

Case Report

Decidualization of intranodal endometriosis in a postmenopausal woman

Hyun-Soo Kim^{1*}, Gun Yoon^{2*}, Byoung-Gie Kim², Sang Yong Song¹

¹Department of Pathology and Translational Genomics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; ²Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea. *Equal contributors.

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Abstract: Here we describe an unusual case of decidualized endometriosis detected in pelvic lymph nodes. The presence of intranodal ectopic decidua in pregnant women has been described. A few cases of decidualization of endometriotic foci in the pelvic or para-aortic lymph nodes have also been associated with pregnancy. However, decidualized intranodal endometriosis occurring in a postmenopausal woman has not been described. A 52-year-old woman presented with a very large adnexal mass. Menopause occurred at the age of 47, and she had been treated with hormone replacement therapy. She received a total abdominal hysterectomy with bilateral salpingo-oophorectomy and pelvic and para-aortic lymphadenectomy for clear cell carcinoma of the right ovary. Histological examination revealed the presence of ectopic decidua in several pelvic lymph nodes. The deciduas consisted of sheets of loosely cohesive, large, uniform, round cells with abundant eosinophilic cytoplasm. Typical of decidualization of intranodal endometriosis, a few irregularly shaped, inactive endometrial glands lined by single layers of columnar to cuboidal epithelium were present within the decidua. An immunohistochemical study revealed that the decidual cells were positive for CD10, vimentin, estrogen receptor and progesterone receptor, which indicated that progestin-induced decidualization had occurred in the intranodal endometriotic stroma. To the best of our knowledge, this case represents the first report of decidualized intranodal endometriosis occurring in association with hormone replacement therapy in a postmenopausal woman. Misdiagnosis of this condition as a metastatic tumor can be avoided by an awareness of these benign inclusions, supported by immunohistochemical staining results.

Keywords: Decidual reaction, endometriosis, lymph node, hormone replacement therapy

Introduction

A variety of benign ectopic inclusions can occur ectopically within lymph node parenchyma, including thyroid follicles, mammary acini and ducts, salivary tissue and mullerian-type glands have been described [1]. The mullerian-type glands are by far the most common type of benign ectopic inclusion and are present in abdominal and pelvic lymph nodes removed from approximately 14% of women. Endometriosis in the pelvic lymph nodes is also a frequent incidental finding. Similar to normal endometrium, endometriotic foci can become decidualized during pregnancy in response to high levels of circulating progestin [2]. Decidualization is the process of conversion of the normal endometrium during pregnancy into a specialized uterine lining adequate for opti-

mal accommodation of gestation. This change is primarily induced by progesterone and involves hypertrophy of the endometrial stromal cells, thickening of the normal endometrium and formation of decidua.

The presence of intranodal ectopic decidua during pregnancy has been described in the literature. A few cases of decidualization of endometriotic foci in the pelvic or para-aortic lymph nodes have also been associated with pregnancy. However, decidualized intranodal endometriosis occurring in a postmenopausal woman has not been described yet. Here we report an unusual case of decidualized endometriosis detected in the pelvic lymph nodes of a postmenopausal woman treated with hormone replacement therapy. We describe these histopathological findings and the results of a thorough immunohistochemical study.

Decidualized intranodal endometriosis

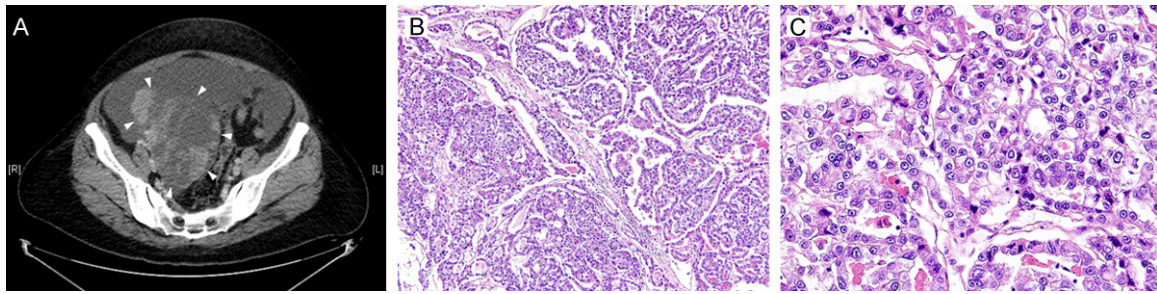


Figure 1. Imaging and histologic findings of ovarian clear cell carcinoma. A. Computed tomographic scan revealed marked ascites and a very large heterogeneous mass in the right lower abdomen. The maximum diameter is 15 cm and it contains solid and cystic components. B. The lesion consists of tumor cell papillae, solid sheets separated by delicate septa and glandular lumina lined by a single layer of tumor cells. C. The tumor cells have clear to eosinophilic cytoplasm and hyperchromatic nuclei with conspicuous nucleoli.

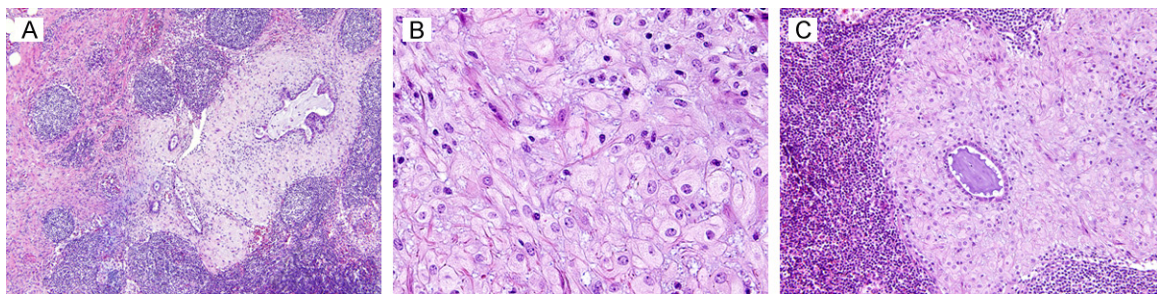


Figure 2. Histologic findings of decidualized intranodal endometriosis. A. Ectopic intranodal decidua surrounding endometrial glands fills the subcapsular region of a pelvic lymph node. B. High-power magnification of the decidualized stroma reveals large polygonal cell aggregates with abundant cytoplasm and round nuclei resembling the pregnancy-like response of the endometrium to progesterin. C. Small inactive glands lined by single layers of epithelium are surrounded by abundant decidualized stroma.

Clinical presentation

A 52-year-old Korean woman (gravid 1, para 1) with an adnexal mass was referred to the Department of Obstetrics and Gynecology, Samsung Medical Center (Seoul, South Korea). She had a 2-month history of progressive abdominal discomfort and a 1-day history of dyspnea. Her medical history included hypothyroidism. She experienced menopause at the age of 47 years, and had taken a combined course of hormone replacement therapy for 6 years. There were no other significant medical history findings and no history of autoimmune disease, thrombosis or bleeding disorders. The physical examination revealed a palpable mass present in the right lower abdomen. Laboratory testing revealed a normal complete blood count and routine biochemistry results. Analysis for tumor markers revealed an increased CA-125 level (1687.3 U/mL). The CA-19-9 level (11.0 U/mL) was within the normal range. A computed

tomographic scan revealed marked ascites and a large, heterogeneous, solid and cystic mass arising from the adnexa (**Figure 1A**). The uterus was normal in size, and no endometrial thickening was apparent. Surgery revealed the presence of 4 L of straw-colored ascitic fluid and a right ovarian mass. There was no gross evidence of intraperitoneal metastasis, but some pelvic and para-aortic lymph nodes were enlarged. A right salpingo-oophorectomy was performed, and the specimen was immediately analyzed by the pathology department. Because a high-grade carcinoma was present in the frozen section of the mass, the surgery was completed with a total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and bilateral pelvic and para-aortic lymphadenectomy. Final histopathologic examination of the right ovarian tumor revealed the presence of primary clear cell carcinoma. The tumor was categorized as stage IA, according to the most recently revised International Federation

Table 1. Immunostaining results of decidualized intranodal endometriosis

Antigen	Decidua	Gland
Cytokeratin, AE1/AE3	Negative	Positive
Cytokeratin, CAM 5.2	Negative	Positive
Cytokeratin 5/6	Negative	Negative
Cytokeratin 7	Negative	Positive
Cytokeratin 20	Negative	Negative
Epithelial membrane antigen	Negative	Positive
p63	Negative	Negative
p16	Negative	Negative
CD10	Positive	Negative
Vimentin	Positive	Negative
Desmin	Negative	Negative
Smooth muscle actin	Negative	Negative
Estrogen receptor	Positive	Positive
Progesterone receptor	Positive	Positive
Calretinin	Negative	Negative
WT-1	Positive	Negative
Ki-67	Positive (1%)	Positive (1%)

of Gynecology and Obstetrics (FIGO) staging system guidelines [3, 4]. The patient's postoperative course was uneventful, and she was discharged from the hospital 5 days after surgery.

Pathologic findings

The right ovarian mass was a 1,680 g multiloculated, solid, cystic tumor measuring 15×12×10 cm. The tumor had a smooth, lobulated external surface. Fleishy, yellow/tan-colored, solid nodular areas were present in the cross-sections. Microscopically, the ovarian tumor displayed tubulocystic, papillary and solid patterns admixed in varying degrees (**Figure 1B**). The tumor cells varied from polygonal, to cuboidal, to flattened in shape. The nuclei were pleomorphic, medium to large in size, and often had prominent nucleoli. The cytoplasm ranged from clear to, less commonly, eosinophilic (**Figure 1C**). Apical hyperchromatic nuclei (hobnail cells) were also present. Mitotic figures were relatively uncommon. This constellation of histopathologic findings was typical of clear cell carcinoma of the ovary.

The histopathologic examination of the pelvic lymph nodes revealed the presence of multiple nodules of ectopic decidua within the subcapsular sinus. They were arranged in sheets of

loosely cohesive, large, uniform, round cells with abundant granular, eosinophilic cytoplasm (**Figure 2A**). The nuclei of the decidual cells were uniform, with an oval to round shape, and were centrally located, along with vesicular chromatin and prominent nucleoli (**Figure 2B**). Mitotic figures were absent. In some areas, the decidual cells were polygonal and closely packed, which is a pattern indistinguishable from the endometrial decidua of pregnancy. A few irregularly shaped endometrial glands lined by a single layer of columnar to cuboidal epithelium were present within the decidua (**Figure 2C**). The decidual nodules were surrounded by normal lymphoid tissue, and there was no evidence of a fibroblastic reaction to their presence. Consistent with these findings, the endometrium showed the morphologic features of progestin effects (particularly the decidual pattern), which are characterized by obvious decidualization of the stroma and small inactive glands lined by a single layer of epithelium. Some ectatic venules were also present.

The immunohistochemical staining results are presented in **Table 1**. The decidual cells were strongly positive for CD10, vimentin (**Figure 3A**), estrogen receptor (ER; **Figure 3B**), progesterone receptor (PR; **Figure 3C**). They were negative for a panel of cytokeratin, epithelial membrane antigen, p63, desmin and calretinin (**Figure 3D**). The glandular epithelial cells were positive for cytokeratin (CK) AE1/AE3 (**Figure 3E**), CAM 5.2, CK 7, epithelial membrane antigen, ER and PR, but negative for CK 5/6, CK20 and calretinin. WT-1 stained the decidual cells (**Figure 3F**), but not the glandular epithelial cells. The histological diagnosis was intranodal endometriosis with marked decidualization.

Discussion

During pregnancy, decidualization can occur external to the uterus; the stromal cells become epithelioid, plump and eosinophilic decidual cells [5]. Many previous reports have described decidualosis of the peritoneal surface of the uterus, ovaries, appendix, lymph nodes and other pelvic organs. This phenomenon has been attributed to progestational effects on endometriosis. This assumption is supported by the fact that the endometrium is the natural precursor of decidua and by the similar topographic distribution of endometriotic and gestational decidual tissue within the peritoneal cavity [6]. Indeed, Moen and colleagues [7] reported that

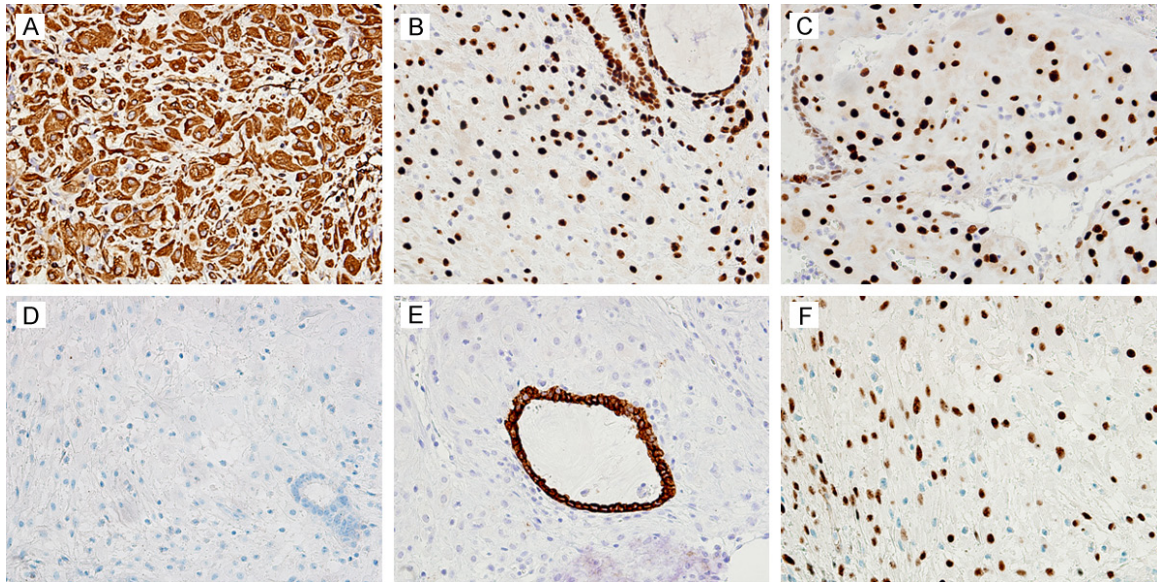


Figure 3. Immunostaining results of decidualized intranodal endometriosis. The decidual cells are strongly positive for (A) vimentin, (B) ER and (C) PR, but negative for (D) calretinin. The glandular epithelial cells are positive for (E) pan-CK. (F) WT-1 immunostaining highlights the decidual cells.

biopsy results revealed decidualization of pelvic endometriotic lesions by biopsy in 10 of 13 (77%) women with proven endometriosis at laparoscopic sterilization during pregnancy, but in only in 31% of women without endometriosis. A useful diagnostic feature of decidualized endometriosis is the presence of endometrial glands within the decidua. We observed that inactive, irregularly shaped endometrial glands were surrounded by decidualized stroma. Furthermore, the endometrium also displayed obvious decidualization with small inactive glands. The present case differs from the previously reported cases in that decidualization of the endometriotic foci occurred in a postmenopausal woman. We assumed that stimulation by exogenous progestins from hormone replacement therapy might lead to a decidual change of both the endometrium proper and intranodal ectopic endometrium. On rare occasions, endometrial tissue can display morphologic features of a progestin effect even though there is no history of exogenous hormone use. These changes may occur in both premenopausal and postmenopausal women, but their etiology is poorly understood. The patterns can be decidua-like changes, with hypoplastic glands and plump stromal cells. This alteration might be due either to abnormal persistence of a functioning corpus luteum or to a luteinized unruptured follicle. The latter entity occurs

when a follicle develops and persists with luteinization of the granulosa and theca cells. If progesterone is produced by the unruptured follicle, a progestin effect from the endogenous source could occur. An intrauterine device may also lead to an enhanced decidual reaction in the endometrium [8, 9]. The patient described in this case had never used an intrauterine device. Neither a functioning corpus luteum nor a luteinized unruptured follicle was present in either ovary, eliminating the possibility of other causes of progestin effects.

The primary importance in recognizing decidual tissues resides in separating them from other morphologically similar entities that are included in the differential diagnosis based on morphology. Malignant mesothelioma can be very similar to decidua. A morphological variant initially thought to afflict only young women has been described and is characterized by large polygonal cells with ample glassy eosinophilic cytoplasm and prominent nucleoli and a poor prognosis. The term deciduoid malignant mesothelioma is used to reflect this similarity [10]. Recently, however, cases involving older women have been reported [11]. The tumors described in these cases retain the classic immunophenotype of conventional mesotheliomas; therefore, these tumors express calretinin and CKs (including CK 5/6) but demonstrate negative

staining for ER and PR [11, 12]. A panel of antibodies should be used to determine this distinction. Samples from the present case did not immunoreact with any of the CKs tested or with calretinin. Additional features suggestive of malignancy (e.g., cytological atypia and increased mitotic activity) were also absent.

This phenomenon is not widely recognized today because few pathologists have the opportunity to examine pelvic lymph nodes from pregnant women. However, with the use of extended hysterectomy and bilateral pelvic lymphadenectomy during the treatment of cervical cancer in pregnancy, the pathologist should be aware that decidualized tissue may be present in the excised nodes. Decidualized endometrial stroma may closely resemble metastatic squamous cell carcinoma, particularly if frozen sections are used for intraoperative staging. The microanatomical distribution of the deposits within the peripheral sinus of the node also mimics metastatic carcinoma. The requirement to make a histologic distinction between metastatic carcinoma and decidualized endometriosis should be anticipated in the patient undergoing salpingo-oophorectomy and/or hysterectomy with pelvic lymphadenectomy. The possibility of metastatic carcinoma should be excluded from the morphological differential diagnosis at this diagnostic stage. The lack of CK reactivity of decidua is one characteristic useful for making this distinction. A detailed clinical history regarding known primary neoplasms is also helpful.

Benign-appearing glandular tissue of presumed müllerian origin but lacking a stromal component is often found in the pelvic lymph nodes. Theories concerning its origin in the lymph node are similar to those for endometriosis. These glandular nests usually represent a diagnostic challenge when metastatic adenocarcinoma is under consideration, but the correct interpretation is usually not difficult. In difficult cases, an immunohistochemical staining can be used to distinguish neoplastic glands from decidualized endometriosis. However, when a frozen section is used, the pathologist is dependent on the light microscopic features apparent with hematoxylin and eosin staining. Awareness that ectopic decidua can occur in pelvic lymph nodes and knowledge of the unique morphologic features that distinguish decidua and metastatic carcinoma should be sufficient for an accurate diagnosis.

The positive WT-1 immunoreactivity in the decidual cells was an interesting finding. It was consistent with previous data indicating WT-1 expression in decidualized endometrial stroma [13, 14]. Anthony and colleagues [14] found that in cultured human endometrial stromal cells, WT-1 mRNA level is significantly elevated along with increasing progesterone concentrations when decidualization is occurring. They also observed that WT-1 protein is localized to the nuclei of the decidual cells. Similarly, Makrigiannakis and colleagues [13] reported that decidualizing stimuli, including progesterone, induce WT-1 mRNA expression and increase the protein levels. These data suggest that the progesterone-induced changes in the expression of WT-1 in endometrial stromal cells may be important for differentiation into the decidualized phenotype. To the best of our knowledge, we have demonstrated for the first time a strong nuclear immunoreactivity for WT-1 in the intranodal ectopic decidual cells. Further investigations will elucidate the role of WT-1 in the process of decidualization of ectopic endometrium and in the cyclic remodeling process occurring in the endometrium.

In summary, we report here a case of postmenopausal woman with decidualized endometriosis in the pelvic lymph nodes. Even though the phenomenon of ectopic deciduosis is common during pregnancy, decidualization of intranodal endometriosis appears very uncommon in postmenopausal women and has not been reported. Surgical pathologists should be aware of this entity, because it can be misinterpreted as a neoplastic process.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Sang Yong Song, Department of Pathology and Translational Genomics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81, Irwon-ro, Gangnam-gu, Seoul 135-710, South Korea. Tel: +82-2-3410-5480; Fax: +82-2-3410-0025; E-mail: yoda.song@samsung.com

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