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Interest of Cytogenetic Study to Invalidate Malignancy Characteristics of an Infiltrative Cardiac Lipoma

Daniel Grandmougin[1*], Damien Mandry[2], Jacqueline Champigneulle[3], Anne Kieffer[4], Agnès Leroux[5] and Juan- Pablo Maureira[1]

[1]Department of Cardiac Surgery, University Hospital of Nancy, France

[2]Department of Radiology, University Hospital of Nancy, France

[3]Department of Cytology and Pathology, University Hospital of Nancy, France

[4]Department of Medical Oncology, Institute of Cancerology of Lorraine - Alexis Vautrin, France

[5]Department of Biopathology, Institute of Cancerology of Lorraine - Alexis Vautrin, France

[*]**Corresponding author:** Daniel Grandmougin, Department of Cardiac Surgery, ILCV Louis Mathieu. CHRU Nancy, Rue du Morvan, 54500 Vandoeuvre les Nancy, France, Tel: +33(0)383157367; Fax: +33(0)383157429; E-mail: d.grandmougin@me.com

Abstract

Purpose: We report the case of a patient with an unusual incidental finding of an epicardial lipoma infiltrating the right atrium and the interatrial groove which was first diagnosed as liposarcoma. In order to definitely validate diagnosis of benign tumor, we sought to assess the interest of cytogenetic study to ascertain diagnosis of benign tumor despite imaging, surgical and histopathological malignancy characteristics.

Methods: Following surgical removal of the tumor, histopathological examination and array-based comparative genomic hybridization were required.

Results: While histopathological examination could not exclude a liposarcomatous transformation, the array-based comparative genomic hybridization showed neither genomic imbalance nor additional evidence of malignancy and hence diagnosis of benign cardiac lipoma was definitely ascertained.

Conclusions: As far as we know, giant cardiac lipoma with similar properties has rarely been reported. This report highlighted the importance of cytogenetic study for invalidation of suspected malignancy properties of a compressive cardiac fatty mass and was an opportunity to review the literature of such a rare tumor with unusual misleading characteristics.

Keywords: ***Cardiac lipoma; Misleading malignancy; Magnetic resonance imaging (MRI); Cytogenetic study; Comparative genomic hybridization (array CGH)***

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Introduction

Cardiac lipoma is a rare primary benign tumor with multiple clinical presentations depending on location [1-6]. Histological as well imaging and surgical characteristics are usually easily validated. We report the unusual observation of a compressive and infiltrating cardiac lipoma presenting with misleading malignancy properties suspected after imaging, surgical and histopathological analysis. Necessity to use cytogenetic study was crucial to ascertain diagnosis of benign tumor and definitely invalidate a liposarcomatous transformation. This exceptional observation was an interesting opportunity to review the literature and highlight the importance of comparative genomic hybridization as a major exam to improve accuracy of the diagnosis.

Case Report

A 63-years-old patient presented with simultaneous chest and lumbar pains and a moderate dyspnea strongly evocating aortic dissection. Decision was made to perform a CT-scan rapidly that showed COPD with emphysema and an asymptomatic 30 mm × 25 mm hamartochondroma in the right lung (Figure 1A). However, it also incidentally revealed a 72 mm × 52 mm mass located into the pericardium with obvious compressive signs on the SVC and the right atrium (Figure 1B - Figure 1C). A transesophageal echography (TEE) confirmed the presence of a solid 70 mm × 50 mm compressive mass attached to both SVC and right atrium extending inferiorly to the coronary sinus and superiorly to the roof of the left atrium and the aortic root. The mass seemed to be encapsulated with smooth contours, nevertheless with strong internal adherences along the interatrial groove. Coronary angiography showed neither obstructive coronary artery disease nor compression of the right coronary artery (RCA). The CT-scan confirmed the mass, showing adipose characteristics consistent with a cardiac lipoma. In order to improve characterization of the tumor the patient underwent a cardiac magnetic resonance imaging (MRI) that showed a 64 mm × 32 mm × 60 mm mass with homogeneous high signal intensity within the intertarial groove in both T1 and T2 weighted images (Figure 2A - Figure 2B). In T1, saturation of the adipose tissue, showed a significant decrease of the signal with a persistent internal heterogeneity of the mass with an external capsule clearly visible (Figure 2C). Additionally, after infusion of gadolinium the mass showed a moderate enhancement of anterior and superior portions leading to suspect a malignancy tumoral transformation such as a liposarcoma (Figure 2D).

Debulking surgery was decided to release complications related to compression of both SVC and RA with concerns about the possibility of a complete tumor resection due to close adherences with the intertatrial groove and MRI features of liposarcoma.

A median sternotomy was carried out and after pericardiotomy, the mass was easily located into the pericardium with obvious signs of right atrial compression (Figure 3A). External border of the mass was well-delineated. Close adherences were found with the interatrial groove, the posterior aspect of the SVC and inferiorly with the coronary sinus.

Normothermic cardiopulmonary bypass (CPB) was applied with bicaval cannulation and tourniquets. Myocardial protection and cardioplegic arrest were achieved with a solution of cold blood cardioplegia infused through the ascending aorta after application of an aortic cross-clamp. After snaring both tourniquets, excision of the mass started at the posterior aspect of the SVC and the roof of the LA and then cautiously reached the interatrial groove and the coronary sinus (Figure 3B). Liberation of close adherences with the interatrial groove was demanding and quite challenging to avoid atrial perforations. The interatrial groove was reinforced with 4-0 polypropylene pledgeted sutures (Figure 3C).

Histopathological examination with additional investigation using array-based comparative genomic hybridization (array CGH) were performed. The tumoral mass was successfully resected. Postoperative outcome was uneventful and the patient was discharged at the 7th postoperative day.

The histopathological examination revealed an encapsulated 90 mm × 70 mm × 25 mm lipoma composed of mature adipocytes (Figure 4A & Figure 4B). Nevertheless, a limited part of the tumor with atrial infiltrations and adherences was consistent with either a lipoma or a well-differentiated liposarcoma despite no MDM2 amplification following fluorescence in situ hybridization (FISH).

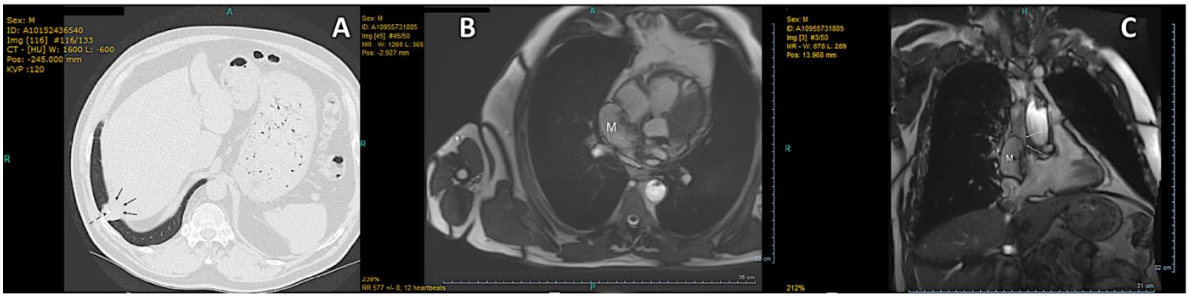

Figure 1: (A) The CT scan shows a typical hamartochondroma (black arrows) with central calcification (dotted black arrow). **(B)** The CT scan reveals a well-delineated compressive mass (M) with heterogenous characteristics infiltrating the interatrial groove. **(C)** The CT scan identifies the compression of the SVC (white arrows) by the mass (M).

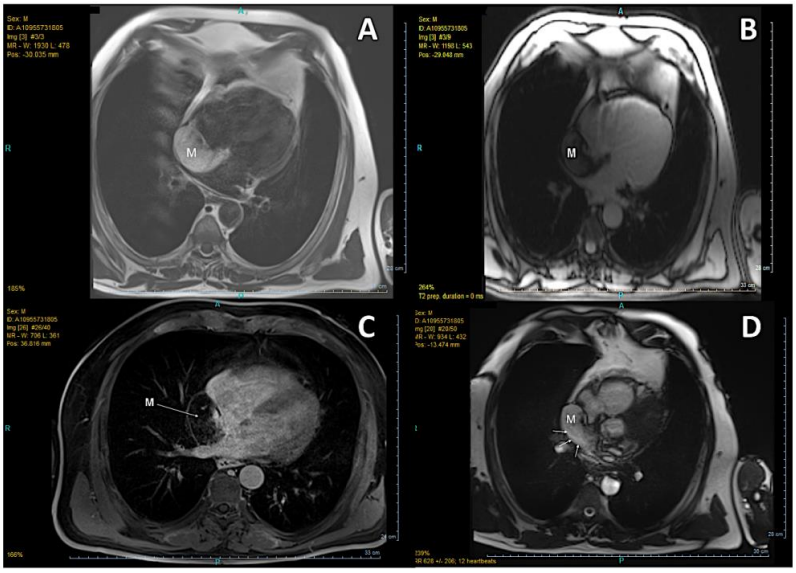

Figure 2: (A) The MRI (T1) displays a hypersignal of the mass (M) with internal heterogenous features. **(B)** The MRI (T2) hypersignal is moderate. **(C)** The MRI (T1), after saturation of the adipose tissue, shows a significant decrease of the signal with a persistent internal heterogeneity of the mass (M). Thse external capsule of the tumor is clearly visible. **(D)** The MRI, following gadolinium infusion reveals enhancement (white arrows) of the mass (M).

The further investigation with array CGH definitely validated diagnosis of benign lipoma. At the 9-month follow-up, the patient remains asymptomatic with no echographic and MRI signs of recurrence.

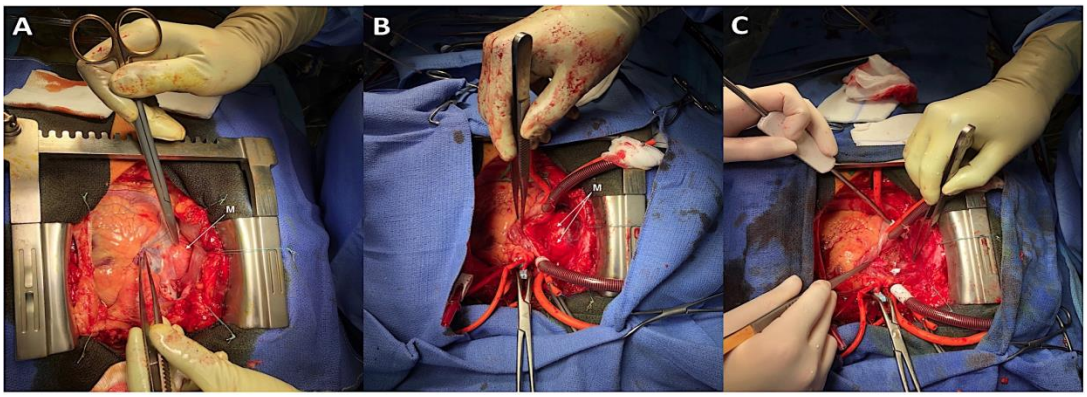

Figure 3: (A) Operative view following pericardiotomy. The mass (M) is deeply enshrined into the interatrial groove and extends superiorly to the posterior aspect of the SVC and inferiorly to the CS. **(B)** Surgical excision of the mass (M). The print of the tumoral compression of the right atrium is clearly visible. **(C)** Final view after resection of the mass. The interatrial groove was reinforced with 4-0 polypropylene pledgeted sutures.

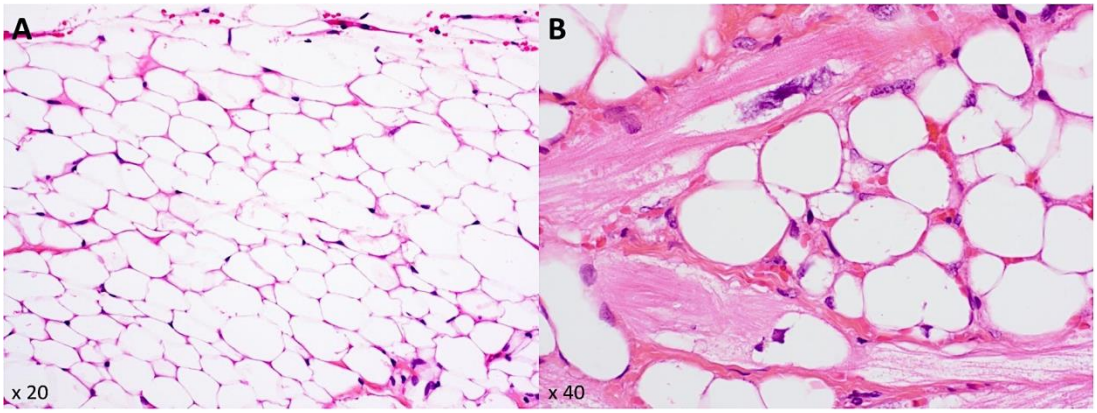

Figure 4: (A) Histological examination showing groups of adipocytes without any cytonuclear atypia separated by thin walls of vascularized conjunctive tissue. Haematoxylin and eosin staining (Original magnification ×20). **(B)** Histological examination showing myocardial cells with dystrophic nuclei dissociated by infiltrative adipocytes consistent with either a lipoma or a differentiated liposarcoma. Haematoxylin and eosin staining (Original magnification ×40).

Discussion

Epidemiology

75% of primary cardiac tumors are benign [1] and among, cardiac lipomas constitute approximately 10%-19% of primary tumors of the heart and pericardium [2] Primary tumors of the heart remain rarely encountered in clinical practice with a reported incidence from 0.001% to 0.19% at autopsy [3,4].

Cardiac lipomas usually represent up 8.4% of all benign ones [2,5,6].

The first case of cardiac lipoma was reported in 1856 [3].

Higher estimates of up to 10% of heart tumors are likely because lipomatous hypertrophy, actually a separate entity, has been included [6,7].

Incidence of cardiac lipomas is not influenced by gender [8] and commonly occur in middle-aged and older adults. Nevertheless, it may also occur in children but account for less than 2% of the heart tumors similar to the relative incidence in adults [8].

Unlike cardiac lipomas which do not have any clear associations, lipomatous hypertrophy is seen more commonly in older, obese people and in females [9].

Rare association of cardiac lipoma with tuberous sclerosis have been reported [10].
The etiology of cardiac lipomas remains undetermined even if some cases of lipomas have translocations involving chromosome 12 [11] with abnormality in HMGA2-LPP fusion gene [12].

Histological characteristics

Histopathologically, cardiac lipoma can be classified into two types.

1. Lipomatous hypertrophy of the interatrial septum and true lipoma. The former one is a non-encapsulated mass of adipose tissue with mature adipocytes resembling brown fat cells intermixed with enlarged cardiac myocytes which is usually in continuity with the epicardial fat and occurring solely in the interatrial septum [13,14].
2. True lipomas are circumscribed masses constituted of encapsulated masses of adipose tissue, typically mature adipocytes [6,13-17].

The capsule is a major differentiation point between cardiac lipoma and lipomatous hypertrophy. The latter is usually an asymptomatic continuation of the epicardial fat, and when arising from the interatrial septum, it usually spares the fossa ovalis [4].

Unlike cardiac lipomas which do not have any clear associations, lipomatous hypertrophy is seen more commonly in older, obese people and in females [5].

Therefore, if lipomatous hypertrophy is the main differential diagnosis, the intramuscular variant of hemangioma, which may contain variable numbers of adipocytes should also be considered [18].

Half of cardiac lipomas commonly originate from the superficial epicardial adipose tissue of the right atrium (RA) and left ventricle (LV) while about the other half develop in subendocardial layers creating septal or parietal defect, septal displacement and cavitary obstructions.

When intracardiac, the most common chambers involved are LV and RA.

They may also involve the ventricular septum and cardiac valves.

Finally, they can be located throughout the heart, including pericardium, epicardium, endocardium and myocardium. According to the literature, cardiac lipoma is extremely variable in size [4-9,14].

Symptoms and potential complications

As benign and slow growing tumors with a low incidence, cardiac lipomas are frequently discovered incidentally at the time of cardiac surgery or autopsy [19] and therefore patients may remain asymptomatic for a long time [3,4] until local mass effect lead to heart dysfunction mainly depending on the location of the tumor. Symptoms are multiple and not specific such as dyspnea, asthenia, hoquet with involvement of the phrenic nerve, arrhythmia due to compression of inferior ventricular septum

[20], conductive system, or intramyocardial location [21,22], chest pain often likely resulting from coronary artery compression [23] and syncope. Life-threatening complications including sudden death [24]**,** stroke-like symptoms and pulmonary embolism are usually related to obstruction of cardiac chambers [25] or acute valve dysfunction [18]. Compression or obstruction of the superior vena cava, as observed in our case, has also been reported [26]. Our patient had no specific symptoms related to the presence of a cardiac tumor and was actually suspected to present with an acute aortic dissection. The Table 1 summarizes the correlations between locations of lipoma and symptoms.

Symptoms	Locations
Ventricular arrhythmia	Intramyocardial [3,4,19] Interventricular septum [1,6,16,19,20] Cardiac chambers [4,19,25] Coronary artery [1,6,19,21]
Atrial arrhythmia (AF, Flutter)	Compression of left atrium [7,15,19, 21]
Junctional ectopic tachycardia	Interatrial septum [4,13,14,15] Right atrium (fossa ovalis) [4,6,9,14,15,19] Proximal right coronary artery compression [1,6,19]
Syncope	Cardiac chambers [3,4,6,7,19,24] aortic valve obstruction [1,6,19,25]
Bradycardia	Proximal right coronary artery (RCA) [1,6,18,20]
Sudden death	Intramyocardial [6,19,22] Cardiac chambers [1,6,7,19,22,23,24] Coronary obstruction [1,3,4,6]
Hoquet	Compression/Displacement of phrenic nerve [21]
Dyspnea	Cardiac chambers [1,3,5,6,7,19,21,25]
Asthenia	Non-specific
Superior Vena Cava syndrome (SVC)	SVC [1,6,19] Intrapericardial [1,2,4,6,19] Rigt cardiac chambers [1,3,5,6,9,26]
Pulmonary embolism	Right cardiac chambers [1,3,5,6,9] RVOT obstruction [1,6,19]
Myocardial infarction	Obstruction of coronary artery [1,6,19,21]
Angina	Compression of coronary artery [1,6,19,21,23]
Systemic embolism	Left cardiac chambers [1,6,19,24,25] LVOT [1,6,19,24,25]

Table 1: Correlations between symptoms and locations of cardiac lipoma.

Diagnosis and characterization of the tumor

Cardiac lipomas are often incidentally discovered by cardiac echography or, like our patient, after a CT scan. Actually, four main exams are used synergistically to complete diagnosis, delineate anatomic involvement of cardiac structures and characterize the structure of the mass.

Cardiac echocardiography is a valuable initial investigation for detection and diagnosis of cardiac tumors. The echographic (TTE or TEE) appearance of cardiac lipomas directly depends on their locations. Lipomas into the pericardial space are often hypoechogenic, showing a relative echolucent shadow of right side of the heart, while intracavitary lipomas are typically echogenic [6]. The reason for this difference remains incompletely known.

Additionally, pericardial lipomas may be sometimes incorrectly diagnosed as loculated pericardial fluid [15].

Therefore, CT scan and MRI both allow for a very specific characterization of the tumor by identifying the adipose structure and definitely validate the diagnosis of cardiac lipoma.

Cardiac CT-scan is a reliable imaging tool to assess cardiac masses, particularly in patients with known contraindications to MR. CT-scan is a fast imaging method with electrocardiographic (ECG) gating that provides high quality images with high spatial resolution. Electrocardiographic gating minimizes motion-related artifacts and allows a more precise delineation of the lesion margins. Main disadvantages with CT-scan include radiation exposure, a small risk of contrast-induced nephropathy, and lower soft tissue and temporal resolutions as compared with magnetic resonance imaging [27].

Cardiac CT-scan may also be useful to detect metastases in suspected malignancies especially when coupled with 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET). The ability of 18F-FDG PET/CT to detect the increased metabolism of glucose may help distinguish malignancy from a benign neoplasm [6].

In our patient, CT-scan highlighted strong adherences of the mass with the interatrial groove leading to suspect a malignancy tumoral process. Therefore, MRI was further applied since it is the optimal imaging modality to improve characterization of the mass [27,28].

Unfortunately, in our case MRI confirmed obvious concerns of malignancy characteristics into the fatty mass strongly suspecting a liposarcomatous transformation.

Finally, despite specific advantages of MRI, such as high temporal resolution, multiplanar imaging capabilities and unrestricted field of view [28], we could not exclude the diagnosis of a liposarcoma.

Additionally, coronary angiography did not show any coronary compression or vascular relation with the mass. This latter investigation may provide ancillary useful informations as some malign tumors have blood supply originating from coronary arteries.

Surgery confirmed adherences of the tumor along the interatrial groove close to the coronary sinus. Histopathological analysis was consistent with a lipoma nevertheless presenting with few characteristics of a well-differentiated liposarcoma [6].

Finally, due to the unusual location of the infiltrative mass enhanced by MRI, surgical and histopathological malignancy suspected features and despite no MDM2 amplification following FISH, additional investigation using array-based comparative genomic hybridization (array CGH) was required. Previous publications have highlighted the major interest of array CGH to delineate the genotypes of liposarcomas [29,30].

The principle of the technique is to perform a competitive hybridization between tumoral DNA (green marked) and normal DNA (red marked) on a normal karyotype. Hence, amplified and deleted genes will respectively appear in green and red into the karyotype. This technique allows a detection of the overall amplifications and deletions as well their accurate locations within the chromosome.

In our case, the array CGH did not detect any genomic imbalances and showed no additional evidence of malignancy.

Conclusion

It is usually admitted that screening between benign and malignant tumors is quite easily obtained with imaging modalities such as echography, CT scan and MRI as well as histopathological examination.

The case herein presented is unique as it mixed imaging, surgical and histopathological properties of lipoma and liposarcoma. Despite accuracy and reliability of our investigations, we could not definitely exclude a liposarcomatous transformation within the fatty mass and definitive diagnosis of lipoma was finally ascertained by cytogenetic study. Additionally, this case provided the interesting opportunity to review the literature in order to assess the optimal management of such a rare cardiac pathology.

Conflict of Interest

The authors and planners have disclosed no potential conflicts of interest, financial or otherwise.

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