Case Report

Left atrial myxoma development after radiofrequency ablation of an atrial flutter substrate

Elpidio Santillo (MD)\textsuperscript{a,}\textsuperscript{*}, Monica Migale (MD)\textsuperscript{b}, Luciano Marini (MD)\textsuperscript{a}, Luca Fallavollita (MD)\textsuperscript{a}, Carlo Massini (MD)\textsuperscript{b}, Fabrizio Balestrini (MD)\textsuperscript{a}

\textsuperscript{a} Geriatrics-Rehabilitative Department, Italian National Research Center on Aging (INR.C.A.), Fermo, Italy
\textsuperscript{b}Unità Operativa di Cardiologia e Cardiologia Salus Hospital, Reggio Emilia, Italy

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\textbf{A B S T R A C T}

A 51-year-old man developed symptoms (palpitations) related to a large left atrial mass attached to interatrial septum discovered by trans-thoracic heart ultrasonography. Six months earlier this patient had undergone radiofrequency ablation (RFA) of an atrial flutter substrate. The left atrial mass was removed surgically using cardiopulmonary bypass with disappearance of symptoms. A post-operative diagnosis of atrial myxoma was made. The present case shows that a big left-attrial tumor could manifest with only mild unspecific symptoms such as palpitations. It is not clear whether the development of myxomas could be related to RFA or occurrence of heart tumors after RFA (already reported in medical literature) or whether it could be just chance without a causal link with ablation procedures.

\textbf{Learning objective:} It is essential to consider myxoma in the differential diagnosis of cardiac masses identified in patients after radiofrequency ablation since some cases of myxoma development after radiofrequency ablation have recently been described in the literature. Transthoracic echocardiography is a precise technique in the evaluation of cardiac masses, but a high index of clinical suspicion is necessary in order to define intracardiac pathologies that could be missed for unspecific symptoms of presentation.

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\section*{Introduction}

Primary tumors of the heart are not common: their incidence has been estimated from 0.0017\% to 0.19\% in autopsy studies performed in groups of unselected subjects. Myxoma is the most frequent cardiac tumor, representing about 50\% of all benign neoplasms of the heart [1]. At present its incidence after radiofrequency ablation (RFA) of an arrhythmic substrate is not well known but some cases have been recently reported [2–6].

We describe the case of a quickly growing cardiac myxoma that developed in the left atrium of a patient with persisting palpitations after procedure of RFA for an atrial flutter.

\section*{Case report}

In February 2014, a 51-year-old man was referred to the cardiology outpatient department of our institute (INRCA Fermo, Italy), with a 2-year history of palpitations in the absence of syncopal events, pre-syncopal symptoms, dyspnea, or chest pain. The patient was a smoker with clinical history of type 2 diabetes mellitus on diet treatment and kidney stones. RFA of a common atrial flutter substrate had been performed 6 months earlier. In particular during the intracardiac electrophysiology study burst pacing (until 200 ms cycles) from proximal coronary sinus catheter and low right atrial catheter induced typical counterclockwise flutter phases (tachycardia cycle: 260 ms). So the patient underwent transcatheter radiofrequency (RF) energy application (30–50 W, 60°C, 120 s) on cavo-tricuspid isthmus obtaining block of isthmus conduction (details shown in supplementary materials). In the weeks following the RFA procedure the patient had only mild reduction of palpitations. The patient’s familial history was unremarkable. In June 2013, for an inconclusive ergometric test he had undergone coronary angiography without evidence of significant coronary atherosclerotic disease.

His current medications were aspirin 100 mg daily and bisoprolol 1.25 mg daily. The beta-blocker was prescribed by the family physician 3 days before the visit, for symptomatic supraventricular extrasystoles also repetitive in unsustained runs evidenced by a Holter electrocardiogram.

On general examination, the patient looked to be a well-nourished man, without dyspnea at rest and without cyanosis and...
pallor. Lymphadenopathy and edema were not present. His temperature was 36.8 °C. Physical examination revealed a blood pressure of 130/70 mmHg and a heart rate of 60 beats/min. Clinical characteristics indicative of familial myxomas (such as Carney complex or familial autosomal dominant syndrome) were excluded. No significant pathological marks were present on heart, lung and abdominal examinations. During the visit the patient showed the results of laboratory analysis made 1 week before. There were no hematological and biochemical abnormalities with the exception of a mild elevation of fasting plasma glucose (119 mg/dL).

The electrocardiogram showed sinus rhythm, mean frontal QRS vector at 60°, rare and isolated atrial ectopic beats, normal duration of PR interval and QRS complex, normal QT length, and pre-existing negative T wave in V5–V6 leads.

Transthoracic echocardiography revealed a large mass in the left atrium. Its dimension was about a 2.7 cm × 4 cm in four chambers apical view and 2.4 cm × 4 cm in two chambers apical view. The mass was attached to the interatrial septum by a broad base, appearing with a smooth surface and presenting both hyperechogenic and hypoechogenic foci in its context. The mass was slightly mobile but did not interfere with mitral leaflet dynamics during all heart cycles (Fig. 1).

The rest of the ultrasonography study showed evidence of mild left ventricular hypertrophy, mild mitral regurgitation, a left ventricular ejection fraction of 55% (by Simpson biplane method), and mild left atrial dilation (antero-posterior diameter: 48 mm).

Surprisingly the patient had undergone 2-dimensional echocardiographic study also at the time of RFA procedure (6 months before), showing no intracardiac masses.

The patient started subcutaneous low molecular weight heparin and was referred for surgical resection which was performed 5 days later, with the assistance of standard cardiopulmonary bypass. The excision of the mass was obtained along with its septal attachment after exposing the left atrium. Macroscopic examination showed the tumor as brownish solid mass which was the size of a citrus fruit, with a smooth and gelatinous surface (Fig. 2).

Microscopic analysis of tumor sections showed a myxoid matrix with polygonal and star-shaped cells disposed in clusters and small areas of hemorrhage and necrosis. The histological aspect was consistent with an atrial myxoma.

After surgical excision of the neoplasm, the patient made a postoperative recovery without complications. Four months later (June 2014), he was in sinus rhythm and asymptomatic for palpitations. A new transthoracic echocardiography revealed no intracardiac mass.

Discussion

We herein reported the case of a large left atrial myxoma discovered on heart ultrasonography in a patient with persisting palpitations after an RFA procedure for an atrial flutter substrate. Due to its great dimensions we think it is improbable that the neoplasm was present but not seen on the echocardiogram performed in the RFA pre-procedural period. The eventual early identification of the neoplasm imposed the consideration of a rapid excision. In fact as described in the present case, myxomas require immediate surgical operation due to their risk of embolism or cardiovascular complications, including sudden death.

RFA represents often the decisive treatment option for symptomatic patients with arrhythmias but it is associated with the risk of several complications including both thrombus and endocarditis in atria. Echocardiographic features of the mass can suggest the right diagnosis. In fact left atrial myxomas appear often as masses attached to the interatrial septum in the area of the fossa ovalis or, less frequently, to the lateral wall of the atrium.

Interestingly, even if several myxoma cases are found incidentally on transthoracic echocardiography, there are few papers of cases in which a cardiac myxoma has been discovered after RFA. At present to our knowledge, five reports before have described the appearance of an atrial myxoma after RFA (Table 1).

Similar to our report, in three cases an early onset of a myxoma after RFA over a few months was highlighted while in two cases the appearance of the tumor has been documented later in life (from 2 to 6 years after RFA) [2–6].

It is not well known whether myxoma development is just a coincidence or if there is a correlation with the previous ablation. Considering that cardiac myxoma cells may result from adult developmental remnants subjected to mitogenic stimuli, surely we can identify three factors associated with RFA procedures potentially able to induce a myxoma’s growth: radiation, heart tissue trauma, and RF-related heat energy.

First, it should be underlined that RFA procedures require often protracted fluoroscopy times. A study has suggested that the use of angiography during RFA could determine a small increase in the lifetime risk of developing neoplasms [7].

Second, heart trauma and subsequent local inflammation have been hypothesized to cause myxoma development. In cases of myxomas that developed after atrial septum trans-septal technique, the iatrogenic puncture could have acted as a stimulus for the development of a reactive lesion. Subsequently, the local tissue injury could have promoted cell proliferation in the endocardium.

Finally, it can be speculated that the heat energy of the ablation may contribute to heart neoplasm development. This mechanism
could trigger development of myxoma in heart regions close to where heat energy is applied.

Moreover, the growth rate of myxomas detected early after RFA appears faster than in all other cases. In fact, in a former observation Walpot estimated that cardiac myxomas present growth rates of 0.49 cm/month [8]. This rate is slightly lower than in two cases diagnosed after RFA as shown in Table 1.

More rapid growth of myxomas identified early after RFA procedures could be attributed to properties of heat energy of RF. In fact, RF has shown the ability to upregulate human cell proliferation and trigger expression of genes and enzymes. The upregulation of inflammatory gene expression could induce cell responses and a faster neoplasm development [9].

Interestingly, it has been demonstrated that quick growth of myxomas is related principally to enlargement of the intercellular matrix, more than to the increase of cellular elements [10]. Whether RFA procedures are also able to induce these changes remains to be established.

Taken together, these observations suggest that, due to its possible rapid growth, a myxoma should always be considered in the differential diagnosis of new intracardiac mass in patients who have previously undergone RFA, also in the presence of a recent normal echocardiogram.

In summary, we reported the case of a man manifesting unspecific symptoms related to left atrial myxoma that developed 6 months after RFA procedure. Causal links between RFA and myxoma growth could be hypothesized but remain to be proven.

Conflict of interest

None declared.

### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jccase.2015.01.001.

### References