Summary: Endometriosis is a common gynecological disorder most often involving the pelvic region. Although it is rare, endometriosis occurring outside of the peritoneal cavity most commonly occurs within scars of the abdominal wall, but it has been reported in the lungs, pleura, kidneys, brain, and the extremities. Herein, we present 2 cases of endometriosis, including 1 case of endometriosis of the wrist that clinically mimicked a soft-tissue neoplasm and 1 case of right-groin endometriosis mimicking synovial sarcoma during the initial pathological interpretation of findings on fine needle aspiration. We also report on a third patient with synovial sarcoma to demonstrate a diagnostic pitfall. To our knowledge, endometriosis within the skeletal muscle of the wrist has not been previously reported in the literature. A literature review was performed, and we discuss how this diagnostic pitfall may be avoided. We review the techniques for diagnosing synovial sarcoma and the importance of a high index of suspicion for endometriosis when investigating any soft-tissue mass in a female patient of reproductive age. Adequate pathological evaluation in conjunction with the correlating clinical and radiological information should help facilitate an accurate diagnosis.

Introduction
Endometriosis is a common, benign, non-neoplastic, chronic gynecological disorder characterized by the presence of uterine endometrial tissue outside of the uterine cavity that occurs in an estimated 6% to 10% of women. Clinically, chronic lower abdominal menstrual-related pain, cramping, dyspareunia, and infertility are all classic presentations of the condition. Within the pelvic cavity, the ovaries are the most common site affected by endometriosis. Although extraperitoneal disease is rare, it most commonly occurs within scars of the abdominal wall, typically following cesarean delivery, or in the lungs and pleura; however, it has been reported in other locations such as the kidneys, brain, and the extremities. In general, a diagnosis of endometriosis is established after recognition of clinical symptoms followed by histological confirmation. Characteristic microscopic features include benign endometrial glands, endometrial stromal tissue, and hemosiderin. Treatment for endometriosis may include anti-inflammatory drugs, hormone therapy, and surgical intervention.

By contrast, synovial sarcoma is a rare malignant tumor that typically presents as a deep-seated, soft-tissue mass located near a large joint. It is one of the most common soft-tissue tumors occurring in adolescents and young adults, with reported cases involving a wide variety of locations. Biphasic synovial sarcoma has both epithelioid and spindle cell components, so it may be high on the list of diagnostic considerations when endometriosis occurs in an unusual soft-tissue location — particularly when the tissue sample is limited.

Herein, we report 2 cases of endometriosis that presented as painful soft-tissue masses in a joint mimicking soft-tissue neoplasms. We also report on a case of synovial sarcoma to demonstrate the diagnostic pitfall and review the diagnostic techniques available for confirming synovial sarcoma.

Case Reports
Case 1
A 23-year-old woman presented with intermittent pain and swelling of her right wrist that she had had for nearly 3 years following a mild injury. Physical examination was performed, the results of which showed swelling and tenderness of her wrist without any definite mass. She was diagnosed with wrist sprain and treated by a hand surgeon with nonsteroidal anti-inflammatory drugs and local steroid injections. Her pain was not adequately controlled with these therapeutic techniques and eventually was noted to be cyclical and...
associated with her menstrual cycle.

Magnetic resonance imaging (MRI) was obtained, and the findings showed a multiloculated mass $2 \times 1.5 \times 1.5$ cm in size on the volar side of the ulnar head with mixed signal intensity on T1-weighted imaging. The mass contained several areas of hyperintensity presumed to be due to hemorrhage (Fig 1). The differential diagnosis included tenosynovial giant cell tumor and endometriosis. However, the patient did not have a history of endometriosis, and findings on transvaginal ultrasonography did not reveal any additional abnormality of the uterus, abdomen, or pelvis.

The patient underwent exploratory surgery that revealed an unencapsulated mass with indistinct borders infiltrating into the distal radial ulnar joint. Sectioning of the mass after removal revealed tan to red-brown cut surfaces with scattered focal areas of hemorrhage (Fig 2). Subsequent histopathological evaluation of the specimen was consistent with endometriosis, with endometrial glands within the connective tissue of the wrist (Fig 3). Immunohistochemical studies for CD10, estrogen receptor, and progesterone receptor were performed and were immunoreactive in the appropriate cells, thus supporting the diagnosis (Fig 4).

Postoperatively, her range of motion improved, her local, intermittent pain resolved, and no additional sites of endometriosis have been discovered to date.

**Case 2**

A 40-year-old woman presented with a small subcutaneous mass in her right groin that was gradually

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**Fig 2.** — Intraoperative photograph of the multiloculated, hemorrhagic wrist mass.

**Fig 3.** — Histological specimen of the wrist mass showing endometrial glands and stroma within the connective tissue (hematoxylin and eosin stain; original magnification, ×200).

**Fig 4.** — Immunohistochemical expression of estrogen receptors by the endometrial glands and stromal cells (original magnification, ×200).

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increasing in size and associated with abdominal discomfort. She reported that she noticed the lesion 2 years prior her presentation.

Findings on physical examination were unremarkable, except for the palpable, soft, mobile mass in her right groin. Findings on MRI revealed a poorly circumscribed, enhancing soft-tissue mass in the right inguinal region that was contiguous with the right rectus sheath (Fig 5). The mass was approximately 2.3 × 1.7 cm on the axial section. Stranding was seen in the subcutaneous fat superficial to this mass with slight thickening of the overlying cutaneous tissue. A mesenchymal neoplasm was initially considered, and the patient was referred to a cancer center for diagnosis and treatment.

Ultrasonographic-guided fine needle aspiration (FNA) was performed, and cytological evaluation revealed a biphasic lesion with glandular and spindle cell components (Fig 6). The differential diagnosis included synovial sarcoma, well-differentiated metastatic adenocarcinoma with desmoplastic stroma, and a primary adnexal skin tumor.

Immunohistochemistry showed cells from the lesion positive for CD10, CD68, and vimentin. The SS18/SSX1 or SS18/SSX2 fusion transcripts were not detected by reverse transcriptase–DNA amplification. Re-examination of the cellblock revealed occasional hemosiderin and cytological features that were overall the most consistent with endometriosis.

Upon questioning, the patient revealed a known history of endometriosis. The mass was excised with nearby fascia due to its deep infiltration into the subcutaneous tissue, and the final pathological evaluation confirmed endometriosis (Fig 7).

**Case 3**

A 66-year-old woman presented with a 5.1-cm size, space-occupying medial mass on her left mid thigh. MRI findings showed evidence of hemorrhage within the tumor (Fig 8). The differential diagnostic considerations included soft-tissue sarcoma, metastatic disease, and hematoma. Findings on biopsy revealed a predominantly glandular tumor with a focal spindle cell component and few scattered cal-

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**Fig 5.** — Findings on magnetic resonance imaging show the endometrial tissue (orange arrow) appearing as soft-tissue outgrowth from the muscles and fascia of the right groin.

**Fig 6.** — Specimen from fine needle aspiration reveals fragments of glandular tissue with no significant nuclear atypia (hematoxylin and eosin stain of the cellblock; original magnification, × 400).

**Fig 7.** — Right groin excision specimen showing benign endometrial glands and surrounding endometrial stroma consistent with endometriosis (hematoxylin and eosin stain; original magnification, × 200).

**Fig 8A–B.** — Magnetic resonance imaging of the (A) coronal and (B) axial section of the deep-seated, left medial thigh mass.
cifications (Fig 9). Both the glandular and the spindle cell components exhibited nuclear atypia, including hyperchromasia, and high nuclear-to-cytoplasmic ratios with no intracytoplasmic mucin.

Immunohistochemical studies showed the tumor cells positive for AE1/AE3/CAM5.2 and KRT7 (CK7) but negative for KRT20 (CK20), S100, TTF1, and CDX2. Due to her previous history of invasive ductal carcinoma, immunohistochemical markers for breast origin, including GATA3, mammaglobin, estrogen receptor, progesterone receptor, and ERBB2, were also performed and were negative. An additional immunohistochemical study for cancer-testis antigen (NY-ESO-1) showed a strong and diffusely positive immunoreactivity, further supporting the diagnosis of synovial sarcoma (see Fig 9). The overall clinical presentation — in combination with the histological features — was most compatible with synovial sarcoma.

Molecular studies revealed the SS18/SSX1 fusion transcript by reverse transcriptase–DNA amplification, thereby confirming the diagnosis of synovial sarcoma.

Radical resection was performed, and the patient was diagnosed with biphasic synovial sarcoma.

**Discussion**

Although it is common within the pelvic peritoneum, ovaries, and the rectovaginal septum, endometriosis rarely occurs outside these locations. Scars of the abdominal wall — in particular, those following cesarean delivery — and the lungs and pleura are the most common extra-abdominal sites involved, followed by the inguinal region or thigh.

Proposed theories for the cause and mechanisms of endometriosis include ectopic transplant due to retrograde menstruation, dissemination by lymphatic or vascular flow, and transformation of intestinal metaplasia. Retrograde menstruation is a widely accepted theory by Sampson that accounts for most of the origin of peritoneal — and possibly rectovaginal — disease. Coelomic metaplasia is another recognized theory. In addition, various modes of inheritance in combination with interactions between specific inherited genes and environmental factors have been proposed.

When endometriosis occurs in its classical, cyclical presentation in a female of reproductive age within the pelvic cavity, the diagnosis is straightforward. However, the patients described in the present report each presented with an infiltrative soft-tissue mass, one in the wrist and the other in the right groin. Without any knowledge of a prior history of endometriosis, and with limited tissue sampling, these lesions could be mistaken for soft-tissue neoplasms, possibly resulting in unnecessary aggressive management.

Microscopically, endometriosis is composed of endometrial-type glands that may be mitotically active and admixed with endometrial stroma, fresh hemorrhage, and hemosiderin. The glands may display metaplastic and hyperplastic changes, as can be seen in the endometrium. Prominent chronic inflammation within small vessels and reactive fibroblasts may also be present. When a limited specimen is obtained via biopsy, some diagnostic features may not be seen; thus, the histological features may be confused with other tumors, such as synovial sarcoma, metastatic, well-differentiated adenocarcinoma, and cutaneous adnexal neoplasms (eg, apocrine tubular adenoma, syringoma, microcystic adnexal carcinoma, mixed tumors). Endometriosis may also present with pseudoinfiltrative growth into normal tissue, which may be misinterpreted as an invasive and malignant process. In such cases, recognizing the presence of endometrial stroma associated with the glands could help the clinician reach the correct diagnosis of endometriosis.

Cases of endometriosis mimicking synovial sarcoma have been previously described, but they are rare. This clinical scenario is challenging when endometriosis presents in an uncommon location and...
when the tissue sample is limited, because both diseases have epithelial and spindle cell components. The epithelial component of synovial sarcoma is arranged in glands or cords and nests, and glandular lumina may contain mucus, simulating endometrial glands.\textsuperscript{4,7,9,11} The spindle cells observed in cases of synovial sarcoma have hyperchromatic nuclei with scant cytoplasm and an increased nuclear-to-cytoplasmic ratio, whereas endometrial stromal cells should lack atypical nuclear features and have paler staining nuclei.

When synovial sarcoma is considered, results from immunohistochemical markers and molecular studies will usually help support the correct diagnosis. The epithelioid portion of synovial sarcoma, if present, is characteristically immunoreactive for cytokeratins, \textit{ETFA (EMA)}, carcinoembryonic antigen, \textit{BCL2}, and \textit{TLE1}, but negative for CD34, smooth muscle and skeletal muscle markers, \textit{WTI}, and \textit{FLI1}.\textsuperscript{26-29} Normal synovial tissue will be negative for cytokeratin markers. Typically, the spindle cell component of synovial sarcoma is positive for vimentin. Confirmation of synovial sarcoma is accomplished by testing for the characteristic translocation t(X;18)(p11.2;q11) via polymerase chain reaction to detect either the \textit{SS18/SSX1} or \textit{SS18/SSX2} fusion transcript.\textsuperscript{27,28}

A promising development for synovial sarcoma is the potential to target the cancer-testis antigen (NY-ESO-1) autologous T cells transduced with a T-cell receptor against NY-ESO-1. Certain immunohistochemical studies detect NY-ESO-1 in a strong, diffuse pattern in as many as 80% of synovial sarcomas.\textsuperscript{30,31} Furthermore, studies have shown that NY-ESO-1 was either rarely or weakly positive in a variety of other mesenchymal tumors (eg, gastrointestinal stromal tumor, malignant peripheral nerve sheath tumor, dermatofibrosarcoma protuberans, leiomyosarcoma, solitary fibrous tumor, cellular schwannoma), making it a potentially useful immunohistochemical marker for distinguishing synovial sarcoma from other soft-tissue tumors.\textsuperscript{30,32}

Another potential target for synovial sarcoma is the enhancer of zeste homolog 2 (EZH2). Dysregulation of EZH2 is associated with a poor prognosis in a variety of tumor types and is highly expressed by poorly differentiated synovial sarcoma.\textsuperscript{33} In vitro study results have suggested a potential role for targeting EZH2-mediated methylation of H3K27 in the treatment of synovial sarcoma.\textsuperscript{35}

Conclusions

Endometriosis mimicking a soft-tissue tumor, such as synovial sarcoma, remains a rare and under-recognized diagnostic pitfall.\textsuperscript{4,9,24} To our knowledge, endometriosis within the skeletal muscle of a distal extremity, especially within the wrist, has not been previously reported. Both of our cases of true endometriosis presented in an orthopedic setting due to location near a joint and were clinically misleading, and each were suspicious for soft-tissue neoplasms. Thus, this report highlights the importance of having a high index of suspicion for endometriosis when investigating an infiltrative soft-tissue mass in any female patient of reproductive age, especially when the mass is painful and associated with the menstrual cycle.\textsuperscript{5,9,24} Clinicians should also be aware of the ancillary techniques available for synovial sarcoma, such as immunohistochemistry for cancer-testis antigen (NY-ESO-1), because the results of such testing may also support the diagnosis and provide useful information for targeted therapy. Careful attention to detail during the pathological examination of biopsy specimens obtained from limited tissue and correlating those results with clinical and radiological information should help the clinician make an accurate diagnosis.

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**References**


