Int Surg 2015;**100:**128–132
DOI: 10.9738/INTSURG-D-13-00203.1

Case Report

Dedifferentiated Liposarcoma Involving the Spleen and Splenic Hilum: A Report of a Case With a Rare Growth Pattern

Gen Nishikawa, Sachiko Minamiguchi, Hiroaki Hata, Satoshi Ogiso, Takashi Yamaguchi, Tethushi Otani, Iwao Ikai

Division of Surgery, National Hospital Organization Kyoto Medical Center, Kyoto, Japan

We present a rare case of dedifferentiated liposarcoma confined to the spleen and splenic hilum. An 81-year-old man was referred to our hospital with a large asymptomatic splenic tumor. The patient underwent splenectomy, and the adipose tissue surrounding the splenic hilum was also resected. Microscopically, the tumor mainly consisted of high-grade spindle cells similar to those seen in undifferentiated pleomorphic liposarcoma. In the splenic hilum, scattered atypical cells were detected in the sclerosing component and adipose tissue. Immunohistochemically, both the spindle cells in the spleen and the atypical cells in the splenic hilum were positive for MDM2 and CDK4. The histopathologic diagnosis was dedifferentiated liposarcoma derived from an atypical lipomatous tumor/well-differentiated liposarcoma of the adipose tissue in the splenic hilum with extension into the spleen. Dedifferentiated liposarcoma in the spleen and splenic hilum should be considered as a differential diagnosis of splenic tumors.

Key words: Dedifferentiated liposarcoma – Spleen – Retroperitoneal tumor – Chondro-osseous differentiation

Malignant lymphoma is the most common type of primary splenic tumorous lesion.[1,2] Non-hematologic splenic tumors, which include hemangioma, littoral cell angioma, hemangioendothelioma, angiosarcoma, hamartoma, and inflammatory pseudotumors, are relatively rare, accounting for approximately 1% of splenic tumors.[3] Metastatic splenic neoplasms, such as metastases from malignant melanoma, breast cancer, lung cancer, and colon cancer, have also been reported.[4] To the best of our knowledge, however, there have been only a few reports about lipogenic tumors in the spleen.[5]

Liposarcoma is one of the most common types of sarcoma in adults and is divided into 3 subtypes:

Corresponding author: Gen Nishikawa, MD, Department of Surgery, National Cancer Center, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan.
Tel.: +081 03 3542 2511; Fax: +081 03 3545 3567; E-mail: gennishikawa@msn.com

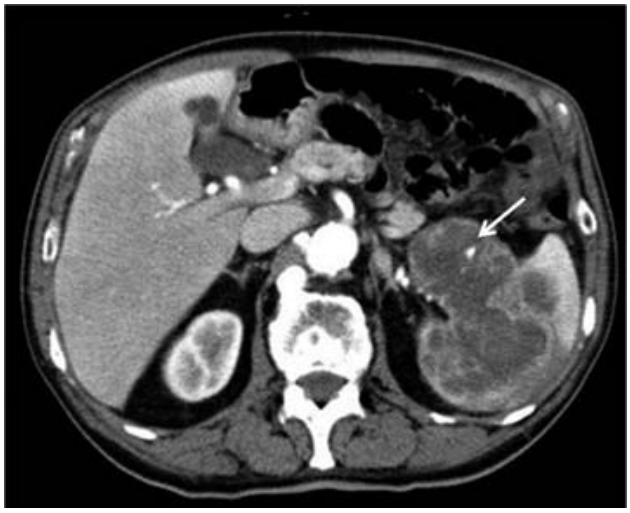

Fig. 1 Axial contrast-enhanced CT scan showing a multinodular tumor that occupied the spleen and extended to the splenic hilum. The margins of the tumor were enhanced, and calcification (arrow) was observed.

atypical lipomatous tumor/well-differentiated liposarcoma (ALT-WDLPS), dedifferentiated liposarcoma (DDLPS), and myxoid liposarcoma. DDLPS is a term that was first introduced by Evans in 1979 to describe liposarcomas that contain ALT-WDLPS cells juxtaposed with areas of pleomorphic non-lipogenic sarcoma cells.[6] DDLPS frequently occurs in the retroperitoneum.

In this report, we present a rare case of DDLPS involving the spleen and splenic hilum.

Case Report

An 81-year-old man was referred to our hospital with a large asymptomatic splenic tumor, which was incidentally detected during an abdominal computed tomography (CT) scan performed as part of a routine medical check-up. His general condition was good, and he did not exhibit any symptoms. CT revealed a large multinodular splenic tumor, which extended into the splenic hilum and exhibited heterogeneous low density and calcification (Fig. 1). In addition, the margins of the tumor were enhanced. The tumor exhibited low signal intensity on T1-weighted magnetic resonance images (MRI) and heterogeneous high signal intensity on T2-weighted images. In addition, it demonstrated a heterogeneous enhancement pattern, which was indicative of a solid tumor containing areas of necrosis (Fig. 2). None of the tumor components displayed signal intensities that were indicative of subcutaneous fat or a lipogenic tumor. Taken together, the abovementioned findings were suggestive of a malignant splenic tumor that exhibited necrosis and hemorrhaging. The patient's preoperative findings and clinical presentation were suggestive of angiosarcoma. Thus, the patient underwent splenectomy combined with resection of the adipose tissue surrounding the splenic hilum with an open laparotomy. The protruded lesion in the splenic hilum was palpable, which served as the gross surgical margin. No adhesion of the tumor to the surrounding organs or proliferation of the adipose tissue around the enlarged spleen was observed. The tumor measured 11 × 8 cm and was found to be a multinodular solid mass that exhibited hemorrhaging and necrosis. In the splenic hilum, a well-demarcated white solid tumor protruded into the adipose tissue (Fig. 3).

Microscopically, the tumor cells in the spleen consisted of densely arranged polymorphic spindle cells, which demonstrated severe atypia and many mitotic figures, similar to the cells found in undifferentiated pleomorphic sarcoma (Fig. 4a). Multifocal chondrosarcomatous and osteosarcomatous components were also detected (Fig. 4b). There were no lipogenic components in the spleen. A small amount of adipo-connective tissue in the splenic hilum contained spindle-shaped atypical cells with a fibrillary collagenous background,

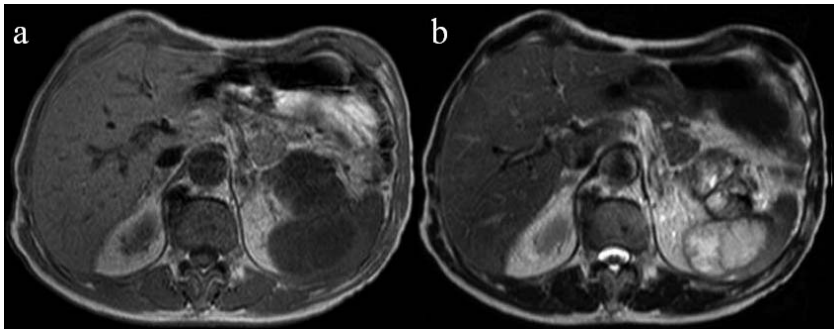

Fig. 2 Axial T1-weighted MR image showing a hypointense mass in the spleen and splenic hilum (a). The mass appeared heterogeneously hyperintense on T2-weighted MR images (b).

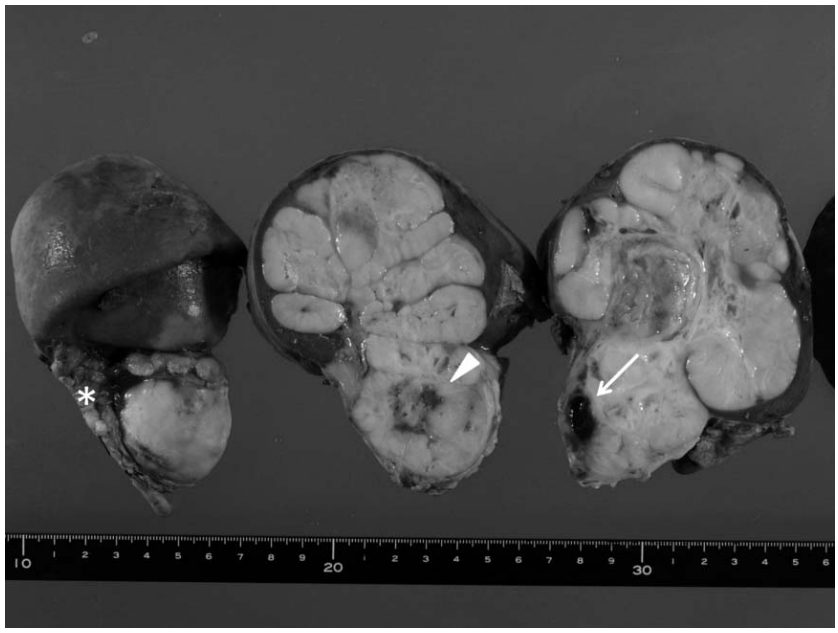

Fig. 3 Gross examination of the spleen showed that the tumor was a well-demarcated, white, solid, multinodular mass that displayed hemorrhaging (arrow) and necrosis (arrowhead) and measured 11 × 8 cm in diameter. There was a small amount of adipo-connective tissue in the splenic hilum (*).

which was compatible with the sclerosing subtype of ALT-WDLPS (Fig. 4c). The high-grade spindle-cell component in the spleen was contiguous with the scattered atypical cells in the hilum. Immunohistochemical staining demonstrated that both the spindle cells in the spleen and the scattered atypical cells in the hilum were positive for MDM2 (clone 1F2, dilution 1:100; Invitrogen, Grand Island, NY) and CDK4 (clone DCS-31, dilution 1:100; Abcam, Cambridge, UK) (Fig. 5). The histologic diagnosis was DDLPS with heterologous chondro-osseous differentiation derived from ALT-WDLPS of the adipose tissue of the splenic hilum. There were no high-grade tumor cells in the hilum, but the ALT-WDLPS component in the hilum was located close to the surgical margin.

The patient was discharged on postoperative day 16 and did not receive additional treatment (includ-

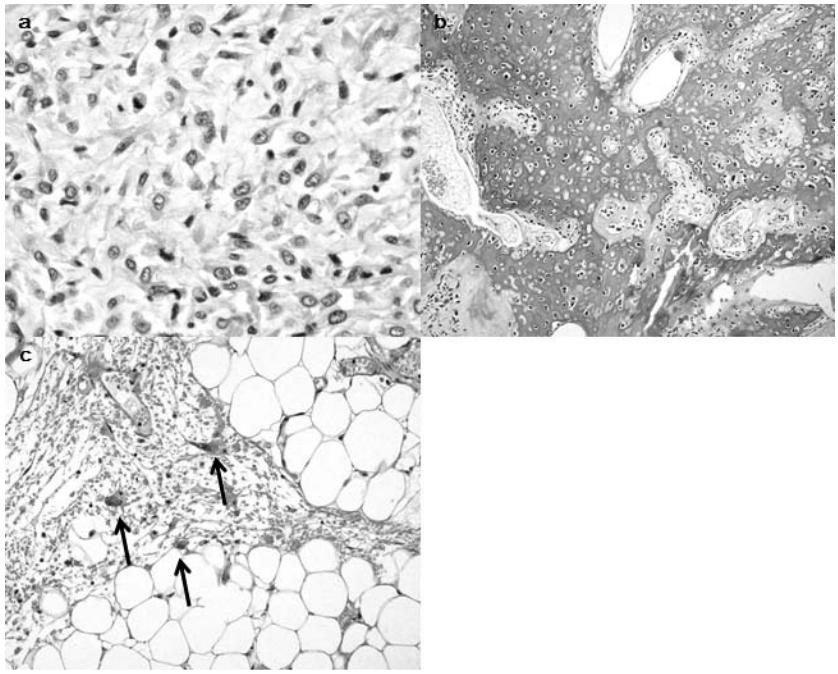

Fig. 4 (a) Microscopically, the tumor mainly consisted of densely arranged polymorphic spindle cells (H&E; ×400). (b) Multifocal chondro-osseous differentiation was also observed (H&E; ×40). (c) Multifocal sclerosing and atypical cells were detected in the fatty tissue of the splenic hilum (H&E; ×40).

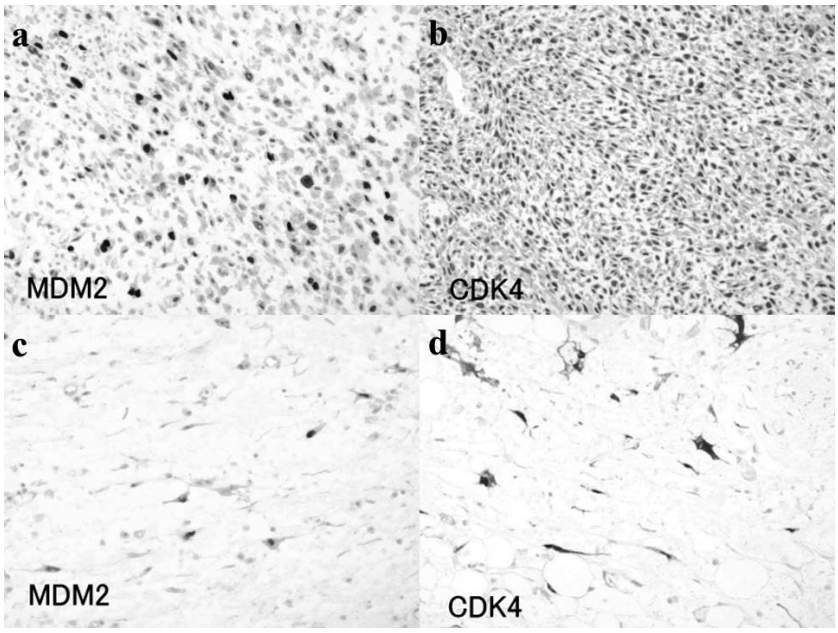

Fig. 5 Immunochemical staining showed that the tumor cells in the spleen were positive for MDM2 (a) and CDK4 (b). The atypical cells in the adipose tissue were also positive for MDM2 (c) and CDK4 (d).

ing radiation therapy). He was alive without recurrence at 4 years after the operation.

Discussion

The spleen is an elastic vascular mass that is covered by the peritoneum, except at the splenic hilum. Easler and Dowlin[5] have described lipogenic tumors that originated from the fatty tissue in the splenic hilum In the latter report, the primary lipoma was distinct from the fatty tissue in the splenic hilum and was entirely enclosed within the splenic capsule. Easler and Dowlin[5] suggested that the tumor in their case had been caused by the differentiation of undifferentiated mesenchymal cells within the spleen into lipocytes. In our case, the tumor was located in the spleen and the splenic hilum and consisted of spindle cells. The keys to diagnosis in this case were the atypical cells in the splenic hilar fatty tissue and the positivity of the tumor cells for MDM2 and CDK4. The dedifferentiated components in the spleen were contiguous with the differentiated components of the splenic hilum. Therefore, we considered that the tumor had originated from the adipose tissue in the splenic hilum.

DDLPS are defined as ALT-WDLPS (either primary or recurrent tumors) that progress to become sarcomas of various histologic grades. It has been reported that up to 10% of ALT-WDLPS subsequently become DDLPS, and retroperitoneal lesions are at particular risk of becoming DDLPS. The histologic hallmark of DDLPS is a transition from ALT-WDLPS to nonlipogenic sarcoma. The resultant dedifferentiated region can exhibit a wide morphologic spectrum but most frequently resembles undifferentiated pleomorphic sarcoma or intermediate- to high-grade myxofibrosarcoma.[7] The detection of the amplification and overexpression of MDM2 and CDK4 by fluorescence in situ hybridization or immunohistochemistry represents an important tool for the diagnosis of ALT-WDLPS and DDLPS. According to an immunohistochemical analysis of a large number of sarcomas, the sensitivity and specificity of MDM2 and CDK4 immunostaining for differentiating DDLPS from other soft tissue tumors were 95% and 92%, and 81% and 95%, respectively,[8] and immunostaining of these molecules played an important diagnostic role in our case.

The imaging characteristics of liposarcoma vary depending on the tumor grade, whereas ALT-WDLPS appear as well-defined, predominantly fat-containing lesions with minimal soft-tissue attenuation. On CT images, ALT-WDLPS appear as well-defined homogeneous masses with fat attenuation, whereas high-grade liposarcomas appear as locally invasive masses that are predominantly composed of soft tissue and contain minimal amounts of fat.[9] On MRI, liposarcomas display a variable appearance depending on their tumor grade, with high signal intensity being seen on T1- and T2-weighted images, and areas of enhancement being detected on

contrast-enhanced images.[10] The identification of a well-defined nonlipomatous mass juxtaposed with a tumor that is predominantly composed of fatty tissue is suggestive of a dedifferentiated liposarcoma. In previous reports, most liposarcomas contained fatty components that occupied more than half of the tumor volume. In our case, however, the tumor mainly consisted of nonfatty tissue, which exhibited heterogeneous attenuation levels. The well-differentiated component, which displayed low attenuation levels, only occupied a small part of the splenic hilum, so it was difficult to diagnose the tumor as a lipogenic tumor. Calcification is sometimes helpful for making a diagnosis. Certain types of sarcoma can exhibit calcification, including malignant fibrous histiocytoma (or undifferentiated pleomorphic sarcoma), synovial sarcoma (in up to 30% of cases), dedifferentiated liposarcoma, extraskeletal osteosarcoma, and other spindle-cell sarcomas.[9] In our case, intratumoral calcification was detected on CT images, and a histologic examination revealed that this was owing to chondro-osseous differentiation. From the patient's clinical symptoms and laboratory data, we were able to rule out some of the possible diagnoses, but it was difficult to reach a definitive diagnosis from the patient's preoperative findings.

The prognosis of lipogenic tumors is mainly determined by whether local recurrence occurs (incidence of local recurrence, 40%–60%) as they display a fairly low metastatic potential (incidence of metastasis, 15%–20%).[11] Complete surgical resection is the optimal treatment for retroperitoneal liposarcoma. Laparoscopic approach might be able to give earlier recovery and shorter hospital stay in our case.[12] The additional postoperative radiation therapy may reduce the risk of local recurrence and lengthen the recurrence-free survival for our patient. But the patient did not receive radiation therapy because of his age.[13]

In studies of patients who were followed up for more than 10 years, it was found that retroperitoneal malignant tumors tended to recur locally.[14,15] Thus, we should follow up the present patient carefully for a long time, as should be done for all patients with retroperitoneal DDLPS.

References

1. O'Reilly RA. Splenomegaly in 2,505 patients at a large university medical center from 1913 to 1995. 1963 to 1995: 449 patients. *West J Med* 1998;**169**(2):88–97
2. Kraus MD, Fleming MD, Vonderheide RH. The spleen as a diagnostic specimen: a review of 10 years' experience at two tertiary care institutions. *Cancer* 2001;**91**(11):2001–2009
3. Abbott RM, Levy AD, Aguilera NS, Gorospe L, Thompson WM. From the archives of the AFIP: primary vascular neoplasms of the spleen: radiologic-pathologic correlation. *Radiographics* 2004;**24**(4):1137–1163
4. Comperat E, Bardier-Dupas A, Camparo P, Capron F, Charlotte F. Splenic metastases: clinicopathologic presentation, differential diagnosis, and pathogenesis. *Arch Pathol Lab Med* 2007;**131**(6):965–969
5. Easler RE, Dowlin WM. Primary lipoma of the spleen: report of a case. *Arch Pathol* 1969;**88**(5):557–559
6. Evans HL. Liposarcoma: a study of 55 cases with a reassessment of its classification. *Am J Surg Pathol* 1979;**3**(6): 507–523
7. Tos APD, Marino-Enriquez A, Pedetour F, Rossi S. Dedifferentiated liposarcoma. In: Fletcher CDM, Bridge JA, Hogendoorm PCW, Mertens F, eds. *WHO Classification of Tumours of Soft Tissue and Bone (WHO Classification of Tumours)*. 4th ed. Lyon France: IARC, 2013: 37
8. Binh MBN. MDM2 and CDK4 immunostainings are useful adjuncts in diagnosing well-differentiated and dedifferentiated liposarcoma subtypes. *Am J Surg Pathol* 2005;**29**(10):1340–1347
9. Shanbhogue AK, Fasih N, Macdonald DB, Sheikh AM, Menias CO, Prasad SR. Uncommon primary pelvic retroperitoneal masses in adults: a pattern-based imaging approach. *Radiographics* 2012;**32**(3):795–817
10. Szklaruk J, Tamm EP, Choi H, Varavithya V. MR imaging of common and uncommon large pelvic masses. *Radiographics* 2003;**23**(2):403–424
11. Coindre JM, Pedeutour F, Aurias A. Well-differentiated and dedifferentiated liposarcomas. *Virchows Arch* 2010;**456**(2):167–179
12. Nomura R, Tokumura H, Matsumura N. Laparoscopic resection of a retroperitoneal liposarcoma: a case report and review of the literature. *Int Surg* 2013;**98**(3):219–222
13. Stoeckle E, Coindre JM, Bonvalot S, Kantor G, Terrier P, Bonichon F *et al*. Prognostic factors in retroperitoneal sarcoma: a multivariate analysis of a series of 165 patients of the French Cancer Center Federation Sarcoma Group. *Cancer* 2001;**92**(2): 359–368
14. McCormick D, Mentzel T, Beham A, Fletcher CD. Dedifferentiated liposarcoma: clinicopathologic analysis of 32 cases suggesting a better prognostic subgroup among pleomorphic sarcomas. *Am J Surg Pathol* 1994;**18**(12):1213–1223
15. Henricks WH, Chu YC, Goldblum JR, Weiss SW. Dedifferentiated liposarcoma: a clinicopathological analysis of 155 cases with a proposal for an expanded definition of dedifferentiation. *Am J Surg Pathol* 1997;**21**(3):271–281