interleukin-6 values were reported in four patients each with a much higher preoperative value than postoperative value, but lacking statistical significance (30.1 ±25.9 *versus* 12.4 ±12.6 pg/mL, p=0.266).

Management of cardiac myxoma was reported for 54 (85.7%) patients: cardiac myxoma resection in 52 (96.3%), and left untreated in two (3.7%) patients. The time interval from cardiac myxoma resection to neurological symptom onset was 53 ±59.6 months (n=18), and to cerebral aneurysm resection was 68.7 ±63.6 months (n=21).

Management of cerebral aneurysm was described in 44 (69.8%) patients, and most patients received follow-up, conservative, or surgical treatments (Table III).

Patients were on a follow-up of 21.4 ±25.1 months (n=27). Prognoses were reported for 49 patients, most were stable by follow-up or treatment (Table IV).

Table III: Management of cerebral aneurysms.

Management	n (%)
Follow-up	13 (29.5)
Conservative	11 (25.0)
Surgical operation	10 (22.7) (including surgical resection in 5, clipping in 2, superior cerebellar arteries reinforced with a cotton wrap in 1, clipping then emergent decompressive craniotomy in 1, and left PCA aneurysm excluded plus biopsy then surgery with a bypass and clipping in 1 patient, respectively)
Interventional (endovascular coiling of aneurysm)	3 (6.8)
Other surgical operation than aneurysmal resection	3 (6.8) (cerebral tumor resection in 2, and evacuation of hemorrhage in 1 patient)
Untreated	2 (4.5)
Hybrid: embolic embolization (right PCA) +1 month later surgical removal of the left parietal lesion and stable occlusion of the right occipital lesion (tiny parent vessel would be difficult to access via endovascular techniques)	1 (2.3)
Low-dose radiation therapy	1 (2.3)

PCA = Posterior cerebral artery

Table IV: Patients' prognoses.

Prognosis	n (%)
Stable	34 (69.4)
Improved	6 (12.2)
Aggravated	2 (4.1)
Recovered	2 (4.1)
Recurred	2 (4.1)
Complicated (cerebral hemorrhage)	1 (2.0)
Died	2 (4.1)

DISCUSSION

The cardiovascular events, as a result of parenchymal brain metastasis of cardiac myxoma, are most commonly caused by left atrial myxoma that represents the vast majority of the benign cardiac tumors than cardiac myxomas arising from any other sites of the heart.[8] As for the cardiac myxoma-related cererbral aneurysms, most of the cases had an origin of left atrial myxoma, while cererbral aneurysms due to a right atrial myxoma have not been previously described in the literature; instead, such a case caused by biatrial myxomas was once reported.[12] The present study revealed that left atrial myoxma was the most common causing cerebral aneurysm than a myxoma arising from any other sites of the heart.

Brain metastases from cardiac myxoma are usually found at the same time or a few months after the diagnosis of primary lesions.[37] However, Brinjikji *et al*. reported that the timing of cerebral aneurysm formation was reported to be 5-78 months after cardiac myxoma resection,[14] and many patients had previous embolic event. The most common type of aneurysms was fusiform in distal branches of the MCAs, ACAs, or PCAs (71.4%), and very few were saccular. The majority of the aneurysms were multiple and a few were solitory.[14] Nussbaum *et al*. reported 60 cerebral aneurysms of 55 patients located on the MCA, PICA, PCA, ACA, superior cerebellar artery, and anterior inferior cerebellar artery in 26 (43.3%), 17 (28.3%), 9 (15.0%), 6 (10.0%), 1 (1.7%) and 1 (1.7%), respectively.[54] They categorised the aneurysms as small (maximum diameter <1 cm) (42/60 (70%)), large (maximum diameter 1-2.5 cm) (7/60 (12%)), and giant (maximum diameter >2.5 cm) (11/60 (18%)). They noted, 68% (41/66) were unruptured, 32% (19/60) were bleeding and 90% (44/60) were very wide-necked or fusiform-shaped. In line with above mentioned results, the present study also revealed a predominance of multiple fusiform MCA aneurysms; however, most of the aneurysmal dimensions were not indicated in individual reports, and statistical analysis could not be performed in this regard.

There has been no consensus about optimal treatment of myxoma-related cerebral aneurysms. Brinjikji *et al*. reported seven (12%) aneurysms which were treated endovascularly, six of which had a narrow neck.[14] Endovascular embolisation, chemotherapy and radiation were attempted with no definite conclusions drawn for therapeutic effects.[14] For the treatment of cerebral aneurysm of any cause, Nussbaum *et al*. applied with direct coil embolisation, endovascular parent artery occlusion across the neck of the aneurysm,[54] but most cases (88%) were indicated for surgical treatment (direct clip reconstruction for 26 patients, trapping/proximal occlusion with distal revascularisation for 21 patients, excision with end-to-end anastomosis for 3 patients, and circumferential wrap/clip reconstruction for 3 patients).

Cardiac myxoma resection usually eliminated early neurologic symptoms, but cannot completely abolish the risk of delayed cerebral aneurysm formation. Thus, follow-up for aneurysmal formation even after myxoma resection is mandatory.[55] The overall event-free survival rate (pateints with a stable or an improved outcome) of this patient setting was 81.6% on a follow-up of a mean of 21.4 ±25.1 months.

The incomplete information of individual patients may lead to multiple potential biases, thereby limiting the interpretation of some results. Data from prospective studies with large patient population would offer precise results of myxoma-related cerebral aneurysms.

CONCLUSION

The present study revealed a predominance of myxoma-related multiple fusiform MCA aneurysms, and left atrial myoxma was the most common causing cerebral aneurysm than a myxoma arising from any other sites of the heart. The cerebral aneurysms developed 53 months after cardiac myxoma resection. Patients' prognoses were promising with 69.4% patients being stable and a mortality of 4.1% by either follow-up, conservative and surgical treatments. Cardiac myxoma resection could not avoid development of cerebral aneurysm, therefore cerebroimaging monitoring is recommended even after cardiac myxoma resection. This lesion showed a relative benign outcome by observation or pertinent treatment with an overall survival rate of 81.6% at a mean follow-up of 21.4 months.

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