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CARDIAC TUMOR

In vivo detection of encapsulated intracardiac paraganglioma by delayed gadolinium enhancement magnetic resonance imaging

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Intracardiac paragangliomas are rare endocrine tumors that are usually benign and can be cured by surgical resection. Both invasive and encapsulated forms have been described and degree of invasion determines surgical complexity. We present in vivo detection of fibrotic encapsulation in a cardiac paraganglioma using delayed enhancement (DE) cardiac magnetic resonance imaging (CMRI), later confirmed on pathology. This finding improved presurgical risk assessment and helped guide management. Tumor necrosis was also easily identified. DE appears useful in the assessment of intracardiac tumor invasion.

Key Words: Delayed enhancement; Encapsulated; Gadolinium; Magnetic resonance imaging; Paraganglioma

1. Introduction

Pheochromocytomas are rare, catecholamine-secreting neoplasms of neuroectodermal origin that usually arise from the adrenal medulla. Excess catecholamine production (primarily norepinephrine) can result in hypertension, arrhythmias, and heart failure (1). In 90% of cases, the tumors are benign and often can be cured with surgery. However, if left undiagnosed or improperly treated, they can be fatal. Pheochromocytomas have thoracic origin in 2% of cases, of which only a small fraction are intracardiac (2, 3). Fewer than 50 cases of cardiac pheochromocytomas have been reported in the literature worldwide with most arising from visceral autonomic paraganglia of the atria or interatrial septum (4). These extra-adrenal tumors are also termed paragangliomas.

Nearly all reported cases of intracardiac paragangliomas are benign and appear sporadically without association to other syndromes (4). In most cases, they arise from the left atrium and receive blood supply from the left coronary system. Unlike typical benign adrenal pheochromocytomas, tumors with intracardiac origin are often infiltrative and densely adherent to myocardium. Infiltrative tumors result in more complex surgery and, in some cases, cardiac transplantation may be necessary (5–7). However, encapsulated intracardiac paragangliomas have also been reported and may result in less complicated excisions with more limited reconstruction (8, 9). As a result, a preoperative evaluation differentiating encapsulated from invasive tumor types has potential to contribute significantly to surgical risk assessment and to guide management.

2. Case study

2.1. *Tumor diagnosis*

A 54-year-old white male presented with complaints of intermittent chest pain and dyspnea on exertion. Past history was remarkable for mild hypertension treated with an angiotensin-converting enzyme inhibitor (ACE-I). Exam and electrocardiogram were essentially unremarkable. Echocardiogram revealed a large, right-sided intracardiac mass compromising the right atrium (RA) measuring greater than 5 cm. The mass was further evaluated on computed tomography (CT) and described as a large, 6 cm contrast-enhancing cardiac mass located in the right atrioventricular

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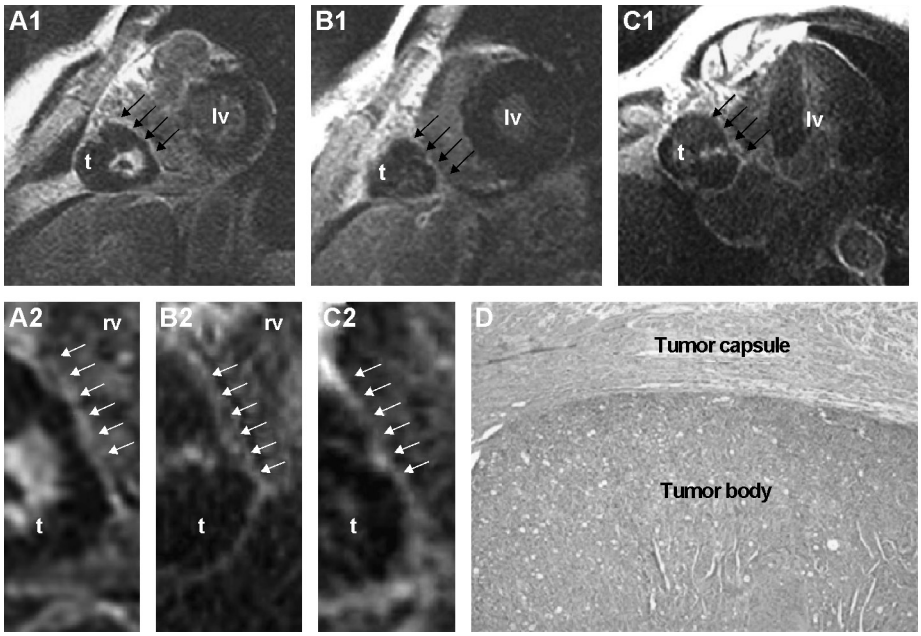

Figure 1. Encapsulated cardiac paraganglioma on DE CMRI. Basal and mid short-axis and four-chamber long-axis cardiac views shown left to right (**A1–C1**) and on magnification (**A2–C2**). Arrows in black and white show thin rim of fibrotic contrast-enhancement at tumor interface with myocardium. Histologic section stained with H&E demonstrate well defined fibrovascular tumor capsule (**D**). Tumor (**t**), left ventricle (**lv**), and right ventricle (**rv**) are marked for orientation.

(AV) groove. While undergoing coronary angiography as part of the preoperative evaluation, the patient developed marked hypertension with blood pressure of 270/103 and was admitted to the ICU with hypertensive urgency. During a secondary work-up for hypertension, 24-hour urine excretion of norepinephrine was increased 46-fold and normetaneprine was increased 16-fold above the upper limits of normal. Abdominal CT was normal. I-131 labeled meta-iodo-benzyl-guanidine (MIBG) scintigraphy revealed positive uptake within the cardiac mass and negative in all other locations including the adrenal glands. Further characterization of the intracardiac mass was performed by cardiac MRI including DE to specifically evaluate for tumor invasion and encapsulation. The patient was diagnosed with a primary intracardiac paraganglioma, which was later confirmed on pathology.

2.2. *Cardiac magnetic resonance imaging*

MR images were acquired with a 1.5-T MR scanner (Signa CV/i, GE Medical Systems, Milwaukee, WI), a cardiac multicoil array, ECG-gating, and breath holds. Selected sequences included steady-state free precession (SSFP) cine,

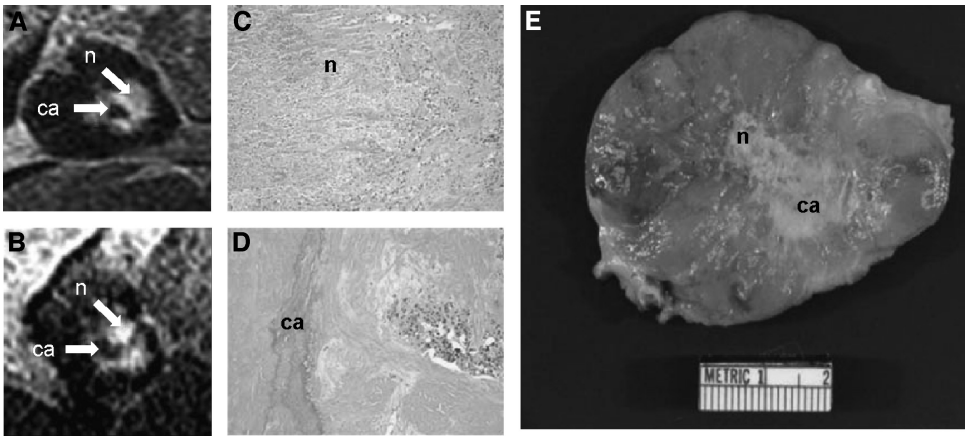

Figure 2. Necrotic tissue deep within tumor and adjacent calcified core on DE CMRI with pathology correlations. Region of tumor necrosis (**n**) is seen bright and calcification (**ca**) dark on CMRI basal short-axis (**A**) and four-chamber long-axis (**B**) views. H&E histologic sections (**C, D**) and gross specimen (**E**) confirmed MRI findings.

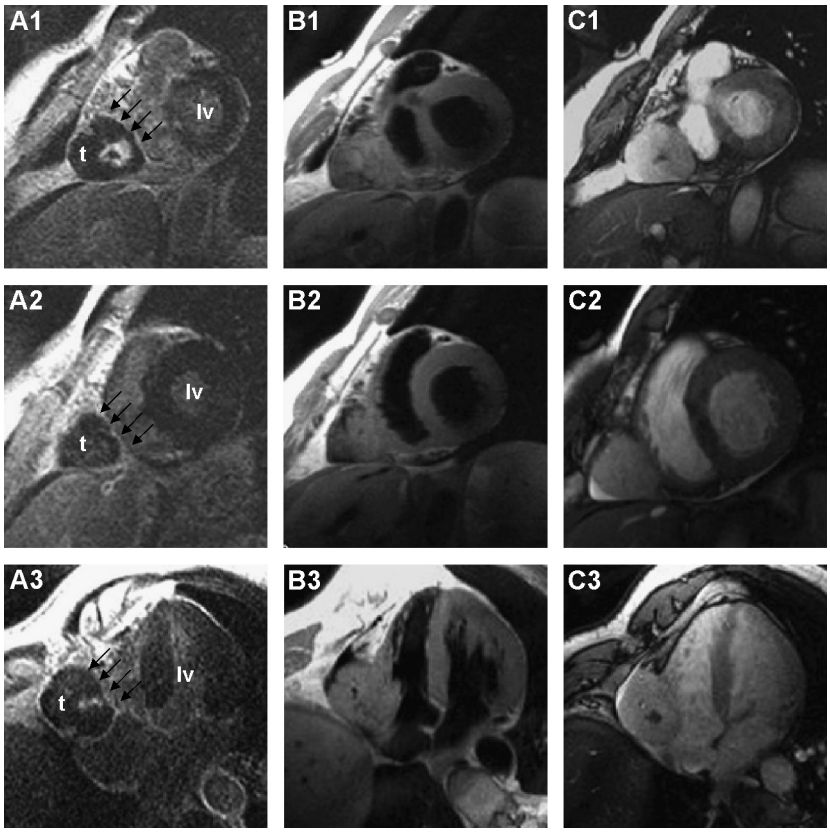

Figure 3. Encapsulated cardiac pheochromocytoma compared on DE, DIR, and SSFP sequences. Black arrows reveal thin rim of fibrotic contrast-enhancement at tumor-heart interface on DE (**A1**, **A2**, **A3**) not seen on similar slices on DIR (**B1**, **B2**, **B3**) or SSFP (**C1**, **C2**, **C3**). Basal (**A1**, **B1**, **C1**) and mid (**A2**, **B2**, **C2**) short axis and four-chamber long-axis (**A3**, **B3**, **C3**) cardiac views are shown. Tumor (**t**) and left ventricle (**lv**) are marked for orientation.

segmented fast spin-echo double inversion recovery (FSE-DIR), fast gradient-echo train (FGRET) dynamic first-pass perfusion, and delayed enhancement (DE). DE images were acquired 15 minutes after 0.2 mm/kg gadolinium-DTPA (Omniscan) intravenous injection.

2.2.1. *Tumor encapsulation and necrosis on DE*

DE revealed a thin, circumferential rim of contrast-enhanced tissue on the tumor's outer surface consistent with the presence of fibrosis. This outer layer of contrast-enhancement was seen in multiple imaging planes and suggested the tumor was encapsulated. The tumor appeared to have a clearly defined border with the myocardium in the right AV groove without invasion into the right ventricle (RV) or tricuspid annulus (Fig. 1, A–C). These findings on DE contributed significantly to the presurgical risk assessment and surgical approach. Histological analysis later confirmed that the tumor was indeed partially encapsulated by a fibrovascular outer layer and clearly distinct from the myocardium (Fig. 1, D).

A second, more prominent region of contrast-enhancement was seen deep within the tumor mass consistent with necrosis. This wide, irregular mass of contrast-enhancing tissue had necrotic features similar to those typically seen in infarcted myocardium on MRI myocardial viability studies, while

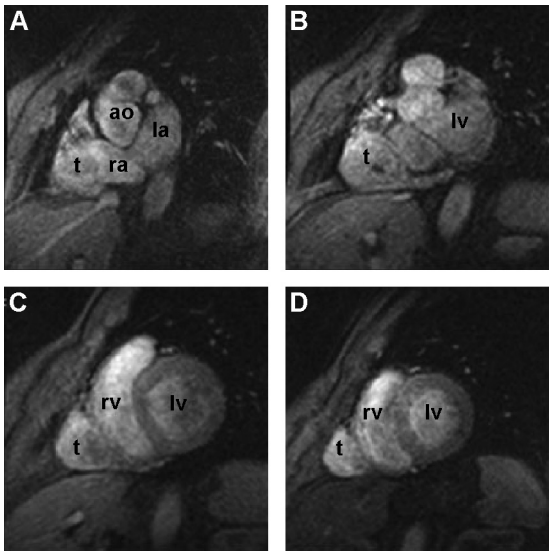

Figure 4. Tumor vascularity with dynamic perfusion FGRET. Perfusion images were acquired only seconds after Gd injection and show a highly vascularized tumor with contrast-enhancement similar to the LV myocardium. There is no obvious tumor capsule. Cardiac short-axis views are shown at atrial level through mid ventricle (**A**–**D**). Left atrium (**la**), aorta (**ao**), right ventricle (**rv**), left ventricle (**lv**), and tumor (**t**) are marked for orientation.

viable tissue appeared nonenhancing. In addition, all sequences including DE, showed the tumor core dark and void of signal consistent with the presence of calcium (Fig. 2, A and B; Fig. 3). Pathologic examination confirmed each of these MRI tissue findings (Fig. 2, C–E).

2.2.2. *Other anatomy on MRI*

Cardiac MRI provides accurate description of tumor anatomy and its relationship to surrounding structures without limitation in the imaging plane. In this case, tumor location, size, and relationship to adjacent cardiovascular structures were accurately assessed by SSFP cine and FSE-DIR sequences. The tumor, measuring up to 6.5 cm, was clearly intrapericardial and adherent to the heart surface in the right AV groove. The tricuspid valve appeared to be functioning normally on cine imaging. MR signal from the tumor was similar to myocardium on both sequences and there was no distinction of the tumor fibrotic capsule as was shown on DE (Fig. 3). Furthermore, first-pass dynamic perfusion with FGRET, acquired prior to DE, revealed a highly vascularized tumor involving the right coronary artery (RCA) with tumor contrast enhancement similar in intensity to that of the left ventricular (LV) myocardium (Fig. 4). As on FGRET, contrasted CT images also showed tumor enhancement (Fig. 5) but a distinct tumor capsule was not obvious on either of these studies.

2.3. *Surgical data*

Intraoperatively, the tumor clearly involved the right atrial wall and encased the RCA. The entire mass was excised en bloc with margins of the RA wall. The RV remained largely intact and there was no tumor involvement of the tricuspid annulus. A pericardial patch was used to reconstruct the resected portion of the RA and an interposition vein graft was placed in the RCA.

2.4. *Pathology*

The neoplasm measured 6.7 × 6.5 × 3.5 cm and was homogenous tan-brown. On gross specimen, calcification and necrosis were evident centrally. Histologic analysis revealed a paraganglioma that was partially encapsulated by a fibrovascular outer layer and clearly distinct from the myocardium. Additional H&E findings included central regions of tumor necrosis and calcification (Figs. 1D and 2C–D).

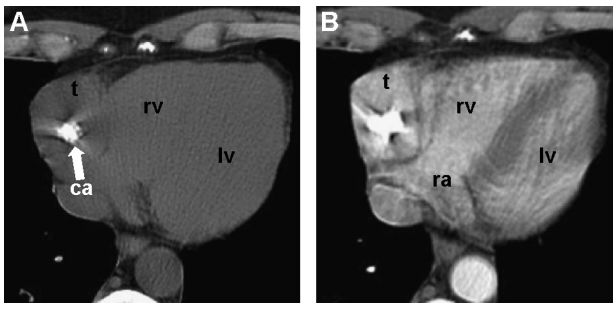

Figure 5. Tumor anatomy on CT. Axial noncontrast (**A**) and contrast (**B**) CT images highlight tumor calcification and vascularity. No obvious tumor capsule is seen as on DE MRI images. Cardiac chambers and pathology are marked as on previous figures.

3. Discussion

Cardiac MRI plays a valuable role in the diagnosis and management of cardiac tumors. Accuracy in tumor size, location, and involvement with surrounding structures is made possible by its excellent spatial resolution and ability to image in any plane. In addition, various tissue characteristics can be determined with an array of imaging sequences to help further determine likely tumor type. Use of gadolinium (Gd) contrast is routinely used to detect tumor vascularity and results in differential enhancement of tumor and myocardium (due to variations in vascularity, capillary permeability, and extracellular space), thereby improving detection of intramural tumors and extent of invasion (10). Similarly, Gd contrast kinetics also allow for differentiation of avascular tissues such as thrombi or tumor infarct, which may appear as nonenhancing regions on MRI (11, 12). However, reported use of delayed Gd-enhancement for characterization of cardiac tumors is more limited. Funari et al. demonstrated regions of high signal intensity on DE in a biopsy-proven intracardiac fibroma (10). But, to our knowledge, data on clinical utility for DE in the detection of tumor encapsulation or tumor infarction has not been presented.

Images acquired with SSFP, FSE-DIR, and FGRET as described above provided detailed anatomical information and assessment of tumor involvement with surrounding structures. However, these pulse sequences did not suggest encapsulation was present. The tumor capsule was evident only on DE, which revealed a clearly enhanced, circumscribed, fibrous capsule later confirmed on histology. The encapsulated rim was enhanced 220% over the myocardium on signal intensity plots (Image J) and was easily distinguished on visual examination. Though cardiac paragangliomas are more often characterized as invasive, DE in this case reliably identified encapsulation, suggesting the tumor would be more easily "shelled out" at surgery. Subsequent surgical results validated the preoperative MRI findings.

Tumor necrosis can be detected on MRI and is a common feature seen in paragangliomas (13, 14). Published reports describe necrosis as nonenhancing areas on MR contrast-enhanced T1-weighted imaging or as areas hypo-intense to surrounding tumor on T2-weighted imaging (12–14). In this case, a relatively large region of necrosis was easily identified on DE with appearance similar to necrotic myocardium seen on routine MRI myocardial viability studies. Though we did not evaluate the paraganglioma with the traditional T2-weighted or contrast-enhanced T1-weighted imaging for

comparison, our findings raise the possibility of improved detection of tumor necrosis using DE.

Central foci of calcification within cardiac paragangliomas have been seen on CT scanning and confirmed after tumor excision (13). Though CT is highly sensitive for calcium, MRI can also detect calcium. In this case, tumor core calcification was clearly identified as a dark signal void on all of the selected MRI sequences, which correlated with the CT images and histologic sections from that region.

4. Conclusions

Though tissue characterization with DE imaging has been well established for detecting myocardial fibrosis and necrosis, its reported use for imaging in cardiac tumors is limited and, to our knowledge, has not been used to identify tumor encapsulation or tumor necrosis as demonstrated here. In this case, in vivo evidence of a tumor capsule provided important presurgical data by indicating minimal tumor involvement with myocardial tissue. Future studies using DE imaging for cardiac (and possibly other organ) tumors will help to clarify its reliability for detecting tumor encapsulation. In addition, encapsulated tumors may be less likely to metastasize or result in local recurrence, which would add further significance to improved in vivo assessment of tumor invasion.

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