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Research Letter

Adenofibroma of the uterine cervix coexistent with endometriosis

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Adenofibromas are rare tumors of the female genital tract, first reported by Abell in 1971 [1], and most arise from the uterus or cervix. Cervical adenofibromas are most commonly seen in peri- or postmenopausal women, and typically present with abnormal vaginal bleeding [1]. Grossly, the tumor usually appears as a polypoid mass at cervix [1,2]. Adenofibromas are composed of an admixture of benign epithelial and mesenchymal elements, and must be differentiated from adenosarcoma, adenomyomas, and carcinosarcoma [2–4]. In rare instances, adenofibromas have been associated with endometriosis [5]. We herein report a case of a 52-year-old woman with a recurrent adenofibroma of the cervix coexistent with endometriosis.

A 52-year-old woman presented with vaginal spotting. Her last menstrual period was approximately 1 month prior, and her history was significant only for endometriosis. Pelvic examination revealed a polyploid mass at the cervix. Ultrasonography revealed a normal uterus and adnexa. Pelvic magnetic resonance imaging (MRI) revealed a focal mass at the posterior lip of the cervix extending to the vagina, with heterogeneous enhancement. Routine hematological and biochemical studies were within normal limits; however, serum CA-125 level (normal values range from 0 to 35 U/mL) was slightly elevated (46 U/mL). Transvaginal biopsy of the mass was performed, and histopathological examination was consistent with an adenomyomatous polyp. The mass was subsequently excised (Table 1).

Two years later, the patient again complained of vaginal spotting, and examination revealed a polyploid mass at the site of the previous lesion. Transvaginal ultrasound revealed two small masses near the cervix, and MRI showed a soft tissue mass at the posterior aspect of the lower uterus/cervix. Excision of the mass was performed, and the histopathological diagnosis was adenofibroma. Three months later, a mass at the same location was noted, and an abdominal hysterectomy was performed. The uterus was normal in size, and a solid whitish nodule with an ill-defined border at the posterior lip of the cervix extended but without infiltrating to the right parametrium was found (Fig. 1). Severe pelvic adhesions were also noted. Histologically, the mass was composed of fascicles and whorls of spindle-shaped cells with low to moderate cellularity. The cells had a moderate amount of pale or eosinophilic cytoplasm with pointed nuclei (Fig. 2). Little cellular atypia was seen, and mitotic figures were rare [<1/10 high power fields (HPF)]. Scattered, bland-appearing endometrial glands surrounding by a thin cuff of endometrial stromal cells embedded in the spindled tumor cells were noted, suggesting a spindle cell tumor possibly arising from pre-existing endometriosis. No focal increased cellularity of the spindle-shaped cells in the proximity of the endometrial glands was noted. In addition, foci of endometriosis were noted at the posterior wall of uterine cervix. Immunohistochemical staining revealed the cells to be diffusely and strongly positive for vimentin, focally positive for actin, and negative for desmin (Fig. 3). The proliferation index (Ki-67) was <5%. The final histopathological diagnosis was Mullerian adenofibroma arising from endometriosis of the uterine cervix.

The majority (90%) of adenofibromas arise from the endometrium, while 10% arise from the cervix, and adenofibromas most frequently occur in peri- and postmenopausal woman, with abnormal bleeding as the primary complaint [2,6]. When the lesion is found to be arising from the cervix, cervical carcinoma must be considered. The present case is similar to one reported by Haberal et al [2]. In their case, a 55-year-old-woman presented with irregular vaginal bleeding for 2 months and was noted to have a hemoglobin level of 7.7 mg/dL. Pelvic examination revealed a 6-cm cervical mass that bled when palpated and transvaginal ultrasonography indicated the mass contained small cysts and measured 6 × 7 cm and normal uterus and adnexa. A biopsy was consistent with a cervical polyp, and because this finding was not consistent

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Table 1
Previous findings in adenofibroma of the uterine.

Author and year of publication	Findings	References
Abell, 1971	The first article reported adenofibromas of the uterine cervix as the mixed mesodermal tumors containing epithelium and mesenchymal stroma.	[1]
Clement, 2007	In adenofibroma, the epithelial component forms a lining on the underlying mesenchymal core, often with cleft-like spaces.	[5]
Zaloudek and Norris, 1981	Adenofibromas had fewer than 4 MF/10 HPF in the most active areas; adenosarcomas had four or more. None of the adenofibromas contained markedly atypical mesenchymal cells. No patient with an adenofibroma had a recurrence following hysterectomy.	[6]
Clement and Scully, 1990	Adenofibromas are described as typically lacking stromal atypia, periglandular cuffing by hypercellular stroma, and very low mitotic activity. Mitoses have been reported as fewer than 2 MF/10 HPF. Tumors were composed of an intimate admixture of benign endometrial-type glands and a moderately cellular stroma containing fibroblasts with benign nuclear features.	[9]
Seltzer et al, 1990	Hysterectomy is the preferred treatment, as adenofibromas may recur if not completely removed.	[11]
Huang et al, 1996	The sonographic finding of adenofibroma must be differentiated from endometrial polyp, endometrial hyperplasia, endometrial carcinoma. The sonographic pattern produced by adenofibroma included an echogenic intracavitary mass containing many irregular cysts, with distinct margins and exhibiting low-resistance blood flow.	[8]
Haberal et al, 2005	The majority (90%) of adenofibroma arise from the endometrium, while 10% arise from the cervix. The sonographic finding of adenofibroma must be differentiated from hyperplasia and molar pregnancy when located in the endometrium, and from cervical carcinoma when located in the cervix.	[2]
Konishi et al, 2006	Adenofibroma is one possible diagnosis when a uterine mass with heterogeneous, multicystic components is identified on computed tomography, MRI and/or ultrasonography. Histological examination is required to reveal the true nature of the tumor.	[7]
Tahlan et al, 2006	The distinction of adenomyoma with adenofibroma and adenosarcoma may be difficult. Adenofibromas show broad papillary fronds covered with epithelium projecting into cystic spaces that are lined by columnar or cuboidal endometrial-type epithelium, and the mesenchymal component is usually fibroblastic.	[4]
Gallardo and Prat, 2009	The characteristic findings of adenosarcomas, which include marked stromal cellularity, prominent mesenchymal cell atypia, mitotic count >4/10 HPF of mesenchymal cells, histologically malignant heterologous elements, and myometrial invasion are not present in adenofibromas. Many tumors diagnosed as adenofibromas are in fact low grade adenosarcomas	[3]
Vellios et al, 1973	In adenofibroma, the stromal component is, by definition, morphologically benign. However, occasional adenofibromas recur or even metastasize. As such, it has been suggested that all adenofibromas should be classified as adenosarcomas, albeit with low-malignant potential.	[10]

with that of the physical examination, an abdominal hysterectomy was performed. The final histopathological diagnosis of the mass was adenofibroma of the cervix extending to the anterior lower wall of the uterus and an endometrial polyp. A case of an adenofibroma of the endometrium presented by Konishi et al [7] also found the lesion to contain multiple cystic components on transvaginal ultrasonography, as well as a heterogeneous high-intensity mass on MRI. Although adenofibromas have a characteristic, multicystic appearance on ultrasonography, MRI, and computed tomography studies [7,8], histopathological examination is necessary for a definitive diagnosis.

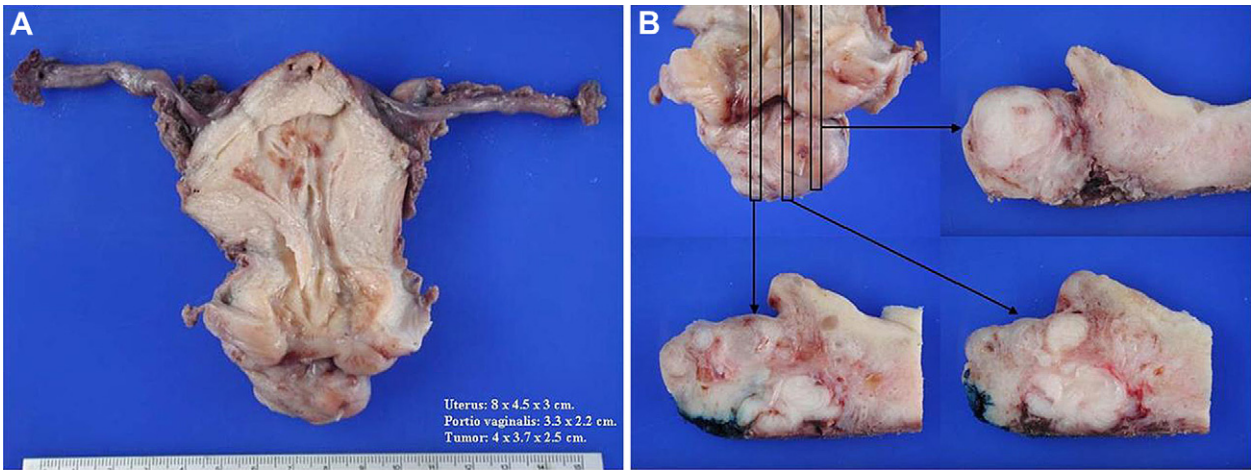

Fig. 1. (A) Hysterectomy specimen from a 52-year-old woman with cervical adenofibroma. (B) A whitish, ill-defined, irregular nodule, the adenofibroma, is seen at the posterior lip of cervix.

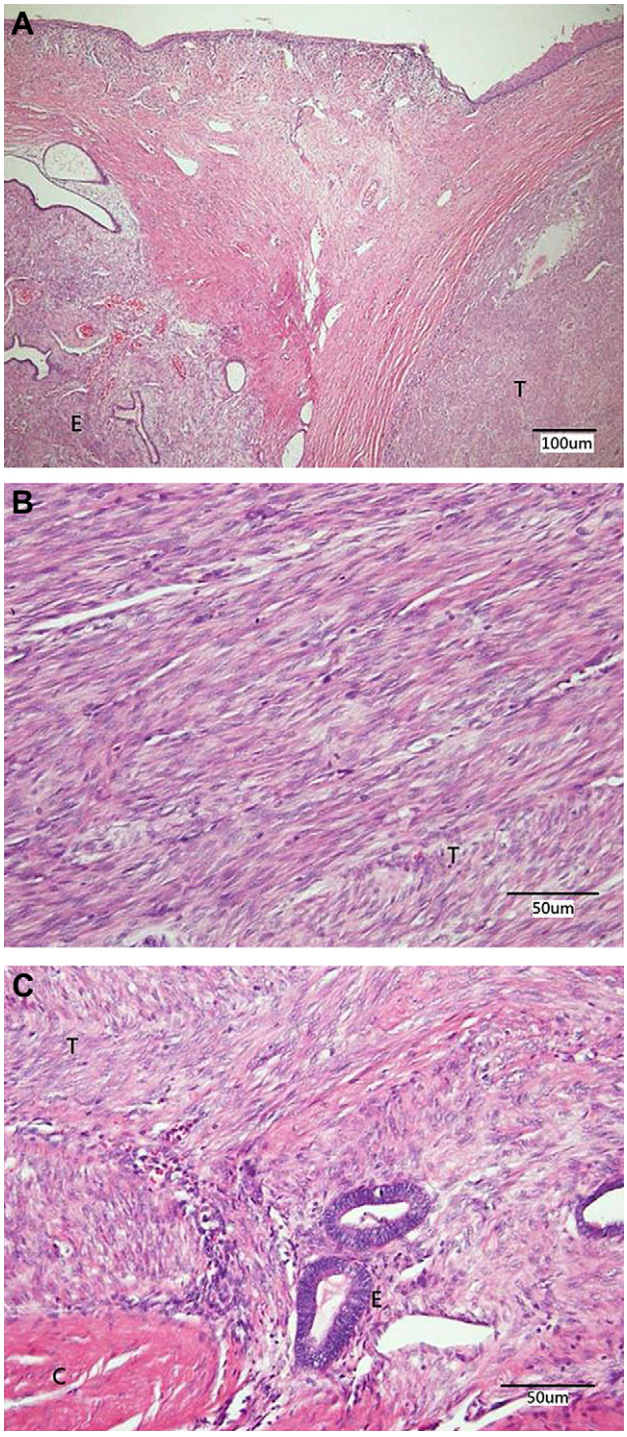

Fig. 2. (A) Histological examination revealed an admixture of benign epithelial and stromal elements in the tumor [hematoxylin and eosin (H&E), ×40]. (B) Fascicles and whorls of spindle-shaped cells with low to moderate cellularity were noted (H&E, ×200). (C) Proliferative-type endometrial tissue is present near the adenofibroma. Absence of cellular atypia or mitotic activity is noted (H&E, ×200).

Adenofibromas are typically described as lacking stromal atypia, lacking typical mesenchymal cell periglandular cuffing by hypercellular stroma, and very low mitotic activity. Mitoses have been reported as fewer than 2/10 HPF, and even <1/10 HPF [9,10]. The characteristic findings of adenosarcomas,

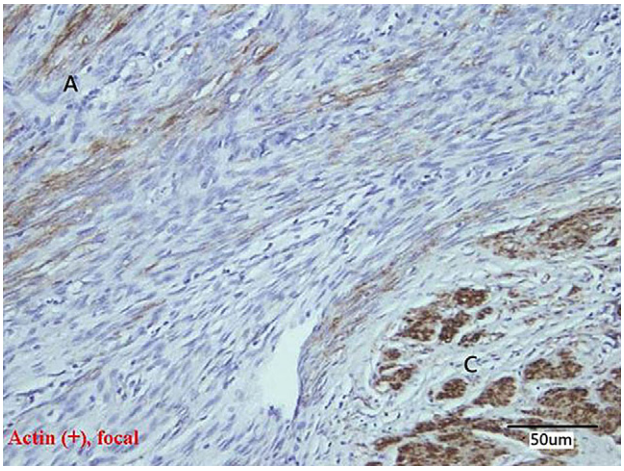

Fig. 3. Immunohistochemical staining revealed the spindle cell component was focally positive for actin. [ABC method using streptavidin and developed by diaminobenzidine (DAB), hematoxylin counterstained, ×200.]

which include marked stromal cellularity, prominent mesenchymal cell atypia, mitotic count >4/10 HPF of mesenchymal cells, histologically malignant heterologous elements, and myometrial invasion, are not present in adenofibromas [3]. In our case, the tumor cells had a moderate amount of pale or eosinophilic cytoplasm and long or pointed nuclei with little cytological atypia. Mitotic figures were rarely found (<1/10 HPF), and the proliferation index (Ki-67) was <5%.

In our case, 3 months after the second surgery, a mass was found at the same location, and an abdominal hysterectomy was performed. A solid whitish nodule with an ill-defined border at the posterior lip of the cervix extending to the right parametrium was found with scattered bland-appearing endometrial glands on histological examination. The pathological characteristics of our case were not similar to those described in the case reported by Clement and Scully in 1990 [9]. In that case, on histological examination the authors found that the lesion was composed of an intimate admixture of benign endometrial-type glands and a moderately cellular stroma containing fibroblasts with benign nuclear features. In our case, the glands were surrounded by a thin cuff of endometrial stromal cells embedded in the spindled tumor cells, suggesting a spindle cell tumor possibly arising from preexisting endometriosis. Furthermore, in our case, a focus of endometriosis was noted at the posterior wall of uterine cervix, suggesting that the adenofibroma of the uterine cervix was coexistent with endometriosis.

Adenofibromas have been associated with endometriosis, and some authors believe they represent a form of endometriosis with extreme smooth muscle metaplasia — that is, endomyometriosis [5]. This is interesting, considering that the patient presented herein had a history of endometriosis.

Hysterectomy is the preferred treatment, as adenofibromas may recur if not completely removed [2,11]. Wide excision via trachelectomy is an alternative treatment for cervical adenofibromas if fertility is desired, or if hysterectomy is contraindicated.

In summary, although rare, adenofibromas should be considered in the differential diagnosis of a patient with a cervical mass and abnormal vaginal bleeding without clinical evidence of malignancy. Detailed histopathological study is required to differentiate adenofibromas from adenosarcoma.

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