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Case Report

Primary cardiac dedifferentiated liposarcoma with homologous and heterologous differentiation: a case report

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Abstract: Liposarcoma originating in the heart is extraordinarily rare. Herein, we report a dedifferentiated liposarcoma arising from the left atrium in a 59-year-old Chinese man. Histologically, the neoplasm predominantly consisted of undifferentiated pleomorphic sarcoma. In addition, the neoplasm exhibited lipoblastic differentiation and osteo-/chondrosarcomatous components. Immunohistochemically, the neoplastic cells were strongly positive for p16, MDM2, and CDK4. Fluorescence *in situ* hybridization showed *MDM2* gene amplification in all of the tumor components. To the best of our knowledge, this is the first published example of cardiac dedifferentiated liposarcoma exhibiting homologous and heterologous differentiation without a well-differentiated liposarcoma component.

Keywords: Liposarcoma, heart

Clinical summary

A 59-year-old Chinese man was admitted to our hospital with a 3-month history of gasping, palpitations and fatigue after activities. Doppler echocardiography revealed a 6.1 cm × 2.5 cm irregular mass with non-uniform echo attached to the atrial wall (**Figure 1**). The mass moved with the heartbeat, and protruded into the left ventricle in diastole. Subsequent computerized tomography and transesophageal echocardiogram showed a nodular mass in the left atrium near the mitral valve. A myxoma was highly suspected, and the surgery was performed in November 2013. The operative findings showed that the mass occupied the whole left atrium and diffusely invaded the myocardium. Additionally, the tumor involved the mitral valve and the left auricle. The intraoperative impression of the frozen section revealed that the lesion was predominantly composed of hyperchromatic spindled cells, and was highly suspicious for spindle cell malignancy. Since complete resection could not be achieved, partial resection was performed only for the floating neoplasms.

A fragmented specimen, 5 cm in aggregate, was subjected to pathological examination. Histological analysis showed that the lesion was predominantly composed of undifferentiated pleomorphic spindle sarcoma (**Figure 2A**, **2B**). In some areas, multivacuolated cells with clear nuclear impression were observed, which were suggestive of lipoblastic differentiation (**Figure 2C**). Additionally, heterologous chondrosarcomatous and osteosarcomatous differentiation was identified (**Figure 2D**). No well-differentiated liposarcoma component was found even extensive sampling. Immunohistochemically, the neoplastic cells exhibited strong positivity for p16, MDM2, and CDK4 (**Figure 3A-C**), and focal positivity for calretinin, desmin and S-100 protein. The tumor cells were negative for CD31, CD34, HBME-1, epithelial membrane antigen, smooth muscle actin, and myogenin. Fluorescence in situ hybridization (FISH) showed *MDM2* gene amplification in the non-lipogenic, lipogenic, and heterologous components (**Figure 4**). Based on the aforementioned findings, the final diagnosis was dedifferentiated liposarcoma (DDLS) with homologous lipoblastic and heterologous osteo-/chondrosarcomatous differentiation. A detailed examination did not show evidence of a tumor in other sites. The patient died within one month following the operation.

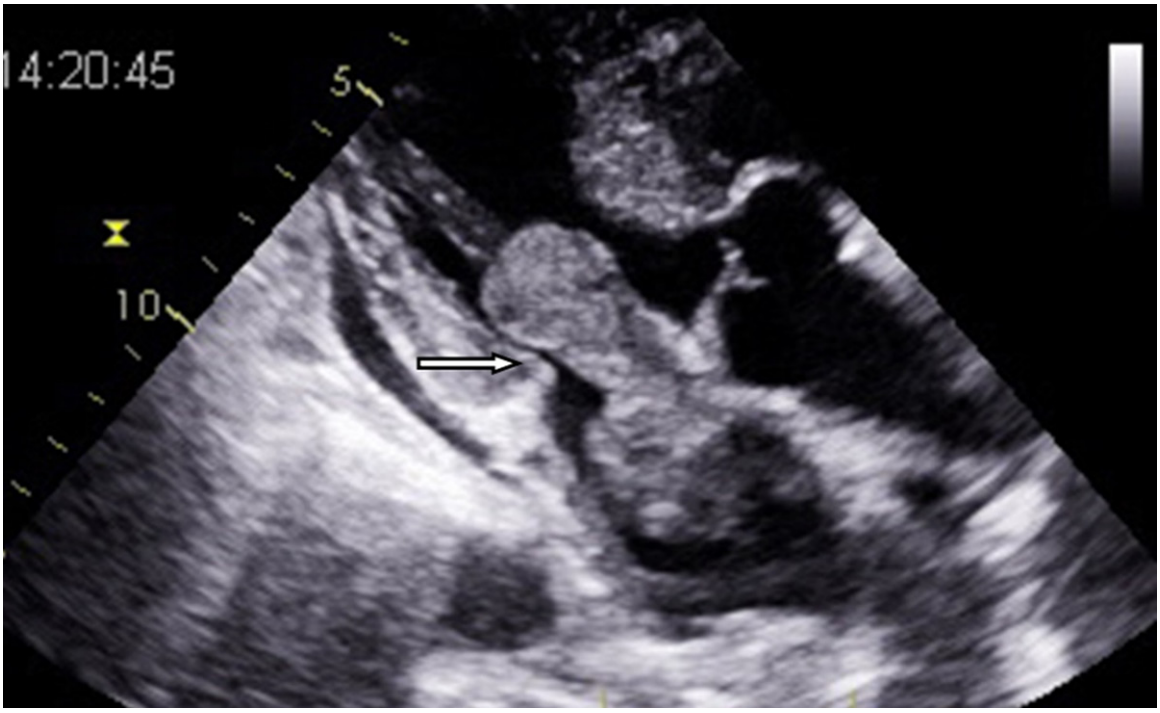

Figure 1. Doppler echocardiography revealing an irregular mass with a non-uniform echo attached to the non-coronary sinus atrial septum side of the aorta (arrow).

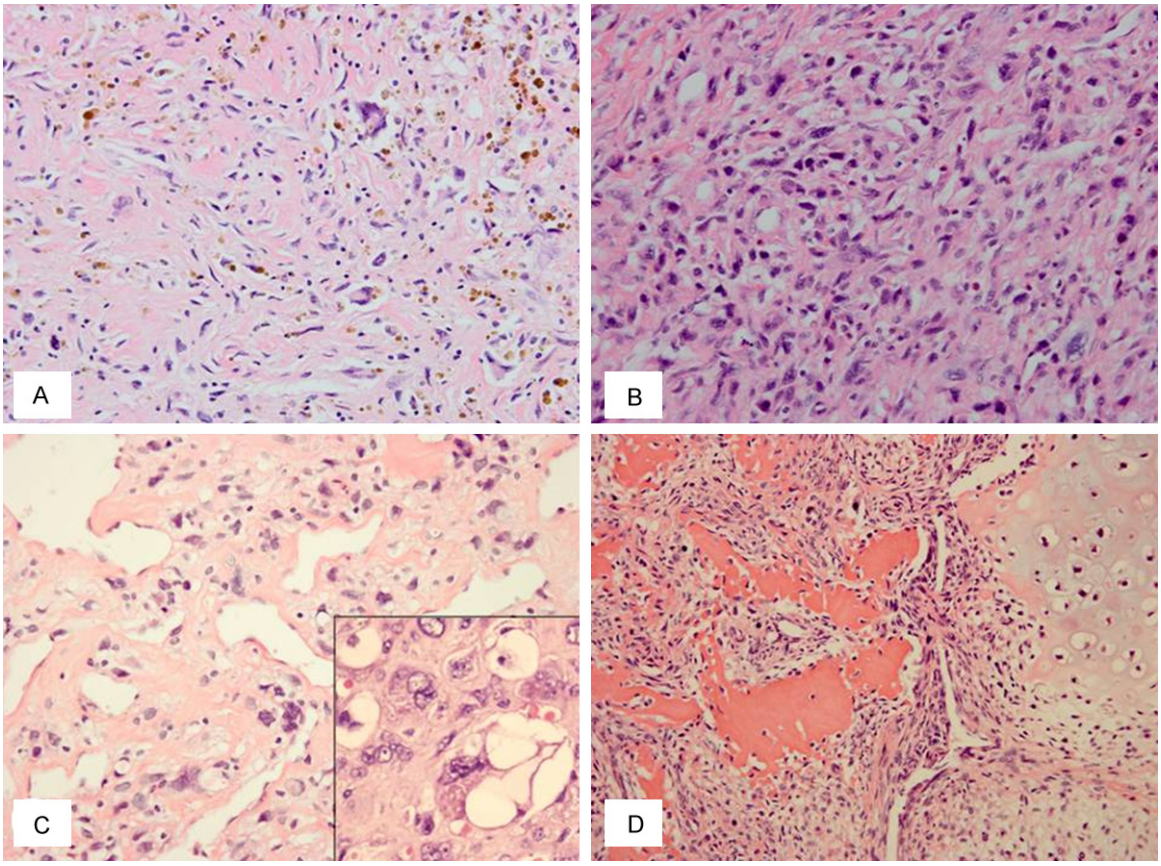

Figure 2. A, B. The majority of the tumor showing morphology identical to undifferentiated sarcoma (H&E, 400×). C. Sheets of lipoblasts with pleomorphism in some areas (H&E, 400×, B inset, 400×). D. The neoplasm exhibiting heterologous chondro- and osteosarcomatous differentiation (H&E, 400×).

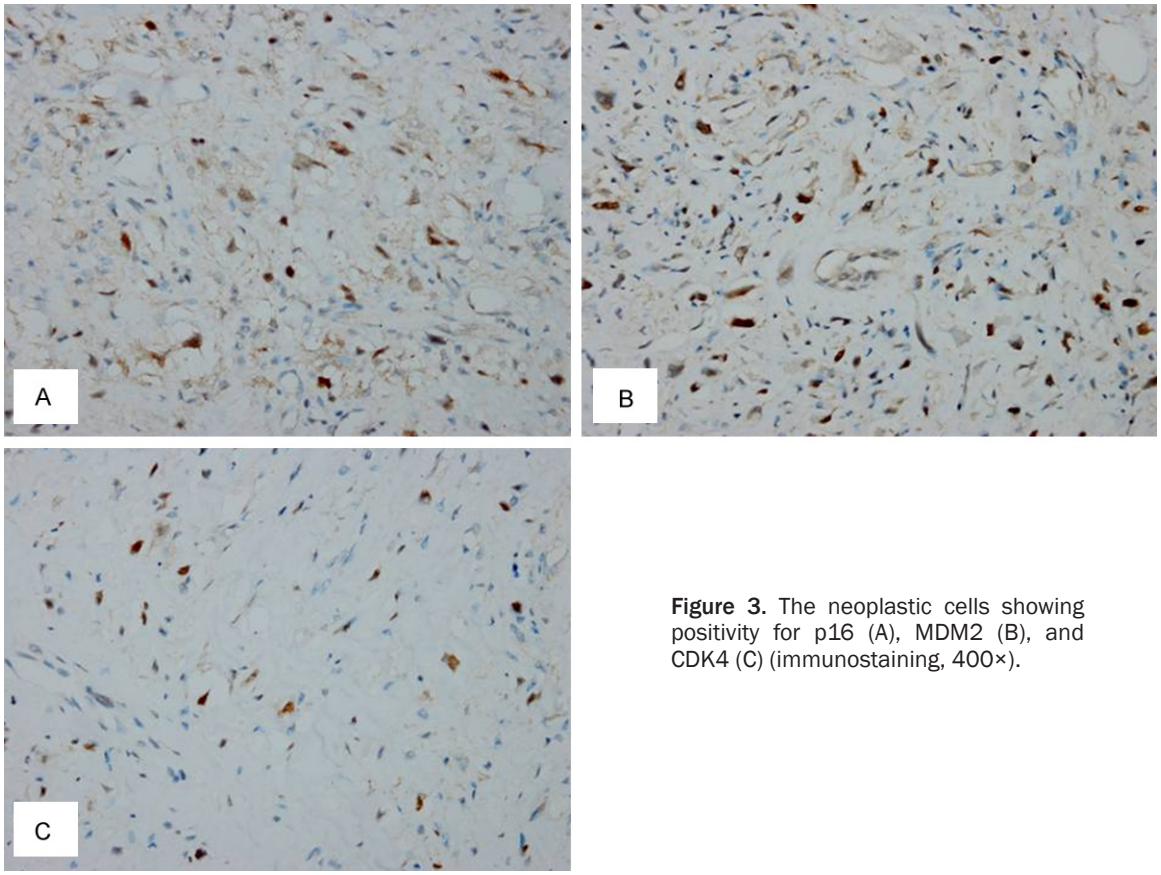

Figure 3. The neoplastic cells showing positivity for p16 (A), MDM2 (B), and CDK4 (C) (immunostaining, 400×).

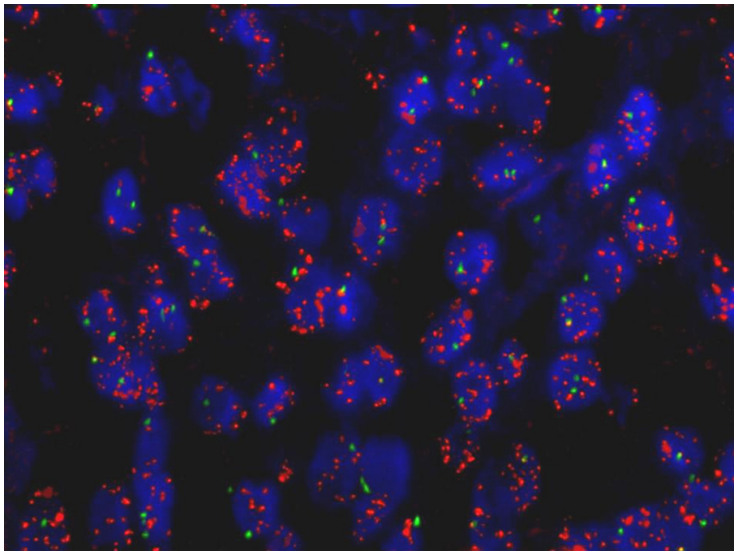

Figure 4. FISH showing a high-level of amplification of the *MDM2* locus in the majority of the neoplastic cells (*MDM2*, red signals; CEP12, green signals).

Discussion

The heart is an extremely rare location for liposarcoma [1, 2], particularly for the DDLS subtype, although this type of neoplasm is well-known to occur in the retroperitoneum and deep soft tissues of the extremities [3]. A search of the English literature indicated that only 31 previous cases of primary cardiac liposarcoma have been reported thus far. Among the 19 known subtypes, there were 7 pleomorphic liposarcomas, 6 myxoid liposarcomas, 4 well-differentiated liposarcomas, 1 DDLS, and 1 mixed liposarcoma (myxoid, round cell, and pleomorphic), respectively. The only one reported case of

DDLS resembled fibrosarcoma [4], which suggests conventional morphology of this entity. To the best of our knowledge, the current case represents the first reported cardiac DDLS with both homologous and heterologous components.

The differential diagnosis of this case should include adipocytic and non-adipocytic sarcomas, such as pleomorphic liposarcoma, intimal sarcoma, extraskeletal osteosarcoma and chondrosarcoma, undifferentiated pleomorphic sarcoma and metastatic liposarcoma. Traditionally, the dedifferentiated component of DDLS was defined as non-lipogenic sarcoma, but a small number of DDLS cases that exhibit lipoblastic differentiation have been described recently [5-8]. Therefore, DDLS with homologous lipoblastic differentiation could be easily confused with pleomorphic liposarcoma on morphologic grounds only, particularly for cases such as this, where the well-differentiated liposarcoma component is not identified. However, the current case exhibited heterologous (osteo-/chondrosarcomatous) differentiation, which is more suggestive of DDLS. More importantly, pleomorphic liposarcoma can be excluded due to the presence of both the high-level amplification of the *MDM2* locus and the diffuse nuclear positivity for MDM2, CDK4 and p16. Intimal sarcomas are usually high-grade sarcomas, and rare cases may show heterologous differentiation [9]. Furthermore, most intimal sarcomas are also manifested by constant *MDM2* gene amplification and overexpression [10] which simulate DDLS. Thus, intimal sarcoma should always be considered in the differential diagnosis. However, intimal sarcomas usually arise in the large blood vessels of the systemic and pulmonary circulatory system instead of the cavity of heart. Additionally, the neoplasm in the present case exhibited overt lipogenic differentiation, which rules out intimal sarcoma. DDLS with heterologous osteo-/chondrosarcomatous differentiation can also mimic osteosarcoma or chondrosarcoma. The detection of lipoblasts and the presence of *MDM2* gene amplification in this case could be valuable to secure the diagnosis. Owing to lack of well-differentiated liposarcoma component in this case, undifferentiated pleomorphic sarcoma should also be enrolled into the differential diagnosis. It is noteworthy to mention that some so-called undifferentiated pleomorphic sarcoma can be classified more specifically. Importantly, undifferentiated pleomorphic sarcomas with 12q14-15 amplification are classified as DDLS in current opinion [11]. The heart is an extraordinarily rare location for this tumor type. Therefore, the possibility of a secondary liposarcoma should always be excluded. In the present case, both imaging studies and physical examinations ruled out the possibility of metastatic lesion.

In conclusion, DDLS is an exceedingly rare neoplasm in the heart, and therefore it should be rigorously distinguished from other types of spindle cell neoplasm, especially when a well-differentiated liposarcoma component is not present.

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Disclosure of conflict of interest

None.

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References

[1] Vander Salm TJ. Unusual primary tumors of the heart. Semin Thorac Cardiovasc Surg 2000; 12: 89-100.

[2] Butany J, Nair V, Naseemuddin A, Nair GM, Catton C and Yau T. Cardiac tumours: diagnosis and management. Lancet Oncol 2005; 6: 219-228.

[3] Goldblum JR, Folpe AL and Weiss SW. Liposarcoma. Enzinger and Weiss's Soft Tissue Tumors, 6th Edition. Philadelphia: Pa: Saunders; 2013. pp. 484-523.

[4] Gałazka K, Ciezarek M, Soja J, Krzanowski M, Szlubowski A, Sydor K, Adamczyk W, Grodecki J and Sładek K. Synchronous primary heart liposarcoma and papillary renal carcinoma–a case report. Pol J Pathol 2003; 54: 153-159.

[5] Dei Tos AP, Mariño-Enríquez A, Pedeutour F and Rossi S. Dedifferentiated liposarcoma.

WHO classification of tumours of soft tissue and bone. 4th edition. In: Fletcher CDM, Bridge JA, Hogendoor P, Mertens F, editors. Lyon: IARC Press; 2013. pp. 37-43.

[6] Mariño-Enríquez A, Fletcher CD, Dal Cin P and Hornick JL. Dedifferentiated liposarcoma with "homologous" lipoblastic (pleomorphic liposarcoma-like) differentiation: clinicopathologic and molecular analysis of a series suggesting revised diagnostic criteria. Am J Surg Pathol 2010; 34: 1122-1131.

[7] Boland JM, Weiss SW, Oliveira AM, Erickson-Johnson ML and Folpe AL. Liposarcomas with mixed well-differentiated and pleomorphic features: a clinicopathologic study of 12 cases. Am J Surg Pathol 2010; 34: 837-843.

[8] Liau JY, Lee JC, Wu CT, Kuo KT, Huang HY and Liang CW. Dedifferentiated liposarcoma with homologous lipoblastic differentiation: expanding the spectrum to include low-grade tumours. Histopathology 2013; 62: 702-710.

[9] Nonomura A, Kurumaya H, Kono N, Nakanuma Y, Ohta G, Terahata S, Matsubara F, Matsuda T, Asaka T and Nishino T. Primary pulmonary artery sarcoma. Report of two autopsy cases studied by immunohistochemistry and electron microscopy, and review of 110 cases reported in the literature. Acta Pathol Jpn 1988; 38: 883-896.

[10] Zhang H, Macdonald WD, Erickson-Johnson M, Wang X, Jenkins RB and Oliveira AM. Cytogenetic and molecular cytogenetic findings of intimal sarcoma. Cancer Genet Cytogenet 2007; 179: 146-149.

[11] Chibon F, Lagarde P, Salas S, Pérot G, Brouste V, Tirode F, Lucchesi C, de Reynies A, Kauffmann A, Bui B, Terrier P, Bonvalot S, Le Cesne A, Vince-Ranchère D, Blay JY, Collin F, Guillou L, Leroux A, Coindre JM and Aurias A. Validated prediction of clinical outcome in sarcomas and multiple types of cancer on the basis of a gene expression signature related to genome complexity. Nat Med 2010; 16: 781-787.