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Original contribution

Benign lipomatous masses of the heart: a comprehensive series of 47 cases with cytogenetic evaluation☆

Melanie C. Bois MD[a], John P. Bois MD[b], Nandan S. Anavekar MB, BCh[b], Andre M. Oliveira MD, PhD[a], Joseph J. Maleszewski MD[a,*]

[a]*Division of Anatomic Pathology, Mayo Clinic, Rochester, MN 55905*
[b]*Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN 55905*

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Summary Benign lipomatous lesions of the heart encompass an apparently etiologically diverse group of entities including neoplastic, congenital, and reparative phenomena. Among these, lipomas and lipomatous hypertrophy of the atrial septum (LHAS) represent 2 commonly encountered mass lesions. To date, no study has systematically and comparatively evaluated the morphologic and genetic characteristics of these lesions. Tissue registry archives of Mayo Clinic were queried for cases of cardiac lipoma and LHAS (1994-2011). Clinical, imaging, and pathologic findings were reviewed. Representative cases in each cohort were evaluated by fluorescence in situ hybridization (FISH) for *HMGA1* and *HMGA2* loci rearrangement and for *MDM2*/*CPM* locus amplification. Five cases of cardiac lipoma were identified (mean age, 67 years; range, 48-101; 3 men): 4 right atrial and 1 left ventricular. Forty-two cases of LHAS were identified (mean age, 75.6 years; range 45-95; 20 men), 39 of which were autopsy derived. The median size was 3.4 cm for lipomas and 2.8 cm for LHAS (n = 14). A single case each of cardiac lipoma and LHAS were found to harbor *HMGA2* rearrangement, whereas no case showed cytogenetic abnormality of *HMGA1* or *CPM*. This represents the largest series of histopathologically confirmed cardiac lipomas from a single institution. In addition, it is the first to evaluate cardiac lipomas and LHAS for genetic alterations associated with extracardiac lipomatous lesions. The genetic and morphologic similarities found provide evidence in support of the neoplastic classification of cardiac lipomas. A single case of LHAS contained an *HMGA2* rearrangement, challenging the currently accepted hypothesis of pathogenesis for this lesion.

1. Introduction

Benign lipomatous lesions of the heart are a diverse group of entities, representing a spectrum of etiologies, imaging characteristics, and histopathologies. Two of these lesions, commonly encountered by pathologists at autopsy or surgical resection, are lipomatous hypertrophy of the atrial septum (LHAS) and cardiac lipoma. Although both contain

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* Corresponding author. Mayo Clinic, 200 First Street SW, Rochester, MN 55905.
E-mail address: maleszewski.joseph@mayo.edu (J. J. Maleszewski).

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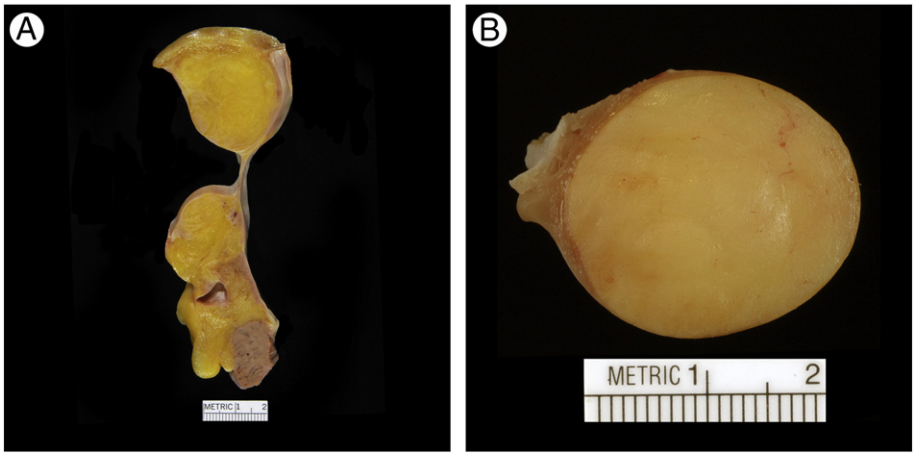

Fig. 1 Gross features of lipomatous lesions of the heart. A, LHAS is grossly characterized by a fatty thickening of the atrial septum. The involvement of the limbus of the fossa ovalis with sparing of the valve of the fossa ovalis imparts a bilobed appearance. B, Cardiac lipoma usually manifests as an encapsulated mass arising endocardially, intramyocardially, or epicardially.

mature adipocytes and generally present as mass lesions, significant differences exist between them.

LHAS was first described by Prior [1] in 1964 as a fatty expansion of the atrial septum. Grossly, it is unencapsulated and often bilobed following the contours of the limbus of the fossa ovalis (Fig. 1A). Histologically, it consists of an admixture of yellow and brown fat with entrapped, usually hypertrophic, cardiac myocytes (Fig. 2A) [2]. Its prevalence is estimated to be around 2.5% in the general population and is primarily encountered incidentally, either on imaging or at autopsy [3-5].

Cardiac lipomas, such as those found in anatomical locations outside the heart, are encapsulated neoplasms of mature adipocytes (Figs. 1B and 2B). Notably, they lack brown fat and cardiac myocytes that, along with the fibrous capsule, help to distinguish them from LHAS [6]. Although less common than LHAS, cardiac lipomas are also usually discovered incidentally on imaging, at the time of surgery, or on postmortem examination [2].

Little is known about the etiology of LHAS and cardiac lipoma. Lipomatous lesions outside the heart have been more extensively characterized. Extracardiac lipomas, for example, are often associated with disruption of 12q13-15, involving the high-mobility group protein genes *HMGA1* and *HMGA2* [7]. In addition, extracardiac liposarcomas are associated with amplification of *MDM2*, an oncogene also located on chromosome 12 [8]. It is conceivable that lipomatous lesions of the heart share common etiologic underpinnings with their extracardiac counterparts. To better characterize the nature of cardiac lipomas and LHAS, we evaluated the clinical, imaging, histopathologic, and cytogenetic features thereof.

2. Materials and methods

2.1. Case selection and review

The study was reviewed and approved by the Mayo Clinic Institutional Review Board and Biospecimens Subcommittee. Autopsy and surgical pathology archives of Mayo Clinic were queried for patients with a diagnosis of LHAS or cardiac lipoma rendered between January 1, 1994, and April 30, 2013. One case of fatty infiltration of the right ventricular wall (FIRV) was also identified from age-matched autopsy specimen to serve as a cytogenetic control. Pathology reports, gross specimens, and hematoxylin and eosin–stained sections (when available) were reviewed for diagnostic confirmation by a cardiovascular pathologist (J.J.M.). For a diagnosis of LHAS, a minimal gross atrial septal thickness of 1.5 cm was used, in the appropriate gross and histologic context. For each case, the patient's age at the time of diagnosis, sex, lesion location, and clinical circumstances (incidental or symptomatic) were recorded. Tumor size was documented from the original pathology reports and also evaluated radiologically (see below) when imaging studies were available.

2.2. Imaging

Transthoracic echocardiography, transesophageal echocardiography (TEE), computed tomography (CT), and magnetic resonance imaging (MRI) images were (when available) reviewed by a cardiac imager (N.S.A.) to document radiologic tumor size, location, morphology, and character. For cases of LHAS, maximal lesional thickness was measured in a 4-chamber, long-axis orientation. When the latter was not possible, the best oblique plane that exhibited the lesion was used.

2.3. Cytogenetics

A representative subset of each cohort was cytogenetically evaluated for molecular alterations commonly associated with extracardiac lipomatous lesions: *HMGA1* and *HMGA2* loci rearrangement via break-apart probes as well as *MDM2*/*CPM* locus amplification via enumeration probes. Six representative cases of LHAS and 4 representative cases