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CASE REPORT

Lipoadenofibroma of the endometrium: a rare variant of benign mullerian mixed tumor

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Abstract
Objective Adenofibroma is a form of mixed mesodermal tumor in which epithelial and stromal components are benign, and usually arises in the endometrium of postmenopausal women. We report a case of lipoadenofibroma of the endometrium that appeared as an intracavitary mass, which is very unusual because endometrioid adenofibroma rarely contains mature adipose tissue, only the second such case described in detail.
Case An endometrial polypoid mass measuring 1,5 cm with maximum diameter was found incidentally during total abdominal hysterectomy for keratinizing large cell carcinoma of the cervix in a 60-year-old woman. The endometrial polypoid mass was found to be a lipoadenofibroma composed predominantly of collagenated fibrous stroma populated by cystically dilated and occasionally crowded glands lined with proliferative endometrium, intermingled with abundant mature adipose tissue.
Conclusion We suggest that uterine adenofibromas with lipomatous areas belong to the family of mixed tumor of Mullerian origin. We discuss the pathogenesis of this entity and review the previously documented similar cases.

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Introduction

Uterine adenofibroma is a rare benign biphasic neoplasm that is classified into the mixed epithelial and mesenchymal tumor group of Mullerian origin [1]. It typically affects the endometrium. Lipomatous component in uterine adenofibroma, first reported in 1995 is an extremely rare phenomenon [2]. To the best of our knowledge, this is the second report of an adipose tissue arising from endometrial adenofibroma.

The origin of adipose tissue in the endometrium is unclear and the pathogenesis of this tumor is still obscure. We report the case of a 60-year-old woman with lipoadenofibroma of the endometrium that was found incidentally during total abdominal hysterectomy for keratinizing large cell carcinoma of the cervix and review previously published reports of similar cases.

Case report

A 60-year-old multiparous woman was admitted to the Department of Obstetrics and Gynecology of Ege University, presenting with postmenopausal bleeding and pelvic pain during the last 6 months. A routine cervicovaginal smear revealed atypical squamous cells of undetermined significance. Colposcopy-directed biopsy of the cervical lesion revealed malignant epithelial tumor with distinctive histologic type of keratinizing large cell carcinoma. A pelvic ultrasound revealed a small polypoid cystic mass apparently arising from the uterus, consistent with an endometrial polyp.

The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy. Postoperative recovery was uneventful.

The uterus with attached cervix measured 6.5 × 5 × 4 cm. The specimen demonstrated a keratinizing large cell carcinoma of the cervix. Tumoral invasion of the lymphovascular spaces was observed. Pelvic lymph nodes showed reactive hyperplasia. The FIGO-stage was evaluated as: 1B2, N0, M0.

Macroscopic examination of the endometrium revealed a 1.5-cm soft, intracavitary mass that has originated in the fundus of the uterus as a pedunculated polypoid mass containing multiple cystic components. The cut surface of the mass was gray-white with yellow areas. The myometrium was thick and there was no sign of myometrial invasion.

Microscopically, the polypoid endometrial lesion contained both epithelial and mesenchymal elements (Fig. 1). The epithelial elements were benign dilated cystic endometrial glands of various sizes, lined by cuboidal-to-columnar endometrioid epithelial cells. Widespread endocervical type epithelium was identified (Figs. 2, 3). The mesenchymal elements were composed of cellular cores of fibrous connective tissue, vascular component and abundant mature adipose tissue (Fig. 4). Mature, bland-looking, uniform lipocytes appeared as isolated cells, small, irregular aggregates and large sheets. Neither the epithelial cells nor the stromal cells showed any cytologic atypia, necrosis and mitotic figures. There was no cambium layer. Pathologic examination confirmed the diagnosis of endometrial lipoadenofibroma. Histopathologic examination of the ovaries and endometrium revealed corpus albicans, inclusion cysts and simple endometrial hyperplasia without atypia, respectively. The patient is well and symptom-free after a 24-month follow-up.

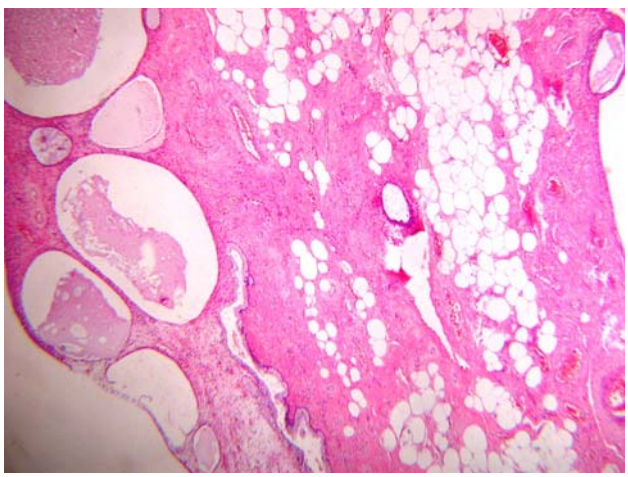

Fig. 1 The tumor is composed of cystic glandular epithelial cells and stromal cells with abundant mature adipose tissue (hematoxylin-eosin, original magnification, ×100)

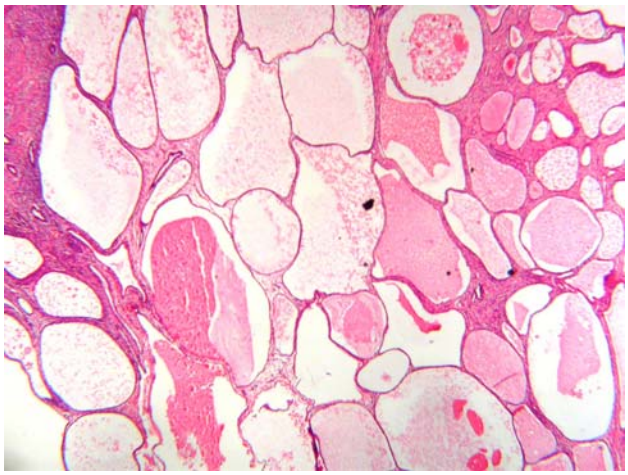

Fig. 2 Low power view of the cystic glandular component lined by columnar or cuboidal epithelial cells, most often of endometrioid type (hematoxylin-eosin, original magnification, ×100)

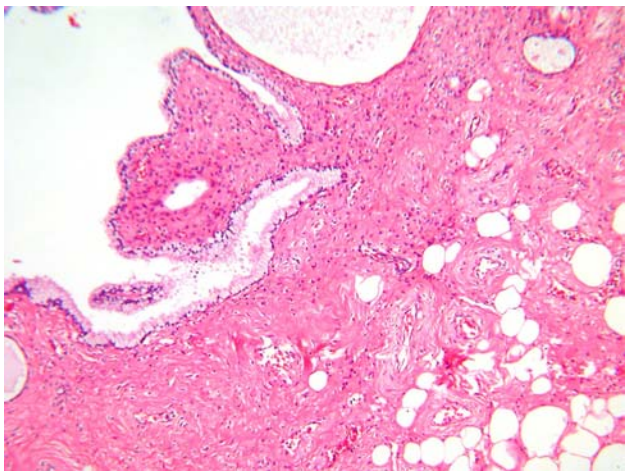

Fig. 3 High power view of the glandular epithelial cells showing features of columnar mucinous epithelium and mature adipose cells in the fibrous stroma (hematoxylin-eosin, original magnification, ×200)

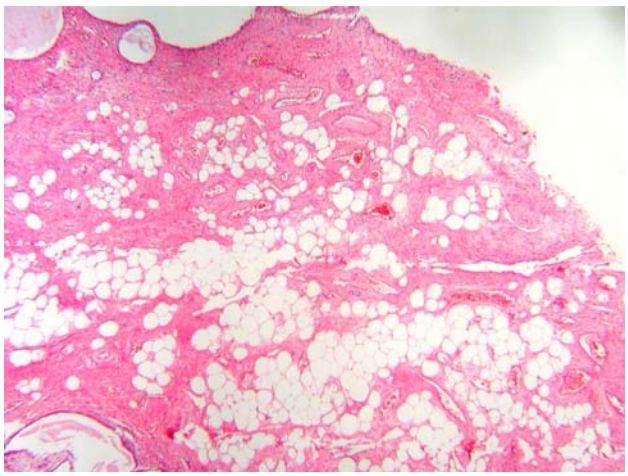

Fig. 4 Fibrous connective tissue, vascular component and abundant mature adipose tissue (hematoxylin-eosin, original magnification, ×100)

Discussion

Uterine adenofibroma was first described by Ober in 1959 as a variant of mixed mullerian tumor in which both the epithelial and mesenchymal elements are histologically benign [3]. Adipose tissue is uncommonly found in the endometrium and myometrium, such as lipoleiomyomas and pure lipomas [4]. However, in normal adenofibromas, the presence of large amounts of adipose tissue is an extremely rare phenomenon. A "mixed tumor" called lipoadenofibroma has recently been described [2].

Adenofibromas may be encountered at any age; however, they are more frequent in postmenopausal women. Adenofibroma most commonly arises from the endometrium, but almost equal to 10% of the tumors originate in the endocervix [1,5–7]. They usually present as broad-based polypoid masses that often have villous and spongy cut surfaces with cystic spaces surrounded by firm tissue [5]. It varies from soft to firm and is tan or brown in color. The tumor size ranges from 2 to 20 cm in maximum diameter, with a median of 7 cm. In the present case, the tumor is very small with a 1.5-cm diameter. The most common presenting symptom of adenofibroma is abnormal vaginal bleeding. Our patient was presented with a postmenopausal bleeding; however, the presence of cervical carcinoma and simple endometrial hyperplasia made it difficult to identify the specific site of bleeding.

The histological differential diagnosis of adenofibroma includes endometrial polyps, endometrial hyperplasia, submucosal lipoleiomyoma and polypoid adenomyoma, which are at the benign end of the histologic spectrum, and adenosarcoma, carcinosarcoma and endometrial stromal sarcoma at the malignant end [2]. Endometrial hyperplasia with multiple cysts is difficult to distinguish from adenofibroma of the endometrium. Histologic features of adenofibroma and endometrial polyp tend to overlap in some cases and distinction between these two lesions may be arbitrary. However; adenofibroma lacks the prominent central vasculature of a polyp [8].

The lipomatous tissue in this lesion without any clinical significance appears benign and is different from the cellular or sarcomatous appearance of the adenosarcoma. However; the awareness of lipomatous differentiation in benign biphasic tumors of the uterus is important. The presence of adipose components in biphasic uterine neoplasms in a small biopsy or curettage specimen requires careful interpretation by the surgical pathologist because the usual setting for heterologous elements in a uterine mullerian mixed tumor is adenosarcoma or carcinosarcoma [1,6,7]. Uterine adenosarcoma is composed of benign endometrial glands and sarcomatous stroma that is usually homologous and may exhibit endometrial stromal, fibroblastic, and rarely, smooth muscle differentiation. Heterologous elements, including skeletal muscle, cartilage, bone and fat are most often observed in adenosarcomas than benign counterpart adenofibromas [1,7]. However, lipomatous differentiation has been only once described in a benign adenofibroma [2]. The polypoid lesion in this case was regarded as an adenofibroma rather than an adenosarcoma because of the absence of the following: a broad-based leaf-like growth pattern, stromal nuclear atypia, stromal mitotic activity, and a cambium layer.

Horie et al. reported lipoadenofibroma in a 67-year-old woman who was presented with lower abdominal pain with higher serum Ca125 levels. The mass was a submucosal tumor measuring 6 × 5 cm in the uterine corpus [2]. In the present case, the patient's age and microscopic features were similar; however, in our case the lipoadenofibroma was small with a 1.5-cm maximum diameter and without high Ca125 levels. Also the presence of synchronous cervix carcinoma makes our case unique.

There is no general agreement on the exact nature of the lipomatous-appearing elements: polypoid lesion considered to be of hamartomatous origin or represent an unusual type of benign Mullerian mixed tumour with a heterologous element. Occasional neoplasms have contained heterologous elements such as skeletal muscle or fat, especially in the cervix [9–14]. We believe it is reasonable to suppose therefore that smooth muscle, skeletal muscle, adipose and cartilaginous tissue should not be an unexpected finding in an endometrial tumor. We consider the mass is not a hamartoma because adipose tissue is not a normal constituent of the endometrium. On the other hand, it is known that mullerian stromal cells have the capacity to transform other mesenchymal-type cells [11]. Although appearance of adipose tissue in adenofibromas of the uterus has very rarely been reported, this case should be a very special form of circumscribed lipomatosis of a uterine adenofibroma.

In conclusion, we reported a case of lipoadenofibroma of the endometrium showing cystic dilatation of the epithelial component and stromal fibrosis. This lesion appears to be clinically and histologically benign and has no malignant implications but leads to consideration of differential diagnosis with other malignant mesenchymal neoplasms of the endometrium, particularly from adenosarcoma, which can be suggestive of adenofibroma due to similar clinical features and gross findings. We suggest that uterine adenofibromas with lipomatous areas belong to the family of adenofibroma (benign mullerian mixed tumor) of the uterine corpus.

References

1. Zaloudek CJ, McUsa M, Norris HJ (1981) Adenofibroma and adenosarcoma of the uterus: a clinicopathologic study of 35 cases. Cancer 48:354–366

2. Horie Y, Ikawa S, Kadowaki K, Minagawa Y, Kigawa J, Terakawa N (1995) Lipoadenofibroma of the uterine corpus: report of a new variant of adenofibroma (benign müllerian mixed tumor). Arch Pathol Lab Med 119:274–276
3. Ober WB (1959) Uterine sarcomas: histogenesis and taxonomy. Ann NY Acad Sci 75:568–585
4. Kondi-Pafiti A, Grapsa D, Kairi-Vassilatou E, Kontogianni-Katsarou K, Koliopoulos C, Botsis D (2006) Mesenchymal tumors of the uterine corpus with heterologous and hematopoietic components: a study of ten cases and review of the literature. Eur J Gynaecol Oncol 27(1):73–77
5. Lee HK, Kim SH, Cho JY, Yeon KM (1998) Uterine adenofibroma and adenosarcoma: CT and MR findings. J Comput Assist Tomogr 22(2):314–316
6. Clement PB, Scully RE (1990) Mullerian adenosarcoma of the uterus: a clinicopathologic analysis of 100 cases with a review of the literature. Hum Pathol 21(4):363–381
7. Clement PB, Scully RE (1988) Uterine tumors with mixed epithelial and mesenchymal elements. Semin Diagn Pathol 5(2):199–222
8. Bettaieb I, Mekni A, Bellil K, Haouet S, Bellil S, Kchir N, Chelly H, Zitouna M (2007) Endometrial adenofibroma: a rare entity. Arch Gynecol Obstet 275(3):191–193
9. Yavuz E, Tuzlali S, Iplikçi A, Ilhan R (2001) Adenomyolipoma of the uterus: a case report. Pathology 33(1):96–100
10. Sinkre P, Miller DS, Milchgrub S, Hameed A (2000) Adenomyofibroma of the endometrium with skeletal muscle differentiation. Int J Gynecol Pathol 19(3):280–283
11. Payne F, Rollason TP, Sivridis E (1992) Adenomyolipoma of the endometrium—a hamartoma? Histopathology 20:357–359
12. Ilhan R, Yavuz E, Iplikçi A, Tuzlali S (2001) Hamartomatous endocervical polyp with heterologous mesenchymal tissue. Pathol Int 51(4):305–307
13. Roth LM, Pride GL, Sharma HM (1976) Mullerian adenosarcoma of the uterine cervix with heterologous elements: a light and electron microscopic study. Cancer 37:1725–1736
14. Perone T, Carson LF, Dehner LP (1990) Rhabdomyosarcoma with heterologous cartilage of the uterine cervix: a clinicopathologic and immunohistochemical study of an aggressive neoplasm in a young female. Med Pediatr Oncol 18:72–76