

# Mixed endometrial stromal and smooth muscle tumor of the uterus in a postmenopausal woman: morphologic and immunohistochemical features

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## Summary

Mixed endometrial stromal and smooth muscle tumor of the uterus is a rare occurrence, and it is truly challenging to diagnose or differentiate mesenchymal tumors of the uterine corpus, due to their many overlapping features. In most cases, the gross pathology of mixed endometrial stromal and smooth muscle tumor differs from that of pure endometrial stromal and pure smooth muscle tumors. A 59-year-old postmenopausal woman presented with vaginal spotting, low abdominal pain, and an uterine mass. Subsequent pelvic magnetic resonance imaging revealed a 4.0×3.8×3.4-cm sized uterine mass with enhancement. The mass showed restricted diffusion on diffusion-weighted images, and thus, was suspected to be uterine sarcoma rather than degenerative leiomyoma. Levels of tumor markers, CA 125, CA 19-9, and SCC, were within their normal ranges. The patient underwent exploratory laparotomy. Morphological and immunohistochemical evaluations were performed, and a final diagnosis of mixed endometrial stromal and smooth muscle tumor of the uterus was rendered. Her postoperative course was uneventful, and aromatase inhibitor adjuvant therapy was administered.

**Key words:** Endometrial stromal tumor; Smooth muscle tumor; Postmenopausal.

## Introduction

Mixed endometrial stromal and smooth muscle tumor arising in the uterus is an under-recognized occurrence due to rarity and its unknown histogenesis. However, Scully *et al.* suggested that multipotential cells in the uterus might differentiate into endometrial stroma or smooth muscle cells [1]. The tumor consists of an admixture of low-grade endometrial stromal sarcoma (ESS) and smooth muscle tumor [2]. Small regions of smooth muscle differentiation are commonly observed in endometrial stromal neoplasms, and insignificant portions of stromal components are present in smooth muscle tumors. Mixed endometrial stromal and smooth muscle tumors can be defined as those containing more than 30% of each component [3]. The tumor mainly occurs within the uterine corpus, and usually has an intramural location. It may sometimes have a submucosal or subserosal location, although an extremely rare case with an extrauterine location has been reported. Its clinical manifestations are non-specific and similar to those of pure endometrial stromal or smooth muscle tumors. Uterine bleeding is the most common complaint followed by an enlarged uterus or mass. Here, the authors present a case of mixed endometrial stromal and smooth muscle tumor of the uterus in a postmenopausal woman and describe its morphologic and immunohistochemical features.

## Case Report

A 59-year-old postmenopausal woman presented with vaginal spotting, low abdominal pain, and an uterine mass. Pelvic examination revealed a slightly enlarged uterus, and transvaginal ultrasonography and pelvic magnetic resonance imaging revealed an enlarged uterus with a 4.0×3.8×3.4-cm sized mass. T2-weighted images depicted a well-defined uterine mass with heterogeneous signal intensity and contrast-enhanced T1-weighted images revealed a markedly enhanced mass. On high b-value diffusion-weighted images, the mass showed restricted diffusion, and thus, was suspected to be uterine sarcoma rather than degenerative leiomyoma (Figure 1). Levels of tumor markers, CA 125, CA 19-9, and SCC, were within their normal ranges.

The patient underwent exploratory laparotomy, and intraoperative frozen examination revealed an endometrial stromal tumor. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed under the suspicion of uterine sarcoma. Grossly, the mass was an intramurally located in the lateral uterine wall, measured 3.5×3.2×3.0 cm, and was soft and yellowish in color (Figure 2). Microscopically, the tumor consisted of an admixture of endometrial stromal tumor and a fascicular proliferation of spindle cells, suggesting smooth muscle differentiation, and a characteristic 'star-burst' appearance was noted. Tumor cells had a bland cytological appearance and mitoses were almost absent. The boundary between the tumor and myometrium was relatively distinct. Only focal minimal myometrial invasion was observed, but lymphovascular involvement was not (Figure 3). Immunohistochemically, smooth muscle cells were immunoreactive for desmin, and a group of cells interspersed between them, probably endometrial stromal cells, were immunoreactive for

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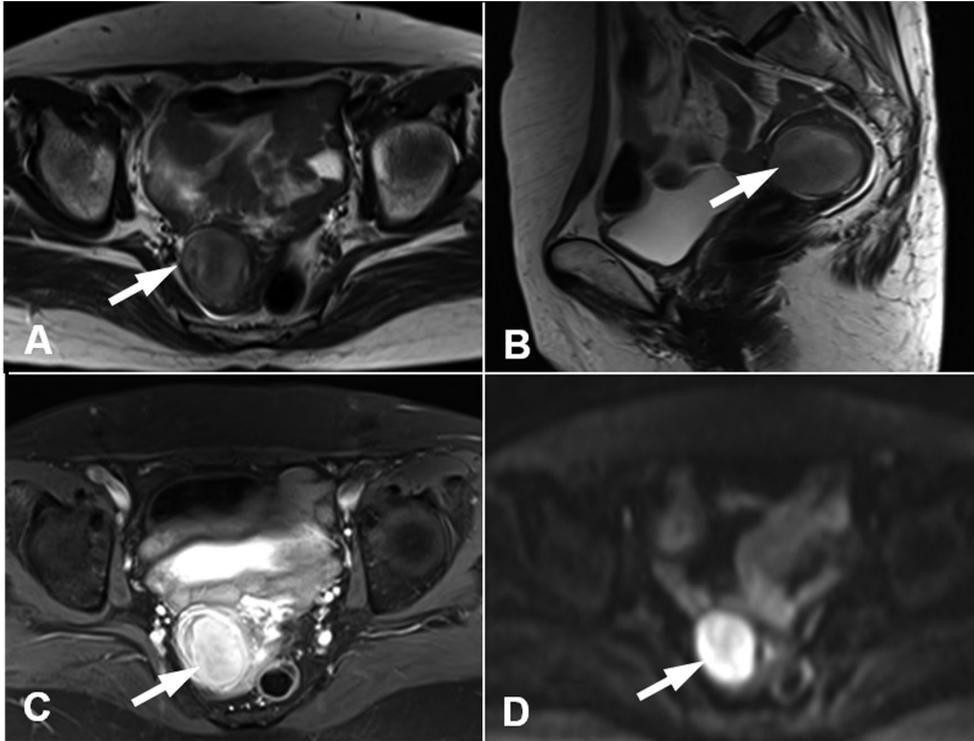


Figure 1. — Mixed endometrial stromal and smooth muscle tumor of the uterus. (A, B) Axial (A) and sagittal (B) T2-weighted images showing a well-defined endometrial mass (arrow) with heterogeneous signal intensity. (C) Contrast-enhanced fat-suppressed T1-weighted image showing the mass with marked enhancement (arrow). (D) Diffusion-weighted image at  $b = 1,000 \text{ s/mm}^2$  demonstrating restricted diffusion in the mass (arrow).

CD10 (Figure 4). The mass was pathologically confirmed to be a mixed endometrial stromal and smooth muscle tumor of the uterus. The patient's postoperative course was uneventful with no recurrence or symptoms after 13 months follow-up. Aromatase inhibitor adjuvant therapy was administered.

### Discussion

Mixed endometrial stromal and smooth muscle tumor is considered a distinct entity and arises in the uterine corpus. However, the differentiation of endometrial stromal tumor and smooth muscle tumor has become increasingly obscure in recent years due to their overlapping pathologic features. In fact endometrial stromal cells and myometrial smooth muscle cells are inextricably related by a common Müllerian-mesodermal derivation [4].

Here, the authors reported a rare mixed endometrial stromal and smooth muscle tumor of the uterus in a postmenopausal woman. The clinicopathological characteristics of this tumor have been previously described by Oliva *et al.* [5]. The tumor consists of an admixture of low-grade ESS and smooth muscle tumor. A characteristic 'star-burst' appearance is observed in most cases [5]. Uterine bleeding is the most common symptom, because the tumor is estrogen dependent.

A diagnosis can be made based on morphological and immunohistochemical evaluations. A literature review showed that almost all cases present as a solitary intramural nodule. On gross examination, this tumor often shows an admixture of soft and firm areas. Some tumors



Figure 2. — Gross appearance of mixed endometrial stromal and smooth muscle tumor of the uterus. Cut section of uterus showing a well-circumscribed mass measuring  $3.5 \times 3.2 \times 3.0 \text{ cm}$  within myometrium and distorting the endometrial cavity.

have a soft tan to yellow nodule and firm white whorl-like nodules, while others have soft nodules with peripheral firm areas. Microscopically, the endometrial stromal component is identical to that observed in endometrial stromal tumors and is composed of packed small, ovoid cells, and numerous small arterioles. Smooth muscle cells vary in appearance. Smooth muscle elements show typical spindle-shaped cells with eosinophilic cytoplasm in fas-

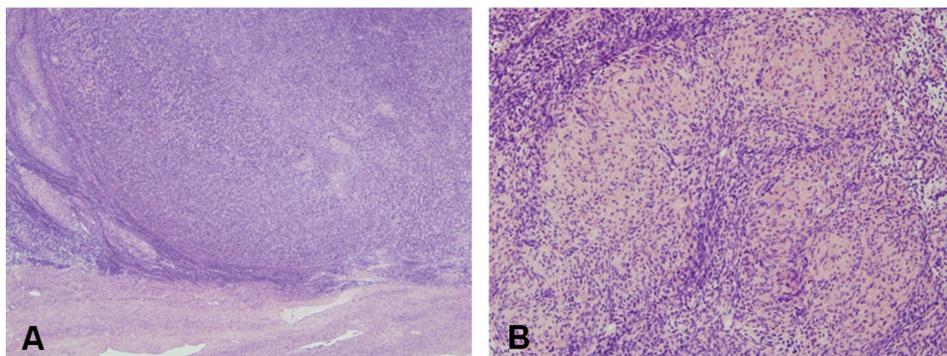


Figure 3. — (A) The tumor consisting of an admixture of endometrial stromal and smooth muscle tumors. The boundary between the tumor and myometrium is relatively distinct (H&E,  $\times 40$ ). (B) A proliferation of spindle cells suggesting smooth muscle differentiation, and the characteristic ‘star-burst’ appearance is observed (H&E,  $\times 200$ ).

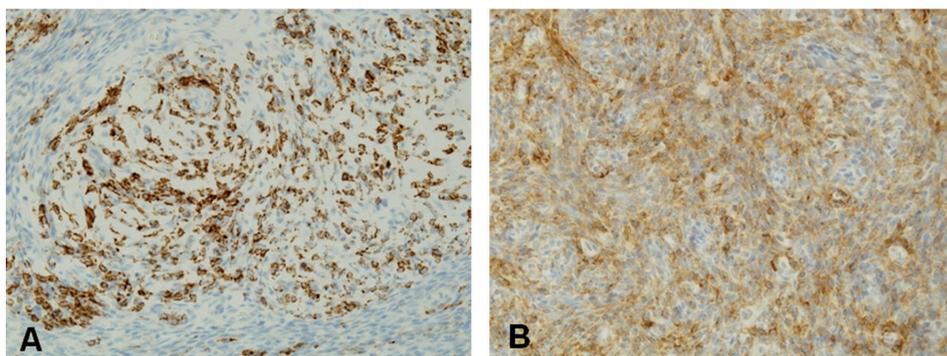


Figure 4. — Smooth muscle cells were positive for desmin (A,  $\times 400$ ) and groups of cells interspersed between them, which are probably of endometrial stromal origin, are positive for CD10 (B,  $\times 400$ ). Immunohistochemical staining for desmin showing cytoplasmic staining in smooth muscle components, and immunohistochemical staining for CD10 showing membranous staining in endometrial stromal components.

cicles or epithelioid cells with clear or amphophilic cytoplasm in nodules. The most characteristic feature in the smooth muscle component is prominent central hyalinization and thin bundles of collagen radiating toward the periphery, referred to as a “starburst” appearance. However, some authors have suggested restricting the use of this term to lesions in which both components comprise at least 30% of the tumor.

It is sometimes difficult to differentiate endometrial stromal cells and smooth muscle cells under a light microscope, and thus, immunohistochemical analysis is an excellent ancillary technique for the diagnosis of mixed endometrial stromal and smooth muscle tumors. Despite their variable appearance, smooth muscle components show strong positive immunostaining for smooth muscle actin and desmin, and immunoreactivity in stromal elements is identical to that in typical endometrial stromal tumors. Typical endometrial stromal tumor should be positive for CD10, but not positive for smooth muscle markers, such as, smooth muscle actin and desmin. In the present case, smooth muscle cells were positive for desmin and endometrial stromal cells were positive for CD10, and the stromal component accounted for more than 30% of the tumor. A characteristic ‘star-burst’ appearance, proliferation of spindle cells suggesting smooth muscle differentiation, was observed.

The main component of the differential diagnosis of mixed endometrial stromal and smooth muscle tumors is

cellular leiomyoma. However, cellular leiomyoma shows different morphological features, such as large blood vessels and no star-burst pattern. Immunohistochemical staining can be very useful for accurate differentiation. Furthermore, the ‘star-burst’ appearance is considered characteristic of mixed endometrial stromal and smooth muscle tumor indicative of a form of smooth muscle differentiation in this tumor [5].

No study has addressed the radiologic features of mixed endometrial stromal and smooth muscle tumors. Radiologically, this tumor might be confused with other uterine mesenchymal tumors, and thus, findings should be interpreted with caution. In particular, soft areas of endometrial stroma may be misinterpreted as either cystic degeneration of leiomyoma or uterine leiomyosarcoma. Therefore accurate diagnosis relies on postoperative pathologic examination. The present case was initially interpreted as uterine leiomyosarcoma.

The smooth muscle component is usually benign. The present case showed no significant cytologic atypia, no tumor cell necrosis, and no mitotic figures. The presence of a smooth muscle component does not significantly impact prognosis, because endometrial stromal tumor determines biologic behavior. Although this rare tumor progress slowly and its prognosis is consistent with low-grade ESS, its malignant behavior causes recurrence and metastasis, even to lung or heart, when endometrial stro-

mal components have an infiltrating margin [4, 5]. A literature review showed four cases of intracardiac extension [6-9], and one case of lung metastasis, which occurred nine months after hysterectomy [4]. For this reason, patients with this tumor should be carefully followed after hysterectomy for cardiopulmonary symptoms and by imaging. Anti-estrogen therapy is usually prescribed, because the tumor is estrogen-dependent.

In summary, accurate diagnosis and differentiation of mesenchymal tumors of the uterine corpus is truly challenging due to their many overlapping features. The authors presented a case of mixed endometrial stromal and smooth muscle tumor of the uterus in a postmenopausal woman that was diagnosed based on its morphological and immunohistochemical features

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