

Letter to the Editor

Myxoid leiomyosarcoma of the uterus with mature adipocytes and numerous bizarre multinucleated giant cells*To the Editor:*

We report the case of a rare variant of uterine leiomyosarcoma, in which the tumor showed a prominent myxoid change and contained numerous multinucleated giant cells with marked nuclear pleomorphism. In addition, mature adipocytes showing no nuclear atypism were scattered. Uterine leiomyosarcomas containing a mature adipocytic¹ or liposarcomatous^{2–5} component are very rare, and a leiomyosarcoma showing a prominent myxoid change with the appearance of numerous bizarre giant cells and containing mature adipocytes has not been reported to date.

A 65-year-old woman presented to our hospital with abdominal distension and pain lasting for one and half months. Magnetic resonance imaging (MRI) demonstrated a large uterine mass showing hyperintensity on a T2-weighted image and heterogeneous contrast enhancement on a T1-weighted image (Fig. 1a). On laparotomy, a large tumor was found to protrude from the left lateral wall of the uterine corpus. It had partly ruptured, and a large amount of jelly-like, dark red material filled the pelvic cavity. The pelvic peritoneum was studded with many small, gelatinous nodules. Despite postoperative chemotherapy, the radiological examination at 7 months after the operation revealed the regrowth of residual intrapelvic tumors.

The tumor, measuring 11 cm × 10 cm × 5 cm, was located within the left lateral wall of the uterine corpus and consisted of a mass of jelly-like material, which was associated with intense hemorrhage (Fig. 1b). A white, firm nodular area, measuring 5 cm × 4.5 cm × 3 cm, was found within the tumor.

On microscopic examination, the greater part of the tumor was occupied by palely basophilic, myxoid material containing stellate or spindle cells and multinucleated giant cells. About 3 mitotic figures were found per 10 high power fields (HPF). In addition, a small number of mature adipocytes showing no nuclear atypism were scattered (Fig. 1c). A plexiform capillary network was not seen. Nuclear atypism and pleomorphism of the stellate or spindle cells were mild to moderate (Fig. 1d). The cytoplasm was scant, but bipolar or multipolar cytoplasmic processes were observed. The multinucleated giant cells had hyperchromatic and markedly pleomorphic nuclei. Osteoclast-like giant cells with bland nuclei were not observed.

The white, firm nodule within the tumor consisted of a dense proliferation of long spindle cells which formed intersecting,

compact cellular fascicles (Fig. 2a). The spindle cells had blunt-ended nuclei and eosinophilic, fibrillary cytoplasm, consistent with the features of well-differentiated leiomyosarcoma (Fig. 2b). About 3 mitotic figures were counted per 10 HPF. These areas also contained scattered mature adipocytes. The nuclei of the adipocytes were bland, and atypical lipoblasts were not observed. Although areas showing hyaline necrosis of the ischemic type were seen, coagulation tumor cell necrosis was not observed. An admixture of malignant epithelial tissue suggestive of carcinosarcoma was not detected.

Most stellate or spindle cells and multinucleated giant cells showed a diffuse and strong immunoreactivity for α -smooth muscle actin (SMA) (Fig. 2c). Tumor cells in the areas of well-differentiated leiomyosarcoma were largely negative for desmin and h-caldesmon, but those within the myxoid areas, including multinucleated giant cells, were strongly immunoreactive for desmin (Fig. 2d). The immunostain for S-100 protein only stained the cytoplasmic rims of mature adipocytes. Tumor cells were not immunoreactive for HMB45, MDM2, estrogen receptor, and progesterone receptor. The Ki-67 labeling indices in the myxoid areas and well-differentiated leiomyosarcomatous area were 36.0 and 32.2%, respectively.

In myxoid leiomyosarcoma of the uterus, stellate or spindle cells with bland nuclei form anastomosing, thin cellular trabeculae.⁶ Although it may focally exhibit marked nuclear atypism and pleomorphism,⁶ the appearance of numerous pleomorphic cells including multinucleated giant cells is extremely rare. Uterine leiomyosarcomas with an admixture of mature adipocytes¹ or a liposarcomatous component^{2–5} have been reported rarely, with some reported under the term of 'lipoleiomyosarcoma'.^{4,5} To our knowledge, uterine leiomyosarcomas which contain mature, benign-looking adipocytes and show a prominent myxoid change with numerous multinucleated giant cells, have not been documented.

In the differential diagnosis, well differentiated and dedifferentiated liposarcomas with prominent myxoid stroma should be considered.⁷ The present tumor differed from them in that it contained distinct areas of well differentiated leiomyosarcoma and lacked both atypical lipoblasts and plexiform or curvilinear blood vessels. Also, nuclear immunoreactivity for MDM2 was not seen in tumor cells.

We interpret the present tumor as a myxoid leiomyosarcoma containing a heterologous, mature adipocytic component. Although some investigators apply the term 'lipoleiomyosarcoma' to uterine sarcomas containing an adipocytic component,^{4,5} this diagnostic term has been used with different connotations among various investigators.⁸ The histogenesis of leiomyosarcoma with an adipocytic

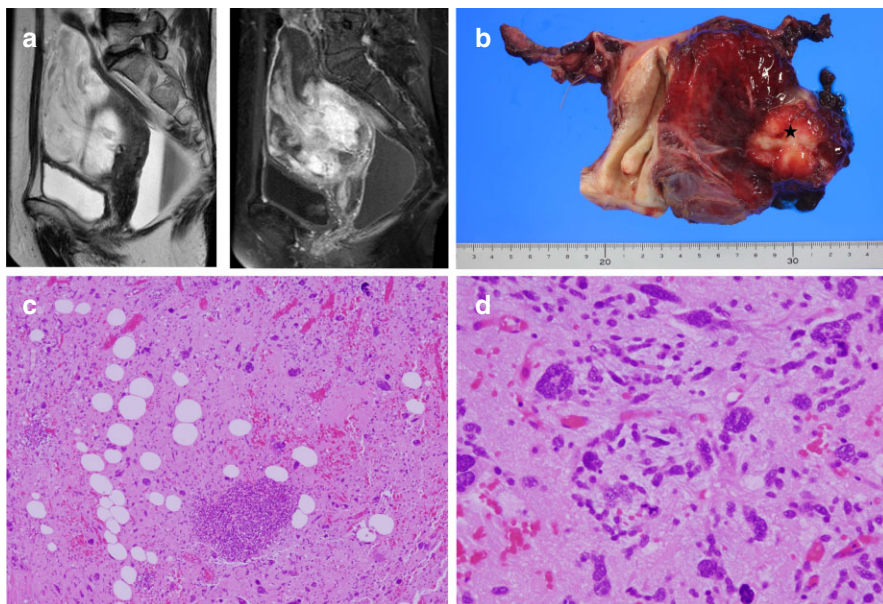


Figure 1 (a) Abdominal MRI (sagittal planes). A large tumor involving the left lateral wall of the uterine corpus showed a high signal intensity on a T2-weighted image (left) and was heterogeneously enhanced by the contrast medium on a T1-weighted image (right). (b) The extirpated uterus and bilateral adnexae. A large tumor in the left uterine wall showed a gelatinous appearance and contained a firm, white nodular region (asterisk). (c) The greater part of the tumor consisted of a myxoid matrix containing sparsely distributed stellate or spindle cells and giant cells. Mature adipocytes were scattered. (d) Stellate or spindle cells had hyperchromatic nuclei and eosinophilic, scant cytoplasm. Multinucleated giant cells showed nuclear hyperchromatism, atypism, and pleomorphism. (c: HE stain, x 25, d: HE stain, x 100).

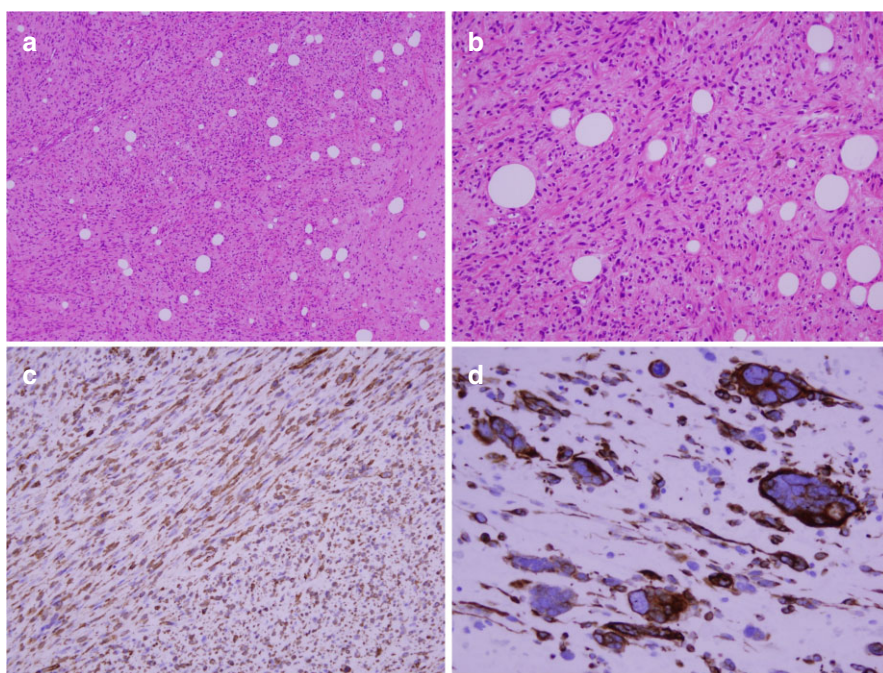


Figure 2 (a) The firm, white, nodular region of the tumor showed a compact fascicular proliferation of spindle cells. Mature adipocytes were scattered. (b) Spindle cells had elliptical nuclei and eosinophilic, fibrillary cytoplasm. Adipocytes were mature and did not show nuclear atypism. (c) Spindle cells were immunoreactive for α -SMA. (d) Multinucleated giant cells within the myxoid areas were immunoreactive for desmin. (a: HE stain, x 25, b: HE stain, x 50, c, d: Immunostain, x 50).

component of the uterus or somatic soft tissue remains controversial. The diverse adipocytic differentiation or adipocytic neometaplasia of sarcoma cells and adipocytic differentiation of non-neoplastic mesenchymal cells in the stroma can be considered as histogenetic possibilities. Some investigators presumed the malignant transformation of lipoleiomyoma, which is an uncommon variant of leiomyoma.^{1,2}

Although it has been generally believed that the vast majority of uterine leiomyosarcoma develops *de novo*, some

recent reports suggested that a subset of leiomyosarcoma arises from the malignant transformation of pre-existent leiomyoma.^{9,10} Scurry and Hack believed their case of leiomyosarcoma to have arisen in a lipoleiomyoma.¹ It is difficult to regard the tumors in their case¹ and our own case as sarcomas showing truly dual lineage differentiation, considering the absence of anaplastic features in the adipocytic component, although the possibility cannot be ruled out that these tumors arose from primitive mesenchymal stem cells and exhibited dual differentiation.

DISCLOSURE

The authors declare no conflict of interest.

Masayuki Shintaku,¹ Takahito Ashihara² and
Takashi Koyama³

Departments of ¹Pathology, ²Gynecology and Obstetrics,
Osaka Red Cross Hospital, Osaka, ³Department of
Diagnostic Radiology, Kurashiki Central Hospital,
Kurashiki, Japan

REFERENCES

- 1 Scurry J, Hack M. Leiomyosarcoma arising in a lipoleiomyoma. *Gynecol Oncol* 1990; **39**: 381–3.
- 2 Vakiani M, Mawad J, Talerman A. Heterologous sarcomas of the uterus. *Int J Gynecol Pathol* 1982; **1**: 211–9.
- 3 Bapat K, Brustein S. Uterine sarcoma with liposarcomatous differentiation. Report of a case and review of the literature. *Int J Gynecol Obstet* 1989; **28**: 71–5.
- 4 Jha A, Sayami G, Adhikari D. Lipoleiomyosarcoma an extremely unusual sarcoma of uterus. A case report. *Nepal J Obstet Gynecol* 2007; **2**: 67–70.
- 5 Lee HP, Tseng HH, Hsieh PP, Shih TF. Uterine lipoleiomyosarcoma. Report of 2 cases and review of the literature. *Int J Gynecol Pathol* 2012; **31**: 358–63.
- 6 Burch DM, Tavassoli FA. Myxoid leiomyosarcoma of the uterus. *Histopathology* 2011; **59**: 1144–55.
- 7 Sioletic S, Dal Cin P, Fletcher CDM, Hornick JL. Well-differentiated and dedifferentiated liposarcomas with prominent myxoid stroma. Analysis of 56 cases. *Histopathology* 2013; **62**: 287–93.
- 8 Folpe AL, Weiss SW. Lipoleiomyosarcoma (well-differentiated liposarcoma with leiomyosarcomatous differentiation). A clinicopathologic study of nine cases including one with dedifferentiation. *Am J Surg Pathol* 2002; **26**: 742–9.
- 9 Yanai H, Wani Y, Notohara K, Takada S, Yoshino T. Uterine leiomyosarcoma arising in leiomyoma. Clinicopathological study of four cases and literature review. *Pathol Int* 2010; **60**: 506–9.
- 10 Mittal KR, Chen F, Wei JJ *et al*. Molecular and immunohistochemical evidence for the origin of uterine leiomyosarcomas from associated leiomyomas and symplastic leiomyoma-like areas. *Mod Pathol* 2009; **22**: 1303–11.