

Review Article



Multi Modality Imaging Features of Cardiac Myxoma

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Conflict of Interest

The authors have no financial conflicts of interest.

ABSTRACT

Primary cardiac neoplasms are rare entities of which approximately 75% are benign and the remaining 25% malignant. Myxomas are the most common benign primary cardiac tumor (30%) and most commonly arise in the left atrium from the interatrial septum at the fossa ovalis. However, they also can originate in any cardiac chamber. Clinical presentation and patient symptomatology are determined by size, location, and mobility of the myxoma. This review will discuss the clinical presentation, natural history, pathology, and multimodality imaging features of cardiac myxomas.

Keywords: Cardiac myxoma; Cardiac mass; Multimodality imaging

INTRODUCTION

Primary cardiac neoplasms are rare entities (0.001%-0.3% of autopsies) of which approximately 75% are benign and the remaining 25% malignant.¹⁾

Myxomas are the most common benign primary cardiac tumor (30%). Other less common benign entities include papillary fibroelastoma, fibroma, rhabdomyoma, haemangioma, lipoma and paraganglioma. On the malignant spectrum, the most common is sarcoma (75%), followed by secondary metastases.¹⁾ Primary cardiac lymphoma and pericardial mesothelioma are both rare entities.

In patients with myxoma, there is a broad range in the age of presentation (11-82 years). Most present in adulthood (mean 50 years), and there is a female predominance.²⁾ Ninety percent of cases are sporadic. The remaining 10% are associated with Carney syndrome where the patients happen to be younger (mean 24 years) and usually men (66% vs 24% sporadic).³⁾ Cardiac myxoma is one of the major diagnostic criteria for diagnosis of this complex, requiring two or more major diagnostic criteria and/or by identification of a heterozygous germline pathologic variant in PRKAR1A on molecular genetic testing (**Table 1**).⁴⁾

Myxomas most commonly arise in the left atrium (LA) from the interatrial septum at the fossa ovalis, however they may originate in any cardiac chamber (75% LA, 20% right atrium [RA], rarely right ventricle or left ventricle). Less common locations include the posterior atrial

Table 1. Diagnostic criteria for carney complex

Major criteria

1. Spotty skin pigmentation with typical distribution (lips, conjunctiva and inner or outer canthi, vaginal and penile mucosal)
2. Myxoma* (cutaneous and mucosal) or cardiac myxoma*
3. Breast myxomatosis* or fat-suppressed magnetic resonance imaging findings suggestive of this diagnosis
4. Primary pigmented nodular adrenocortical disease* or paradoxical positive response of urinary glucocorticosteroid excretion to dexamethasone administration during Liddle's test
5. Acromegaly as a result of growth hormone (GH)-producing adenoma*
6. Large-cell calcifying Sertoli cell tumour* or characteristic calcification on testicular ultrasound
7. Thyroid carcinoma* (at any age) or multiple hypoechoic nodules on thyroid ultrasound in prepubertal child
8. Psammomatous melanotic schwannomas*
9. Blue nevus, epithelioid blue nevus (multiple)*
10. Breast ductal adenoma (multiple)*
11. Osteochondromyxoma*

Supplemental criteria

1. Affected first-degree relative
2. Activating pathogenic variants of PRKACA (single base substitutions and copy number variation) and PRKACB
3. Inactivating mutation of the PRKARIA gene

Minor criteria (findings suggestive of or possibly associated with carney complex, but not diagnostic for the disease)

1. Intense freckling (without darkly pigmented spots or typical distribution)
2. Blue nevus, common type (if multiple)
3. Café-au-lait spots or other 'birthmarks'
4. Elevated IGFI levels, abnormal glucose tolerance test, or paradoxical GH response to thyrotropin-releasing hormone testing in the absence of clinical acromegaly
5. Cardiomyopathy
6. History of Cushing's syndrome, acromegaly or sudden death in extended family
7. Pilonidal sinus
8. Colonic polyps (usually in association with acromegaly)
9. Multiple skin tags or other skin lesions; lipomas
10. Hyperprolactinemia (usually mild and almost always combined with clinical or subclinical acromegaly)
11. Single, benign thyroid nodule in a child younger than age 18 years; multiple thyroid nodules in an individual older than age 18 years (detected on ultrasound examination)
12. Family history of carcinoma, in particular of the thyroid, colon, pancreas and ovary; other multiple benign or malignant tumors

To make the diagnosis of carney complex, a patient must either (1) exhibit two of the major criteria confirmed by histology, imaging or biochemical testing or (2) meet one major criterion and one supplemental one.¹¹⁾

*With histologic confirmation.

wall, anterior atrial wall, and atrial appendage. Very rarely they may occur on the heart valves. Multiple tumors and atypical locations are more frequent in cases of familial myxoma.⁵⁾

This paper will review the clinical presentation, natural history, and pathology of cardiac myxomas and provide an overview of imaging features.

CLINICAL PRESENTATION

Clinical presentation and patient symptomatology are determined by the size, location and mobility of the myxoma.

Most patients present with one or more of the triad of (1) embolization, (2) intracardiac obstruction, and (3) constitutional symptoms,⁵⁾ therefore, presentation may mimic infective endocarditis.

The most common symptom relates to valvular obstruction and occurs in approximately 50% of patients. Systolic murmurs may occur if there is interference with closure of the atrioventricular (AV) valves or ventricular outflow tract narrowing; diastolic murmurs are due to obstructed ventricular filling. Valvular obstruction may also result in heart failure, syncope or sudden death.

Polypoid and extensively myxoid lesions, or those that are irregular are more likely to form surface thrombi with subsequent embolization, the second most common manifestation of myxoma occurring in 30%–40% of patients.²⁾ Embolization may result in central nervous system symptoms including transient ischaemic attacks, stroke or seizure; visceral infarction and pulmonary embolism may also occur.

Constitutional symptoms including weight loss, malaise, fever, arthralgia and myalgia are due to tumor production of IL-6. There is a positive correlation between tumor size and IL-6 production levels; in addition, the higher the IL-6 levels, the more intense the constitutional symptoms.⁶⁾

Twenty percent of cases are asymptomatic.²⁾

NATURAL HISTORY

Because myxomas are usually excised following diagnosis, their rate of growth is generally unknown. Previous case reports have demonstrated lesion stability on serial imaging up to a period of 15 years,⁷⁾ with growth rates of up to 1.36×0.27 cm/month.⁸⁾

HISTOPATHOLOGY

Myxomas are neoplasms of endocardial origin, projecting into the cardiac chamber.

They are generally polypoid, often pedunculated, rarely sessile, and round or oval with a smooth or gently lobulated appearance. The less common villus type has friable, frond like contours, which have a greater propensity for fragmentation and subsequent embolization.⁹⁾ Most are 5-6 cm, and can range from 1-15 cm in diameter (**Figure 1**).⁵⁾

Myxomas are composed of stellate or globular myxoma cells with abundant eosinophilic cytoplasm, indistinct cell borders, oval nucleus with open chromatin and indistinct nuclei (**Figure 2**). Myxoma cells form complex structures including rings, syncytia, and cords that are typically infiltrated by lymphocytes and macrophages.²⁾



Figure 1. Excised left atrial cardiac myxoma with a pedicle.

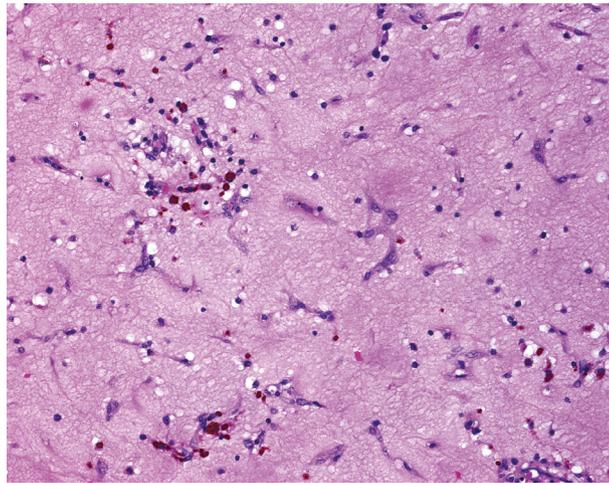


Figure 2. H&E stain: stellate cells in abundant myxoid matrix (image used with permission of WebPathology)

Histologically, myxomas may exhibit variable fibrosis (41%), calcification (20%), Gamna-Gandy bodies (17%), ossification (8%), extramedullary hematopoiesis (7%), mucin forming glands (3%), atypia (3%), and/or thymic rests (1%).¹⁰

IMAGING FEATURES

Echocardiogram

Echocardiogram is typically the primary imaging modality with high sensitivity and specificity, allowing to assess the size, morphology, attachment site, mobility and haemodynamic consequences of the tumor.

Trans-oesophageal echocardiogram (TOE) is superior to trans-thoracic echocardiogram (TTE), providing more detailed evaluation,² particularly with smaller lesions.

Myxomas manifest as spherical masses attached to the endocardial surface, with occasional internal hypoechoic areas, speckled echogenic foci (**Figure 3A**), and frond-like surface projections.² Areas of calcification are typically echogenic (**Figure 4A**); Doppler images may demonstrate internal flow (**Figure 5B**), particularly in those with capillary-like channels that communicate with the surface of the myxoma.⁵

Echocardiogram contrast agents may be useful to assess vascularity of the tumor, with highly vascular lesions demonstrating hyper-enhancement. Real-time three dimensional (3D) echocardiogram allows for a volumetric assessment of a mass over a linear measurement as it is obtained with 2-dimensional imaging. With the cropping techniques available with 3D, various aspects of the mass can be better visualized including point of attachment, homogeneity, vascularity, and calcification.¹¹

Limiting factors of echocardiogram include a narrower field of view compared to computed tomography (CT) and magnetic resonance imaging (MRI), a poor acoustic window, and artifacts that may be misinterpreted as pathology.

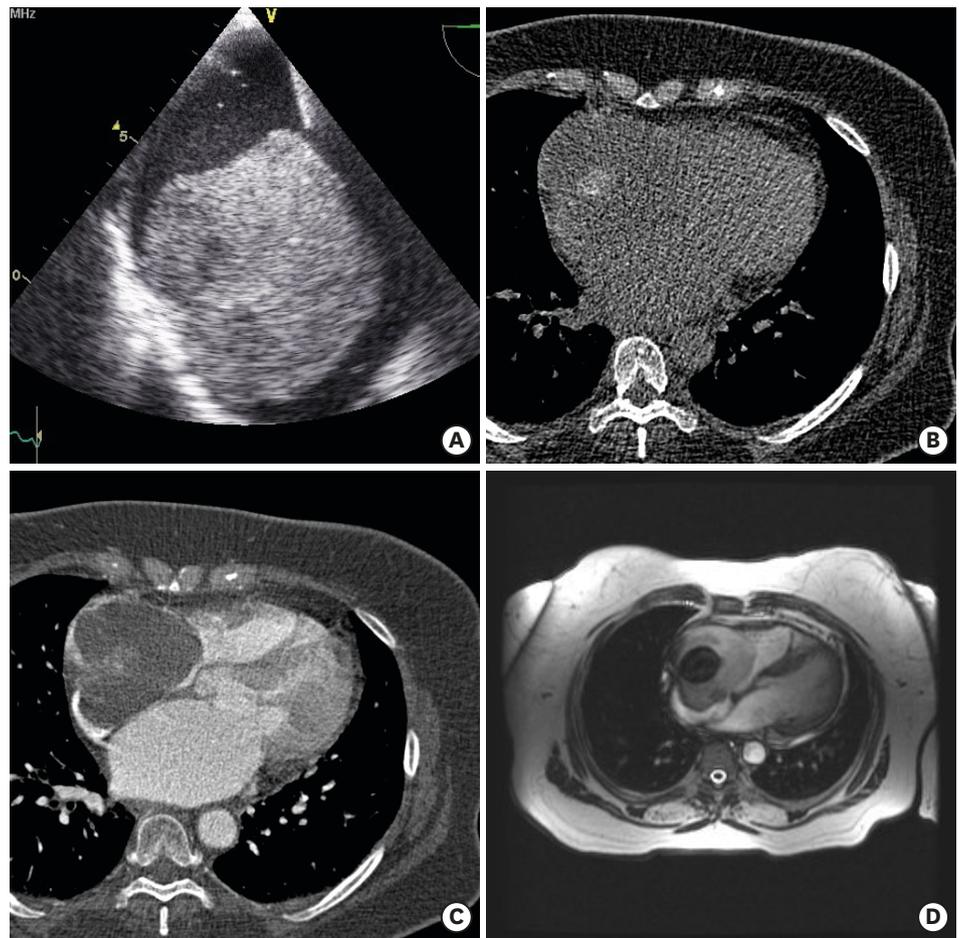


Figure 3. (A) TTE demonstrates the large right atrial mass with small, speckled echogenic foci, prolapsing in to the right ventricle and bulging the inter atrial septum to the left. (B) Right atrial myxoma is slightly lower attenuation than blood pool, and is heterogenous in density secondary to calcification; (C) post contrast CT better demonstrates the massive myxoma attached by a pedicle to the posterior wall of the right atrium. The mass occupies almost the entire chamber. There is minimal contrast enhancement; (D) corresponding T2 MRI demonstrating central low signal secondary to calcification. The remainder of the mass is of high signal intensity; CT: computed tomography, MRI: magnetic resonance imaging, TTE: trans-thoracic echocardiogram.

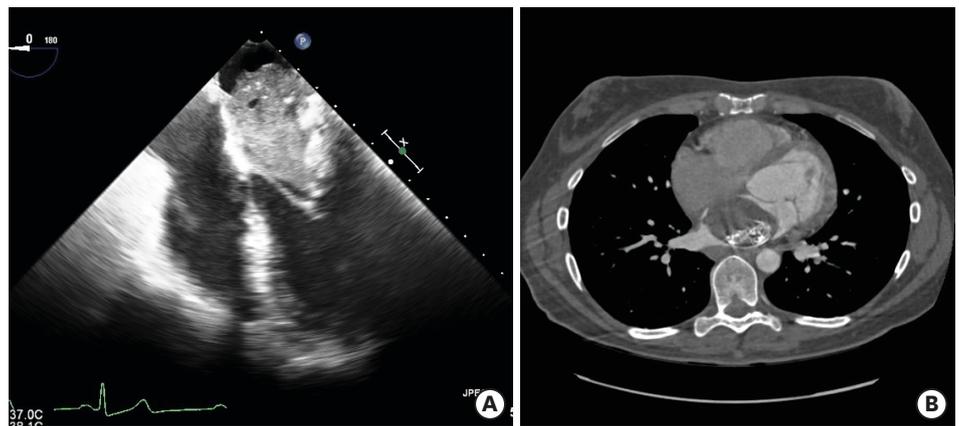


Figure 4. (A) TOE demonstrating hyperechoic foci corresponding to the calcification on CT. There is mild prolapse through the mitral valve leaflets during diastole. (B) Post contrast CT chest demonstrating a large left atrial myxoma attached to the interatrial septum at the level of the fossa ovalis. High density in the posterior aspect of the mass is secondary to calcification. CT: computed tomography, TOE: trans-oesophageal echocardiogram.

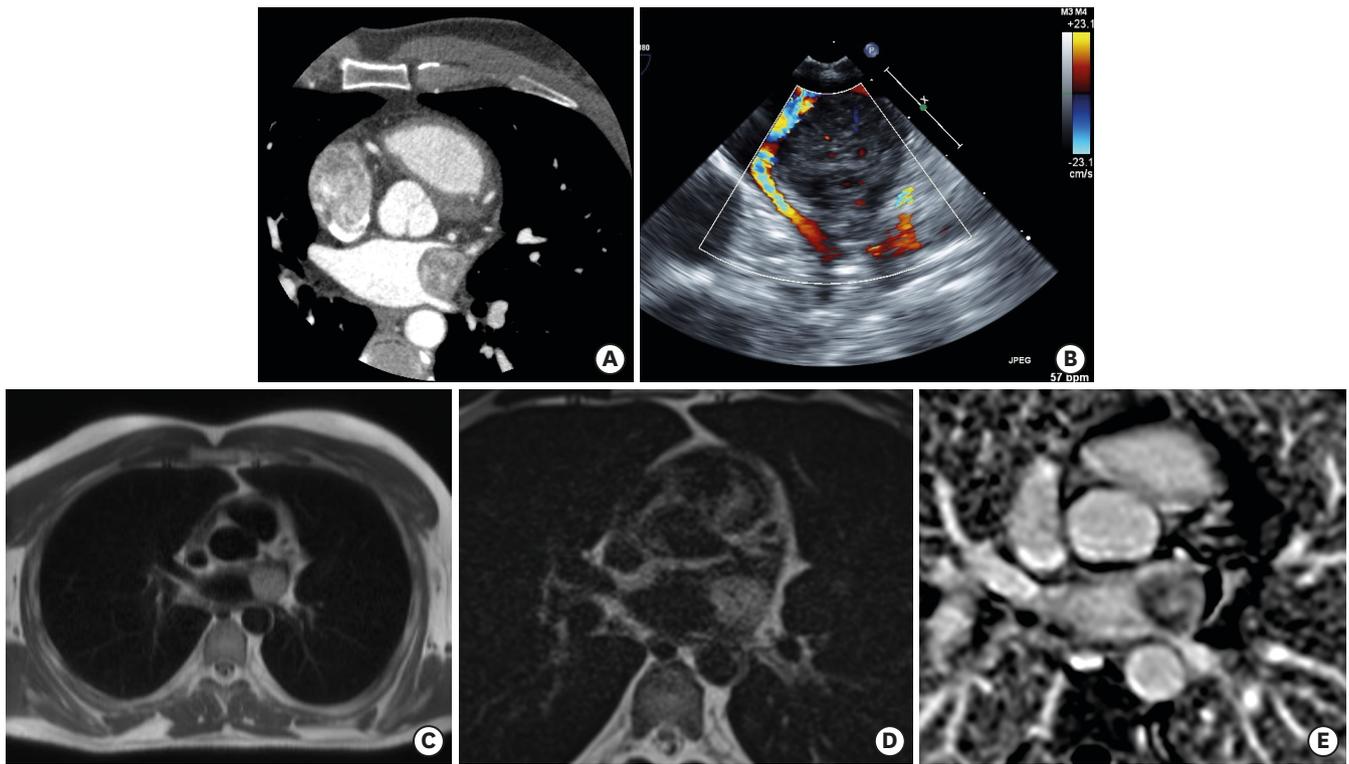


Figure 5. (A) Cardiac CT with a heterogenous mass at the base of the left atrial appendage with foci of contrast density, seen with capillary-like channels that communicate with the surface of the myxoma; (B) TOE Doppler showing small areas of flow within the myxoma; (C) T1 and (D) black blood MRI images, the mass is hyperintense; (E) central contrast enhancement on LGE helps to distinguish this tumor from thrombus. CT: computed tomography, LGE: late gadolinium enhancement, MRI: magnetic resonance imaging, TOE: trans-oesophageal echocardiogram.

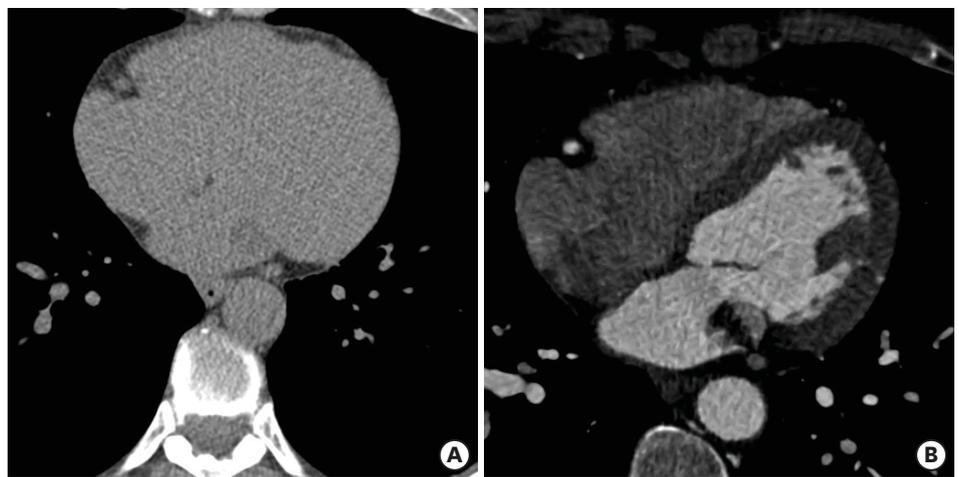


Figure 6. (A) Non contrast cardiac computed tomography with myxoma arising from the posterior wall of the left atrium, contacting the posterior mitral valve leaflet. Note the density of the mass is lower attenuation than blood pool. (B) Contrast enhanced image performed in diastole. The mitral valve is open, there is no prolapse of the mass into the left ventricle. There was mild enhancement.

Computed tomography

On non-contrast CT, tumor attenuation is typically lower than non-opacified blood (**Figure 6A**). Myxomas often appear heterogenous due to hemorrhage, calcification/ossification (**Figures 3B, 3C, and 4**), necrosis, cyst formation or fibrosis. Tumors may visibly enhance post contrast administration, but typically enhancement is less evident than with MRI

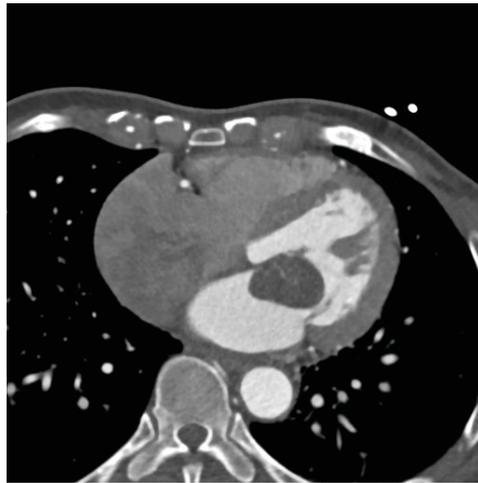


Figure 7. Cardiac computed tomography. Left atrial myxoma contacting the anterior leaflet of the mitral valve, prolapsing in to the left ventricle during early diastole.

Table 2. MRI protocol for suspected cardiac mass

MRI protocol
Localiser images
4-chamber/3-chamber/2-chamber long axis cine SSFP sequences
Cine SSFP images in 2 planes oriented perpendicular to the lesion
T1/T2/T2FS black blood imaging sequences in 2 planes oriented perpendicular to the lesion
Short axis LV stack cine SSFP (optional)
First pass perfusion imaging in 2 perpendicular planes through the lesion
LGE in at least 2 planes oriented perpendicular to the lesion

FS: fat saturated. LGE: late gadolinium enhancement. LV: left ventricle. SSFP: steady state free procession.

(**Figure 6B**) and can be difficult to appreciate due to surrounding high contrast blood pool. Dual energy CT with mean iodine concentration is an accurate approach for defining whether a cardiac mass visibly enhances.¹²⁾

Functional retrospective cardiac CT is able to demonstrate tumor mobility (**Figure 7**).

Magnetic resonance imaging

MRI is the modality of choice for evaluation and assessment of cardiac tumors due to its superior tissue characterization and ability to aide in differential diagnosis. With cine and phase contrast sequences, one is able to assess the functional impact of the mass. See **Table 2** for a standard MRI protocol for patients with suspected cardiac myxomas.¹²⁾

Myxomas can be substantially variable in appearance and of heterogenous signal intensity on MRI owing to myxoid tissue, fibrous tissue, blood and calcification.

T1 and T2 weighted double inversion recovery fast spin echo sequences with nulling of the blood pool in relation to the myocardium (“black blood”) and black blood fat saturated T2 weighted sequences are able to assist tissue characterization.⁹⁾ On T1 the tumors are usually iso-intense to myocardium (intermediate signal intensity), and occasionally hyperintense.

Myxomatous components are low on T1, high on T2.²⁾ Low signal on both T1 and T2 may be due to calcification (**Figure 3D**); haemorrhage within the tumor is variable in signal, depending on age.

Late gadolinium enhancement sequences performed 10-15 minutes after contrast administration are helpful to differentiate these tumors from thrombus, particularly if they arise in the LA appendage (**Figure 5E**). Enhancement is typically heterogenous, and areas of enhancement have been shown to correspond with regions rich in myxomatous tissue and focal inflammation.⁹⁾ There may be non-enhancing areas secondary to internal cysts or necrosis. First pass perfusion studies may demonstrate mild heterogenous enhancement.

An additional sequence that can aid in the differentiation between myxoma and thrombus is inversion time (TI). TI varies between patients but is typically approximately 300 ms, depending on the cardiac output and time after contrast injection.¹³⁾ Compared with normal myocardium, Pazos-López et al.¹⁴⁾ found the majority of thrombi (94%) tend to be hyperintense/isointense with short TI (150 ms), and hypointense with long TI (500 ms); tumors rarely follow this pattern of signal (2%).

Cine steady state free precession images are useful in the functional assessment of the myxoma, as mobile lesions can prolapse through the AV valve during diastole.

If there is associated mitral valve obstruction, features such as LA enlargement and pulmonary venous hypertension with pulmonary vascular redistribution and pulmonary oedema may be seen on radiographs, CT and MRI.

CONCLUSION

Myxomas are the most frequently diagnosed primary cardiac tumor. They have characteristic imaging features that may frequently suggest the diagnosis and aid in differentiating these lesions from other intracardiac masses, facilitating the choice of appropriate therapeutic management.

Whilst echocardiogram can readily assess cardiac myxomas and suggest the diagnosis in many cases, further imaging with contrast enhanced CT and MRI is beneficial in providing greater anatomical detail for surgical planning. MRI is most useful for differential diagnoses, the most common of which include metastases and thrombus, as well as other primary benign and malignant neoplasms, and valvular vegetations. Once diagnosed, treatment consists of urgent surgical excision due to potential life threatening sequelae including embolic complications and sudden cardiac death. Surgical excision has excellent long-term prognosis and low risk of recurrence.²⁾

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