Supplementary Materials

Oncological features of intravenous leiomyomatosis: involvement of mesenchymal tumor stem-like cells

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Supplementary material 1

Tissue Collection. A total of 101 patients between 32 and 83 years of age and diagnosed as having smooth muscle tumors of the uterus were selected from pathological files. Serial sections were cut from at least 2 tissue blocks from each patient for hematoxylin and eosin staining and immunostaining. All tissues were used with the approval of the Ethical Committee of Shinshu University after obtaining written consent from each patient. The pathological diagnosis of uterine smooth muscle tumors was performed using established criteria (Hendrickson and Kempson, 1995) with some modification. Briefly, usual leiomyoma (usual LMA) was defined as a tumor showing typical histological features with a mitotic index (MI) [obtained by counting the total number of mitotic figures (MFs) in 10 high-power fields (HPFs)] of <5 MFs per 10 HPFs. Cellular leiomyoma (cellular LMA) was defined as a tumor with significantly increased cellularity (>2000 myoma cells / HPF) and a MI<5, but without cytologic atypia. Bizarre leiomyoma (BL) was defined as a tumor either with diffuse nuclear atypia and a MI<2 or with focal nuclear atypia and a MI<5 without coagulative tumor cell necrosis. A tumor of uncertain malignant potential (UMP) was defined as tumor with no mild atypia and a MI<10 but with coagulative tumor cell necrosis. Leiomyosarcoma (LMS) was diagnosed in the presence of a MI>10 with either diffuse cytologic atypia, coagulative tumor cell necrosis, or both. Of the 105 smooth muscle tumors, 52 were diagnosed as LMA, 3 were BL, 2 were intravenous leiomyomatosis, 58 were uterine LMS, 1 was uterine LANT-like tumor, and 2 were uterine rhabdomyosarcoma. Of the 58 LMS, 48 were histologically of the spindle-cell type and 10 were of the epithelioid type. The clinical stage of the LMS patients was stage I in 11 cases, stage II or III in 31 cases, and stage IV in 16 cases. Protein expression studies with cervix epithelium and carcinoma tissues were performed using tissue array (Uterus cancer tissues, AccuMax Array, Seoul, Korea). Details about tissue sections are indicated in manufacture's information (AccuMax Array).

Supplementary material 2

Case 1: Patient background

In February 2003, Uterine Artery Embolization (UAE) was performed for a uterine leiomyoma in a 40-year-old woman at a nearby hospital. Because of subsequent excessive bleeding during the necrotic uterine leiomyoma delivery that developed under the mucosa, the vaginal leiomyoma was resected by short-term hospitalization or outpatient visit a total of 5 times from June 2003 to July 2009. During the histopathological diagnosis for resected uterine leiomyoma, it was determined that the cell density was rather high. No malignant findings were noted in the surgical pathological diagnosis and the patient was diagnosed with uterine leiomyoma with hemorrhage and necrosis. Afterwards, she did not feel any physical abnormalities with no complaints and did not go to the outpatient clinic for 12 years. At the age of 52, she had menopause. In March 2021, the abdominal bulge became evident and the blood clot was excreted from May 9 to 10, 2021. She received an outpatient visit at a nearby hospital. She was referred to our hospital because of a significantly larger mass in her abdomen. On May 31, 2021, she arrived at our hospital with a markedly swollen abdomen and swelling of the left supraclavicular lymph node.

Virchow: LNs: Palpate multiple bulky tumors
Abdomen: A neonatal-sized hard bulky tumor was found on the right side of the lower abdomen. This tumor has poor mobility

Vaginal discharge: small amount

Cervix: The cervix was not red and sore

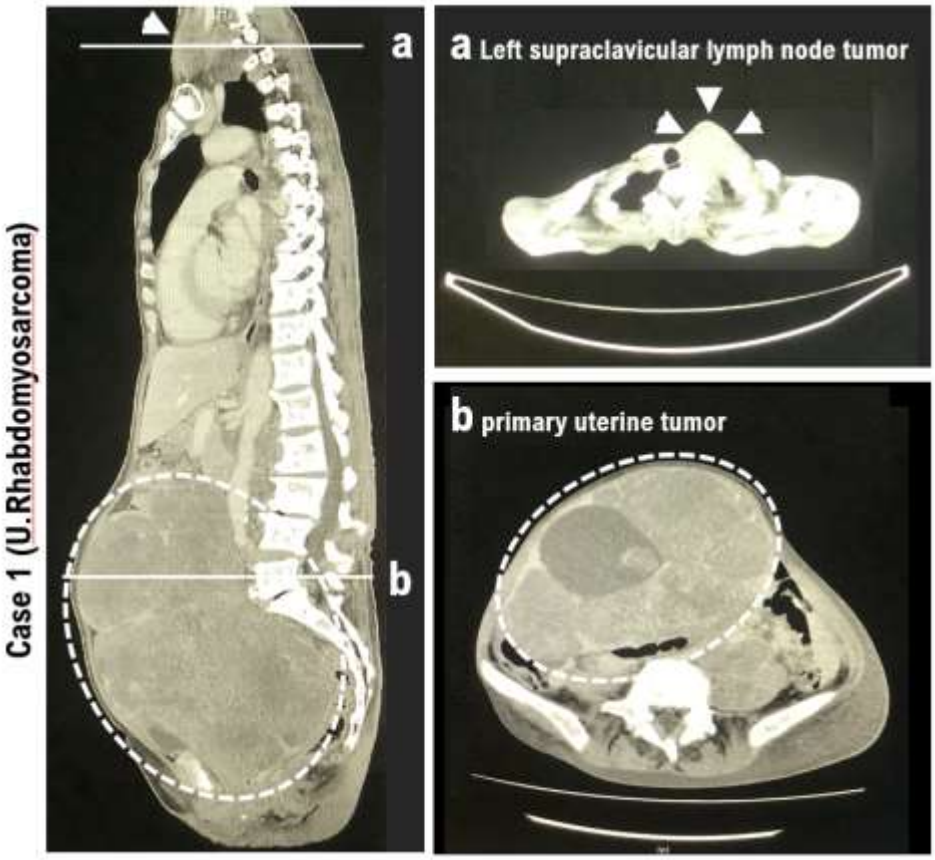
Transvaginal ultrasonography (TV-USG): Only the area around the uterine ostium that is markedly swollen can be confirmed. The intensity of the echo is almost uniform. ascites (-)

Transabdominal ultrasonography (TA-USG): A bulky tumor measuring 246 x 140 mm in diameter, with a blood reservoir inside. Hemorrhagic necrosis and lumen are observed. An irregularly shaped ridge measuring 43 x 49 mm was found in the lumen.

CT and MRI images: The uterus is large enough to occupy most of the abdomen. Calcification due to some uterine leiomyoma is observed. Suspected onset of uterine leiomyosarcoma or uterine carcinosarcoma. Bulky tumors were found in the pelvis, para-aorta, and left supraclavicular lymph node.

Malignant lymphoma was suspected because of multiple lymphadenopathies.

Differential diagnosis: Polymorphic rhabdomyosarcoma



Contrast CT images
The mass of the left supraclavicular lymph node is indicated by the white arrowheads.
The white dotted circle indicates the uterine tumor.

Case 2: Patient background

A 16-year-old girl went to a general hospital for an outpatient visit because of lower abdominal pain and bleeding. Based on the results of various tests, she was suspected of having a malignant tumor originating from the uterus. The tumor was resected by a total abdominal hysterectomy and bilateral salpingo-oophorectomy. The surgical pathological diagnosis of the excised tissue indicated that the excised tumor was a uterine alveolar rhabdomyosarcoma. A response to VAC therapy was confirmed.

Supplementary material 3

Case 1: Results of surgical pathological diagnosis

Diagnosis: Pleomorphic rhabdomyosarcoma

Tumor size: at least 23 cm in greatest dismension

Lymph-vascular invasion: present (LVI1)

Positive IHC: CD56 (partial), synaptophysin (partial), desmin (partial), myogenin (partial), AE1/AE3 (focal), Cam5.2 (focal), CD99 (partial, main dot-like), p53 (diffuse).

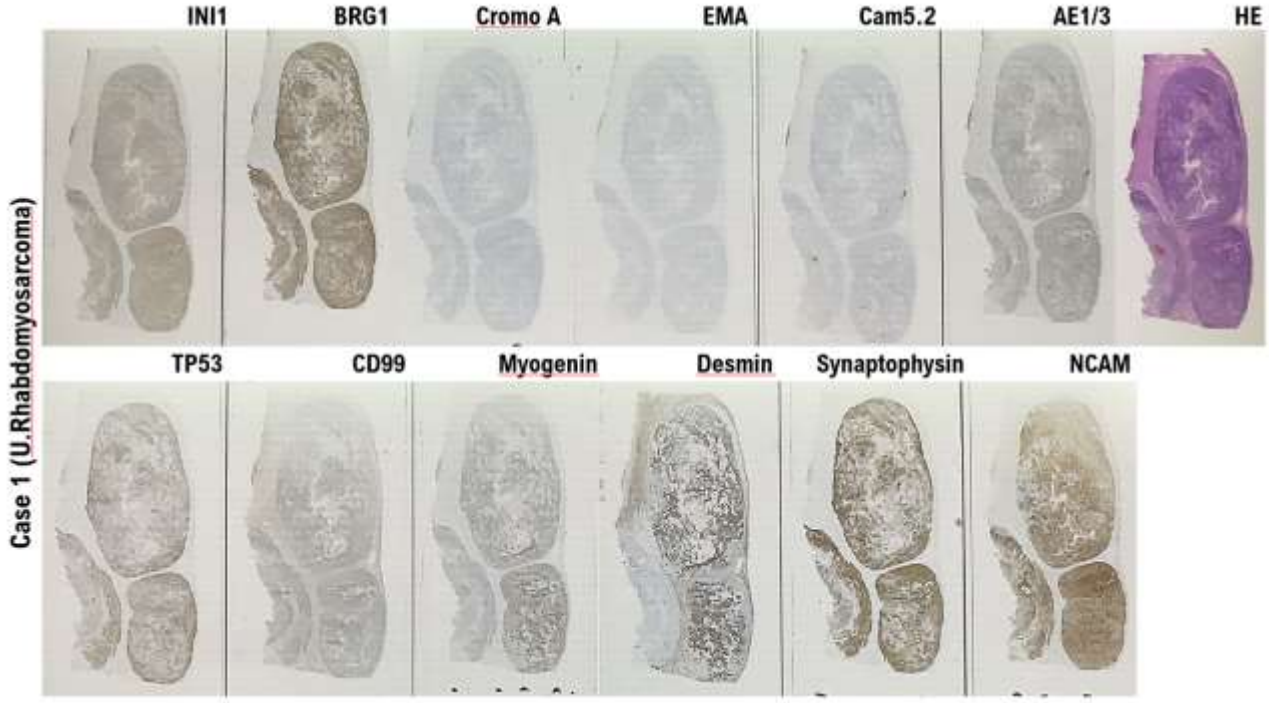
Negative IHC: EMA, chromogranin A.

Margins: uncertain

-Leiomyoma

Ovary and tube, bilateral, salpingo-oophorectomy: involved by pleomorphic rhabdomyosarcoma.

Omentum, biopsy: A small amount of necrotic cells and tumor cells are mixed.



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