Case Report

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대한영상의학회지

A Rare Case of Cardiac Neurofibroma in a Patient with Neurofibromatosis Type 1: Radiologic Findings

신경섬유종증 1형 환자에서 드물게 발생하는 심장 신경섬유종: 영상의학적 소견

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Neurofibromatosis type 1 (NF1) is a relatively common inherited disorder characterized by the formation of neurofibromas, pigmentary abnormalities of the skin, Lisch nodules of the iris, and skeletal abnormalities. Multiple cutaneous neurofibromas are benign nerve sheath tumors and the main manifestation of NF1. Cardiac neurofibroma associated with NF1 is very rare, and few cases have been reported in the literature. Herein, we present the CT and MRI findings of a surgically confirmed left ventricular neurofibroma in a 32-year-old female with NF1.

Index terms Neurofibromatosis Type 1; Neurofibroma; Computed Tomography, X-Ray; Magnetic Resonance Imaging

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INTRODUCTION

Neurofibromatosis type 1 (NF1), also known as von Recklinghausen disease, is the most common phakomatosis or neurocutaneous disorder (1, 2). NF1 is characterized by the formation of neurofibromas and abnormalities related to mesodermal dysplasia. Moreover, it affects multiple organ systems, with skeletal abnormalities seen in up to 50% of patients (1). Neurofibromas are benign tumors that arise from peripheral nerve sheaths. Although neurofibromas are found mostly in the skin and subcutaneous tissue, deeper anatomical structures of many organs may be involved.

Paravertebral and anterior mediastinal regions in the thorax, and retroperitoneal, para-psoas, mesenteric, and paraspinal regions in the abdomen and pelvis are the commonly affected sites of neurofibromas (2). It rarely occurs in the heart. Few cases of cardiac neurofibromas have been reported in literature, and these cases were studied using

echocardiography and MRI only (3-9). Of these, four cases were associated with NF1 (4, 6-8). Herein, we present the CT and MRI findings of a left ventricular neurofibroma in a patient with NF1.

CASE REPORT

A 32-year-old female with NF1 was admitted in our hospital for the evaluation of pericardial effusion on breast ultrasound. She presented with exertional dyspnea that persisted for 2 weeks. On physical examination, her breath sounds were clear and the heartbeat was regular, without murmur. Electrocardiography revealed a normal sinus rhythm and a non-specific T-wave abnormality. A chest radiograph showed an abnormally bulging left cardiac silhouette. A non-contrast-enhanced axial chest CT scan showed an ovoid mass (average CT value: 30 Hounsfield unit) along the left ventricle (Fig. 1A). A contrast-enhanced axial chest CT scan showed the mass (average CT value: 50 Hounsfield unit) measuring 8.6 cm × 6.8 cm was heterogeneous and moderately enhanced (Fig. 1A). Pericardial effusion was also observed. Echocardiography revealed a large intra-pericardial, echogenic, inhomogeneous mass, with smooth margins, in addition to pericardial effusion.

Cardiac MRI was performed using a 3.0 Tesla scanner (Ingenia, Philips Healthcare, Best, the Netherlands). Black-blood T1-weighted imaging before and after contrast enhancement with fat saturation, black-blood T2-weighted imaging, cine imaging with a steady-state free-precession sequence, and delayed gadolinium enhancement imaging were performed. Delayed gadolinium enhancement images were acquired 12 minutes after the injection of 0.1 mmoL/kg of gadobutrol (Gadovist, Bayer Healthcare, Leverkusen, Germany). A solitary, well-defined, and ovoid mass broadly attached to the posterolateral wall of the left ventricle, showing an obtuse angle, compressed the left ventricle and left atrium, and showed heterogeneous high signal intensity on cine images (Fig. 1B). Pleural effusion also showed a homogenous high signal intensity. Collectively, cine images showed a mass arising from the lateral wall of the left ventricle. The mass demonstrated heterogeneous iso to high signal intensity relative to the myocardium on T1-weighted images and heterogeneous high signal intensity on T2-weighted images (Fig. 1C). The mass showed markedly heterogeneous contrast enhancement on gadolinium-enhanced T1-weighted fat-saturation images (Fig. 1D). Additionally, delayed gadolinium enhancement images showed persistent heterogeneous intense enhancement separated by a thin wall of non-enhanced normal myocardium (Fig. 1D). If any cardiac mass is identified in patients with NF1, cardiac neurofibroma should be suspected as a differential diagnosis, although it is rare.

Excision of the cardiac mass was performed with median sternotomy. Intraoperatively, a huge mass was found attached to the posterolateral wall of the left ventricle and posterior aspect of the left atrium. The encapsulated mass was isolated from the myocardium of the left ventricle and was removed, confirming that the tumor originated from the left ventricle. On gross appearance (Fig. 1E), the mass was encapsulated and measured 9.8 cm × 8.0 cm × 5.0 cm. Histopathological examination of the sections stained with hematoxylin and eosin showed that the tumor was well-marginated and encapsulated by a fibrous capsule. The wavy nuclei (arrows) were arranged haphazardly, and thin and thick collagen bundles (arrowheads) had

Fig. 1. CT and MRI features of a neurofibroma in the LV.
A. A non-contrast-enhanced axial CT image (left) shows an ovoid mass (average CT value: 30 HU) along the LV. A contrast-enhanced axial CT image (right) shows that the mass (average CT value: 50 HU), measuring 8.6 cm × 6.8 cm, is heterogeneous and moderately enhanced (arrowheads), with moderate pericardial effusion.
B. Axial (left) and short-axis (right) cine images of the mid-LV show a solitary, well-circumscribed, and ovoid mass attached to the posterolateral wall of the LV at an obtuse angle (arrows) compressing the LV and LA. Heterogeneous high signal intensity is also observed. Pleural effusion is also shown as homogeneous high signal intensity.
C. The mass demonstrated heterogeneous iso to high signal intensity relative to the myocardium on T1-weighted images of the LV (left) and heterogeneous high signal intensity on T2-weighted images of the LV (right).
HU = Hounsfield unit, LA = left atrium, LV = left ventricle, RV = right ventricle

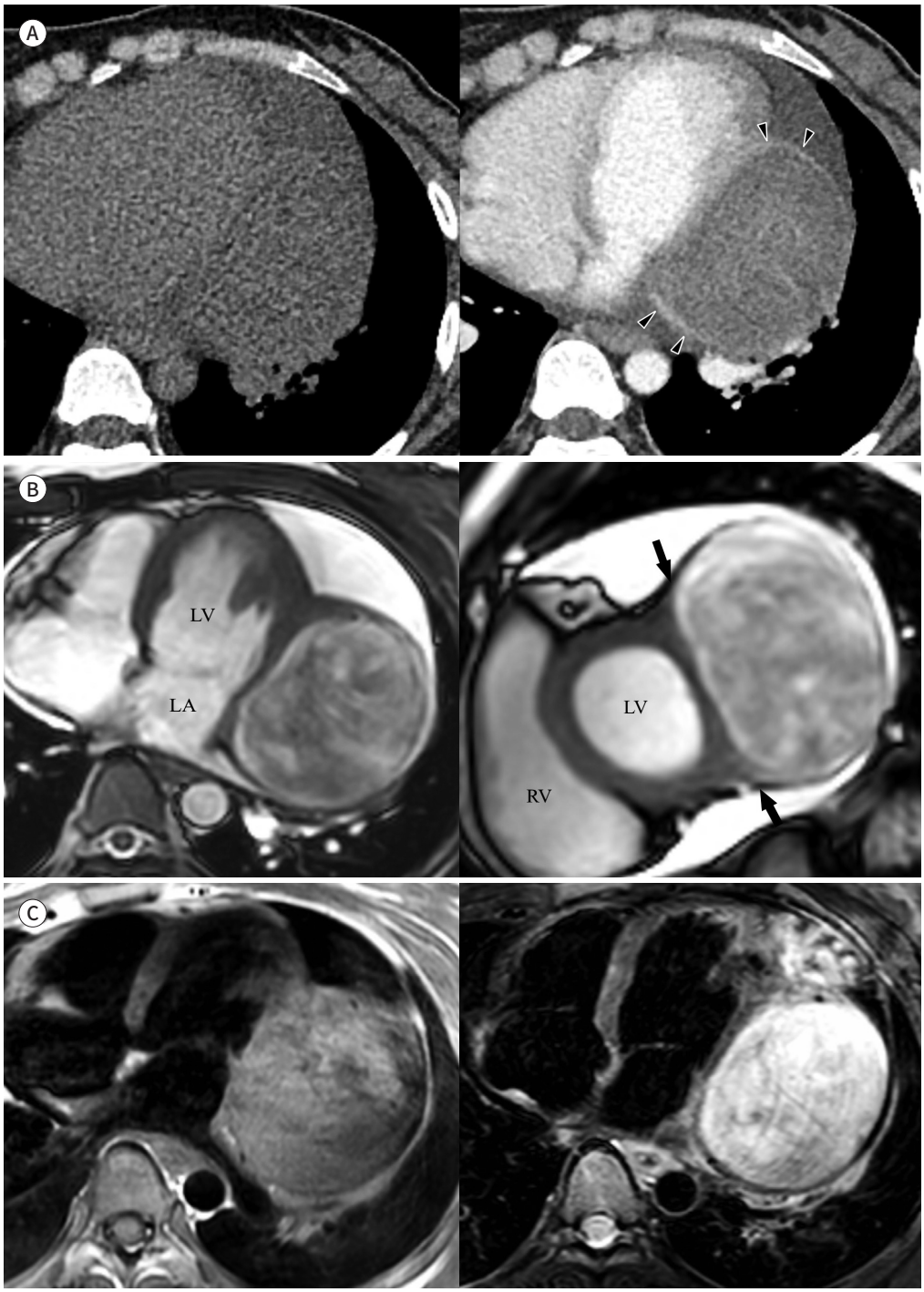
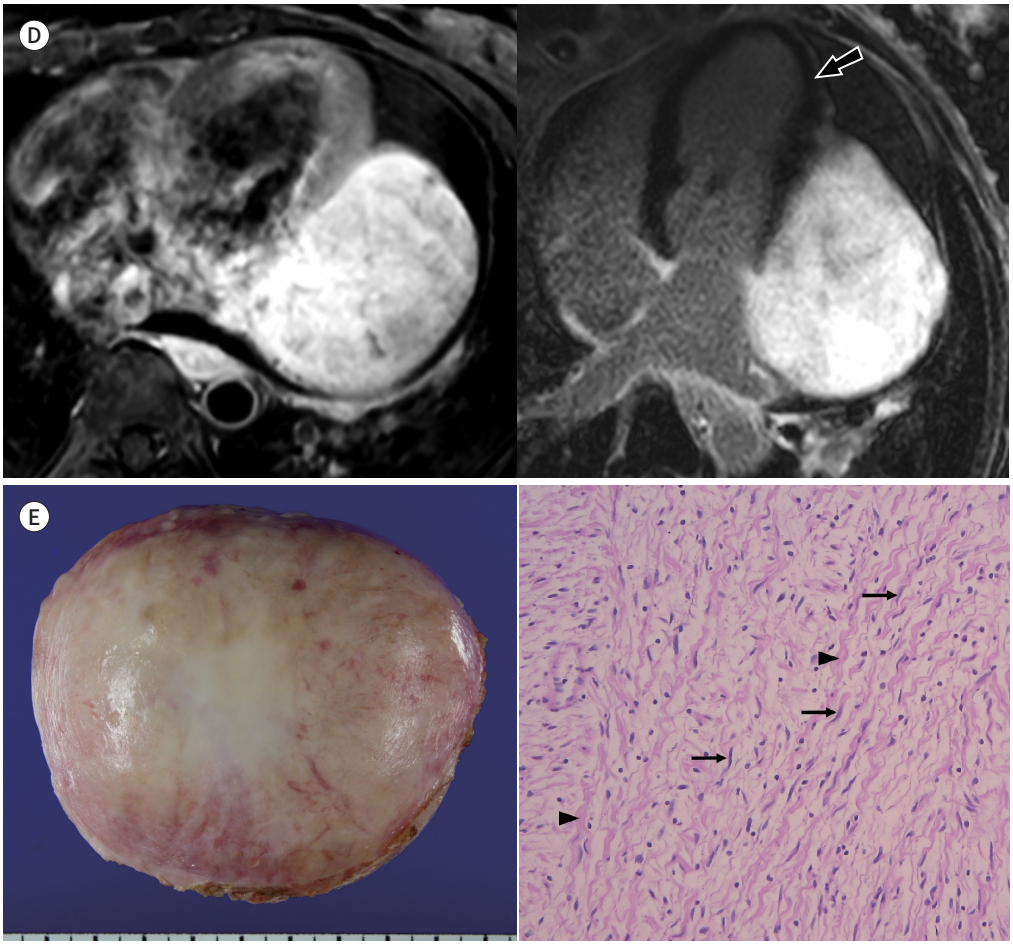


Fig. 1. CT and MRI features of a neurofibroma in the LV.
D. Axial gadolinium-enhanced T1-weighted fat-saturated image of the LV shows significant heterogeneous contrast enhancement of the mass. The mass shows an intense persistent heterogeneous enhancement, separated by a thin wall of non-enhancing normal myocardium (arrow) on delayed gadolinium enhancement image (right).
E. Gross pathological image (left) shows that the mass is encapsulated and measures 9.8 cm × 8.0 cm × 5.0 cm. Histopathological examination (right) shows that the wavy nuclei (arrows) are arranged haphazardly, and the thin and thick collagen bundles (arrowheads) have "shredded carrots" appearance (hematoxylin and eosin stain, × 200).
LV = left ventricle



"shredded carrots" appearance (Fig. 1E). Immunohistochemistry studies showed that these wavy Schwann cells were positive for S100 protein and negative for smooth muscle actin. Ki-67 was less than 5%, with no cell necrosis, suggesting benign neurofibroma. The patient was discharged without any complications.

This retrospective study was approved by the Institutional Review Board of our hospital, and the requirement for informed consent was waived (IRB No. WKUH 2020-09-020).

DISCUSSION

Neurofibromas originating from the heart are extremely rare. To date, very few reports of

Table 1. Previously Reported Cardiac Neurofibromas in the Literature

Reference	Year	Age/Sex	NF1	Location	Imaging
Li et al. (3)	2020	39/F	-	LV	Echo, MRI
Moghadam et al. (4)	2018	6/M	+	LV, LA	Echo, MRI
Alimi et al. (5)	2016	24/F	-	LV	Echo, MRI
Iino et al. (6)	2006	46/F	+	LV	Echo
Alaeddini et al. (7)	2000	29/M	+	RA, septum	Echo
Henderson et al. (8)	1997	36/F	+	RV	Echo
Gotoh et al. (9)	1992	7/M	-	LV	Echo
Current case	2020	32/F	+	LV	Echo, CT, MRI

Echo = echocardiography, LA = left atrium, LV = left ventricle, NF1 = neurofibromatosis type 1, RA = right atrium, RV = right ventricle

cardiac neurofibromas have been published (Table 1) (3-9). Of these, four cases associated with NF1 were identified (4, 6-8). In the eight reported cases, including this case, five tumors were located in the left ventricle, while one tumor each was located in the left ventricle and atrium, right ventricle, and right atrium and septum. The anatomic distribution of the vagus plexus provides nerve tissue that may produce these tumors. The left heart also has an extensive parasympathetic plexus, which surrounds the heart in the mitral valve region, passing through the epicardium and myocardium and extending to the subendocardial surface (3, 6).

However, little is known about the image characteristics of cardiac neurofibroma, as some studies of cardiac neurofibroma included only echocardiography and MRI. In the 3 case reports that described cardiac MRI findings (3-5), two tumors showed delayed contrast enhancement with iso or low signal intensity on steady-state precession sequences; one tumor showed iso signal intensity on the T1-weighted image, and low signal intensity on the T2-weighted image without contrast study. These cases only showed some figures of the cardiac MRI sequence and description with no figure, so detailed MRI findings of cardiac neurofibroma were not available. This case demonstrated MRI findings using the proposed core protocol for MRI imaging of cardiac masses (10). The mass showed heterogeneous high signal intensity without a classic target sign on the T2-weighted image (Fig. 1C). The classic target sign appearance, which is less common but nearly pathognomonic, is seen on T2-weighted images with high signal intensity myxoid material peripherally and a relatively low signal intensity fibrous component centrally (1). We also performed delayed gadolinium enhancement of the mass, which showed heterogeneous and persistent intense enhancement (Fig. 1D). On delayed gadolinium enhancement imaging, gadolinium washes out of the normal myocardium over time. However, it persists in any expanded interstitial space, which can occur owing to acute inflammation, fibrosis or after myocardial infarction. It also persists in the intracellular space owing to cellular breakdown in acute myocardial infarction or direct tumor invasion (10). Any combination of these factors can contribute to the hyperenhancement patterns of the various tumor types (10): thrombus, pericardial cyst, and lipoma show no uptake, rhabdomyoma, and lymphoma show no or minimal uptake, fibromas show hyperenhancement, and myxoma, sarcomas, or metastases show heterogeneous or homogeneous enhancement. It is believed that the fibrous and collagenous components of neurofibromas

may be responsible for the delayed gadolinium enhancement. Delayed enhancement study is thought to provide additional information for characterizing tumors. In our case, the cardiac MRI finding was suggestive of a benign neurofibroma rather than a malignant peripheral nerve sheath tumor. Malignant peripheral nerve sheath tumors may arise from various neurofibromas in patients with NF1. MRI findings suggesting malignant transformation include large size, a peripheral enhancement pattern, perilesional edema, cystic changes in the tumor, and heterogeneity on T1-weighted images (1). MRI also helps in the differential diagnosis of common benign cardiac tumors or tumor-like conditions (10). A myxoma is seen as a mobile intra-atrial mass in cine images. A fibroma shows low signal intensity on T2-weighted images, and a thrombus shows no enhancement on postcontrast T1-weighted images.

In conclusion, a well-defined mass, high signal intensity on T2-weighted images, and heterogeneous persistent intense enhancement on delayed gadolinium enhancement images may be suggestive MRI findings of cardiac neurofibromas with NF1, although rare.

Author Contributions

Conceptualization, all authors; investigation, all authors; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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신경섬유종증 1형 환자에서 드물게 발생하는 심장 신경섬유종: 영상의학적 소견

서상현 · 노지영*

신경섬유종증 1형은 비교적 흔한 유전 질환이며 신경섬유종 형성, 피부의 색소 이상, 홍채의 리쉬결절 및 골격 이상들을 특징으로 한다. 다발성 피부 신경섬유종은 양성 신경초 종양이며 신경섬유종증 1형의 특징적인 병변이다. 신경섬유종증 1형과 관련된 심장 신경섬유종은 매우 드물며 문헌에 몇 가지 사례가 보고되었다. 이에 저자들은 신경섬유종증 1형을 가진 32세 여성에서 수술로 확진된 좌심실 신경섬유종의 컴퓨터단층촬영 및 자기공명영상 소견을 보고한다.

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