Myxoma-related cerebral aneurysms: a cerebral MRI cohort study

Poster No.: C-1380
Congress: ECR 2013
Type: Scientific Exhibit
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Keywords: Neuroradiology brain, MR-Angiography, MR, Diagnostic procedure, Experimental investigations, Aneurysms
DOI: 10.1594/ecr2013/C-1380

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Purpose

Cardiac myxomas are the most common primary cardiac tumours which are rare neoplasms with an autopsy estimated prevalence ranging from 0.0017% to 0.19%. They are mainly located in the left atrium (75-80%). Age of onset is very variable, ranging from childhood to elderly [2], with a higher prevalence in female patients (57-78%) [1,2].

Other than cardiac and general symptoms, patients may present embolic and neurological symptoms, mainly involving central nervous system, reported in up to nearly 26% of patients [1,2], the most frequent being ischemic events [1,3,4]. Further acute or delayed neurological events include development of intracranial aneurysms and intracranial or subarachnoid haemorrhages [3,4]. Up to 17% of patients with neurological symptoms were reported to have a cerebral bleeding [3], possibly due to ruptured cerebral aneurysms. Myxoma-related cerebral aneurysms were firstly reported by Marchand in 1894 and follow-up by cerebral imaging after myxoma resection for the development of myxoma-related aneurysms has been recommended [5].

Nevertheless, knowledge about this association derives only from case-reports and retrospective studies [5-7]. Thus, despite great knowledge of acute neurological complications, little is known about delayed neurological events, especially cerebral aneurysms. Pathogenesis is not fully understood and natural history is unclear.

Different authors described cases with stable aneurysms [7] or progressively enlarging or new developing aneurysms [7,8].

Latency between myxoma resection and diagnosis of cerebral aneurysms is very variable. They may be diagnosed before cardiac surgery but also many years after [5-7]. Some authors showed that the development of cerebral aneurysms can occur after myxoma resection [7]. Although surgical removal of primary cardiac neoplasm may prevent early neurological embolic events, late events such as cerebral aneurysm formation cannot be excluded [8].

Moreover, a standardized therapy has not been established for myxoma-related cerebral aneurysms and there is no general consensus on their management.

Prevalence of cerebral aneurysms in patients treated for left cardiac myxoma (LCM) has been reported to be higher if compared to general population, real prevalence of cerebral aneurysms in patients treated for CMs is unknown and no prospective studies have been conducted.

Thus, our aim was to prospectively assess cerebral aneurysms prevalence in patients previously treated for LCM.
Methods and Materials

This prospective study was has been approved by the local ethics committee (ASL Milano 2). Inclusion criteria was previous surgical excision of left cardiac myxoma. We tried to contact by phone the patients surgically treated for LCMs at our institution (IRCCS Policlinico San Donato) between 1990 and 2009. Clinical data about neurovascular events were collected.

Exclusion criteria were site of myxoma other than left cardiac chambers; contraindication to magnetic resonance imaging (MRI); any status precluding the ability to sign the informed consent. After signing informed consent, patients enrolled underwent the mini mental state examination in order to evaluate their cognitive status. This score was normalized for school level.

MR Imaging Protocol and analysis

Patients enrolled in the study underwent 1.5-T unenhanced brain MRI (Magnetom Sonata Maestro Class, Siemens Medical Solution, Erlangen, Germany)

1. three-plain gradient-echo localizer;
2. sagittal T1-weighted turbo spin-echo (repetition time 635 ms, echo time 17 ms, slice thickness 5 mm, matrix 256x256, acquisition time 2 minutes and 47 seconds);
3. axial T2-weighted turbo spin-echo (repetition time 4760 ms, echo time 94 ms, slice thickness 5 mm, matrix 256x256, acquisition time 2 minutes and 52 seconds);
4. axial fluid-attenuated inversion-recovery (repetition time 8650 ms, echo time 109 ms, inversion time 2500 ms, slice thickness 5 mm, matrix 256x256, acquisition time 3 minutes and 28 seconds);
5. axial echo-planar diffusion weighted sequences (b=0 s/mm$^2$, b=500 s/mm$^2$ and b=1000 s/mm$^2$; repitition time 3900 ms, echo time 87 ms, slice thickness 5 mm, matrix 128x128, acquisition time 1 minutes and 34 seconds);
6. three-dimensional time-of-flight angiographic sequence with multiplanar and 3D maximum intensity projection reconstructions (repitition time 34 ms, echo time 4.45 ms, slice thickness 0.8 mm, matrix 384x384, acquisition time 6 minutes and 55 seconds).

MRI exams were evaluated by two neuroradiologists with 3 and 12 years of experience, in consensus.

Workup of MRI findings
In the case of detection of MRI findings suspected as cerebral aneurysms, the patients was referred to interventional neuroradiologists for evaluating the possibility of further diagnostic imaging and of therapeutic approach.

Statistical analysis

Demographics data are presented as mean and standard deviation. The prevalence of cerebral aneurysms was calculated as number of patients diagnosed with the disease on cerebral MRI divided by the number of patients who underwent cerebral MRI, with 95% confidence interval (CI) calculated according the binomial distribution.

Results

Patient Population

From 1990 to 2009, 84 patients underwent surgery for cardiac myxoma at our institution. We excluded 8 patients: 5 had a cardiac myxoma in right cardiac chambers; in 3 patients the final pathological diagnosis was not available (2 of them deceased during the intervention). Thus, 76 patients were eligible for the study. The mean age at the time of tumor resection was 60±13 years (range 23-83 years), with a median age of 62 years. Forty-seven of them were women (63%). For 49 of these 76 patients (64%), we obtained by phone information regarding current status and clinical history since tumor resection. For 4/49 cases (8%), the person answering the call told us that the patient was deceased, one of them caused by cerebral hemorrhage due to a ruptured cerebral aneurysm about 8 years after tumor resection. Moreover, one patient had a pacemaker which contraindicated MRI.

Enrollment and MRI results

Of the remaining 44 patients, 31 (70%) declined and 13 (30%), 10 females and 3 males, were enrolled and accepted to underwent brain MRI at our institution. No cognitive impairment was found at mini mental state examination, the score ranging between 25 and 30. Out of 13 patients, 3 (23%) were diagnosed with a cerebral aneurysm on MRI:

1. one female of 59 years of age, operated for cardiac myxoma at 49, diagnosed with a berry aneurysm of 2 mm in diameter in M1 tract of the right middle cerebral artery, nearly its bifurcation at the origin of the frontal-orbitary artery (Fig 1); this patient reported episodes of vertigo and headache;
2. one female of 66 years of age, operated for cardiac myxoma at 62, diagnosed with a small saccular aneurysms of 3-4 mm in diameter in the
proximal M1 tract of the right middle cerebral artery (Fig 2); this patient reported headache;

3. one male of 78 years of age, operated for cardiac myxoma at 68, diagnosed with a saccular of 4-5 mm in diameter in the C4 tract (according to Fischer classification) of the right internal carotid artery, arising from the lateral side of the vessel (Fig. 3); this patient reported no neurological symptoms.

Moreover, MRI showed a right cerebellar lacunar infarction in the first patient and multiple lacunar infarcts in basal ganglia in the third patient. Among the remaining 10 patients, MRI showed anatomic variants of P1 tract of cerebral posterior artery in 2 patients and hypoplasia of the A1 tract of the right anterior cerebral artery in another patient; small lacunar infarcts were found in basal ganglia, left parietal lobe, ascendent gyrus of the right frontal lobe and right cerebellum were found in 3 patients. One patients reported an episode of drop attack; the same was surgically treated for pituitary macroadenoma. The other 9 patients did not report relevant neurological symptoms.

All the 3 patients diagnosed with cerebral aneurysm at MRI, were evaluated by experienced interventional neuroradiologists who confirmed the diagnosis. None of the patients was asked to perform digital subtraction angiography and for all of them a diagnostic follow-up was advised within 2-3 years. The prevalence of cerebral aneurysms in our group of patients previously treated for LCMs who underwent brain MRI resulted to be 3/13 (23%, 95% CI 5-54%). If we include the case of the patient deceased from ruptured cerebral aneurysm, the prevalence of cerebral aneurysms becomes 4/14 (29%, 95% CI 8-58%).

Images for this section:
Fig. 1: Case 1 - A female patient, 59 years old, operated for cardiac myxoma 10 years before. MIP reconstruction from 3D time of flight sequences disclosed a berry aneurysm (arrow and circle) of 2 mm, on M1 tract of the right middle cerebral artery, nearly bifurcation.
**Fig. 2:** Case 2 - Brain MRI of a female patient, operated for cardiac myxoma at 62 years. Cerebral MRI showed on 3D time of flight sequences and MIP reconstruction a small saccular aneurysms of 3-4 mm in diameter in the proximal M1 tract of the right middle cerebral artery.

![Brain MRI of a female patient](image)

**Fig. 3:** Case 3 - Male patient of 78 years of age, operated for cardiac myxoma at 68, diagnosed with a saccular aneurysm(arrow) of 4-5 mm in the C4 tract of the right internal carotid artery, arising from the lateral side of the vessel which can be seen both in 3D time of flight sequences and MIP reconstruction.

![Male patient MRI](image)
Conclusion

Our **prospective study** was aimed at assessing cerebral aneurysms **prevalence** in patients previously treated for LCMs. We found 3 patients with cerebral aneurysms among 13 who underwent MRI while 1 patient was reported to be deceased from ruptured cerebral aneurysm, for an overall prevalence ranging from **23% to 29%**. Cognitive function were normal in all these 13 patients, as expected.

Formation of myxoma-related cerebral aneurysms has been described and documented since 1894, but current knowledge on this association derives only from case reports and retrospective studies [1-8]. Standard of care was not established. While cardiac surgery for removing the myxoma can eliminate early neurological symptoms, the risk of **delayed neurological events**, as cerebral aneurysms development, cannot be completely abolished [5,7].

The prevalence of myxoma-related cerebral aneurysms varies among previous studies, especially due to the fact that **no systematic investigation** using neuroradiological imaging was done. Lee et al [4] reviewed 74 patients treated for cardiac myxoma and reported one patient with cerebral aneurysms and hemorrhage among 9 patients presenting with neurological symptoms. Patients with neurological events underwent neuroimaging: cerebral aneurysms prevalence resulted to be **11%** (1/9). Ekinci et al. [3] considered 113 patients treated for cardiac myxoma with neurologic symptoms (6 from their own center and 107 from literature). Cerebral aneurysms were reported in 6 of them at the time of myxoma diagnosis, giving a prevalence of **10%** (11/113). Lee et al. [1] reported cerebral aneurysms prevalence of **2%** (1/59) in patients treated for cardiac myxoma and **8%** (1/13) among patients with cardiac myxoma and embolic signs. Interestingly, the case of cerebral aneurysms was not reported in a patient with brain emboli, but it was an **incidental finding** in a patient presenting with only systemic embolic symptoms. Pinede et al [2] found 3 cases of cerebral aneurysms among 29 patients treated for cardiac myxoma with neurological symptoms (**10%**); considering all the 112 patients with cerebral aneurysms reviewed in this study, having neurological symptoms or not, cerebral aneurysms prevalence would be **3%** (3/112). Tamuleviciute et al. [7] retrospectively matched two databases, one concerning 2,246 patients with cerebral aneurysms and the other one concerning 40 patients treated for cardiac myxoma; a single patient was present in both databases.

Our prevalence of myxoma-related cerebral aneurysms (**23%-29%**) was higher than that previously reported, probably due to the aforementioned lack of systematic imaging evaluation in previous studies. In addition, we prospectively looked for cerebral aneurysms using a protocol including MR angiography, while other studies did not report standardized imaging protocol. Another explication is our selection of only **LCMs**, reported to be more likely to **embolize** and promoting aneurysm formation [3].
Moreover, our prevalence of cerebral aneurysms appears to be higher if compared to that reported for the general population, ranging from 2.3% to 6% according to study design and population as well as aneurysm characteristics [9,10]. Vlak et al [9] reported unruptured aneurysms prevalence of 3.2% in the general population (mean age 50 years) with a higher prevalence in females (6%). For adults without specific risk factors, Rinkel et al. reported a prevalence of 2.3% while it was found to be 3.6% in prospective autopsy studies, 3.7% in retrospective angiography studies, and 6.0% in prospective angiography studies [10]. Thus, our unruptured myxoma-related cerebral aneurysms (3/13), was from 4 to 11-fold that in general populations.

While myxoma-related cerebral aneurysms were mainly reported to be multiple, fusiform, and located in distal arterial branches [6,7], our aneurysms were unique, saccular, and located in proximal tracts of brain arteries. This would be due to our use of a 1.5-T unenhanced MRI, using a non-multicoil and relatively low-resolution protocol, potentially missing small peripheral cerebral aneurysms. However, our results are consistent with previous studies which reported saccular and central aneurysms as myxoma-related aneurysms despite being less frequent [6,7]. Stollberg and Tamulevičiūtė [5,7] retrospectively reviewed previously case-reports including a case presenting with saccular and fusiform, proximal and distal aneurysms; they also reported a patient with a giant aneurysm in the proximal tract of the middle cerebral artery [7]. Lee et al [4] reported one patient with a 3-mm myxoma-related aneurysm of the left internal carotid artery. The 3 aneurysms found in our series are consistent with these results. A similar reasoning holds for the right-sided location of all our aneurysms, in agreement with previous findings and consistent with data on embolic strokes [6].

The association between myxoma-related aneurysms and brain infarcts was already reported [7]. For patients who underwent left myxoma resection presenting with ischemic stroke or transient ischemic attack secondary prevention with anticoagulant or antiplatelets has been proposed [3]. In that case, necessity to exclude cerebral aneurysms has been claimed. One of our patients was reported to have had fatal ruptured cerebral aneurysm 8 years later myxoma resection. In fact, even though myxoma-related aneurysms can remain stable over years [2,7], they may grow or rupture [4,6-8], up to 25 years later [7]. Our three patients were conservative treated with follow-up due to aneurysms characteristics, as already suggested [2,7]. However, we should consider the paucity of long-term follow-up in the literature.

Our study has limitations. Apart from the abovementioned non-high field non-multicoil MR technique, we had also a small sample of patients who underewent MRI.

In conclusion, we prospectively showed a prevalence of about 23%-29% of cerebral aneurysms in patients treated for LCM, suggesting brain MRI study as appropriate
in these patients. Transversal studies investigating the brain when cardiac myxoma is diagnosed and longitudinal large studies are needed to further clarify this matter.

References


Personal Information