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Case Presentation

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Uterine Lipoadenofibroma: A Case Report of a Rare Variant of Adenofibroma

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Abstract

Objective: Adenofibroma is a benign mixed mesodermal tumour comprising fibroblastic stromal tissue and epithelial tissue, usually arising in the uterine cavity of postmenopausal women. It rarely has an adipose component.

Case: We describe a nodular lesion found incidentally in the uterine corpus of a 73-year-old multiparous woman in the setting of surgical treatment of a high grade serous carcinoma of the ovaries, histologically consistent with a lipoadenofibroma. The cystic lesion is composed of two distinct benign contingents: a fibroblastic cellular stromal component with foci of abundant adipose tissue, and an epithelial component of endometrial epithelial cells. This is a variant of adenofibroma with the presence of mature adipose tissue.

Conclusion: Due to the rarity of this lesion, we describe this tumour in a case report. Proposed differential diagnoses are discussed, in relation to the literature review of similar cases previously described.

Keywords: Uterine corpus; Adenofibroma; Adipose tissue; Mixed müllerian tumor; Uterine lipoadenofibroma

Introduction

Uterine adenofibroma is a rare tumour classified as biphasic benign lesion: epithelial and mesenchymal fibroblastic stroma, tumour group of müllerian origine **[1].** It affects the endometrium and does not have an adipose contingent. Afterwards, the first case of a lipomatous component in an adenofibroma was described in 1995 **[2]** and the second in 2008 [3].

We report the case of a 73-year-old woman with lipoadenofibroma of the endometrium, found incidentally during a total hysterectomy and adnexectomy for an ovarian carcinoma after neo-adjuvant chemotherapy. The main differential diagnoses are discussed. A few identical cases as mentioned above of uterine lipoadenofibromas have been reported in the literature.

Case Presentation

A 73-year-old post-menopausal multiparous woman was admitted to the Department of Gynecology at the University Hospital of Geneva, presenting a right pelvic mass with high serum levels of CA125. Diagnostic radiology, laparoscopy and histological analysis revealed a high-grade serous carcinoma of the right ovary with a FIGO III stage. The tumour invades one ovarie and metastasizes to the retroperitoneal lymph nodes.

The patient was first treated with neo-adjuvant chemotherapy (Plaxitacel, 4 cycles) and then surgically by total hysterectomy with bilateral adnexectomy, epiploic resection and extended pelvic curage. Samples are sent to the pathologist to estimate the tumour residue and to establish the pathological stage after chemotherapy.

The uterine corpus measures 6.5x6x3 cm. The endometrium is smooth and has a polyp at the bottom of the uterine cavity measuring 3.5 cm long. Fallopian tubes, ovaries, ovarian serosa, uterine serosa, cervix and epiplon are without suspicious lesion. Extended pelvic curage found a white, indurated metastatic lymph node.

Macroscopically, in submucosal, intramural and subserosal, there were seventeen white, firm, homogeneous, fasciculated, well-limited, non-encapsulated nodules, without necrosis or haemorrhage, the largest measuring 1.5 cm in length, localised to the anterior and posterior myometrial walls, into the cervical isthmus. None of them really stood out. A sample of the twelve largest nodules was taken.

Microscopically, our nodule of interest measuring 1.2 cm in maximum diameter, is well limited, non-polypoïd, non-encapsulated, intra-mural at low magnification. It has large slits and cystic spaces **(Figure 1),** lined by a simple epithelium of glandular epithelial cells. These epithelial cells have the morphology of inactive benign endometrial cells, varying in shape from flat, to cuboidal to cylindrical. The mesenchymal component includes fibro-conjunctive tissue, small vessels and abundant mature adipose tissue with no smooth muscle component **(Figures 2 and 3).** No cytonuclear atypia, no necrosis and no haemorrhagic focus are seen in the epithelial and mesenchymal components. There is no cambium layer. The mitotic count is 0 mitosis per 10 fields at high magnification in the mesenchymal component. The morphological character of this image is benign. The final report makes the pathologic diagnosis of a "uterine lipoadenofibroma".

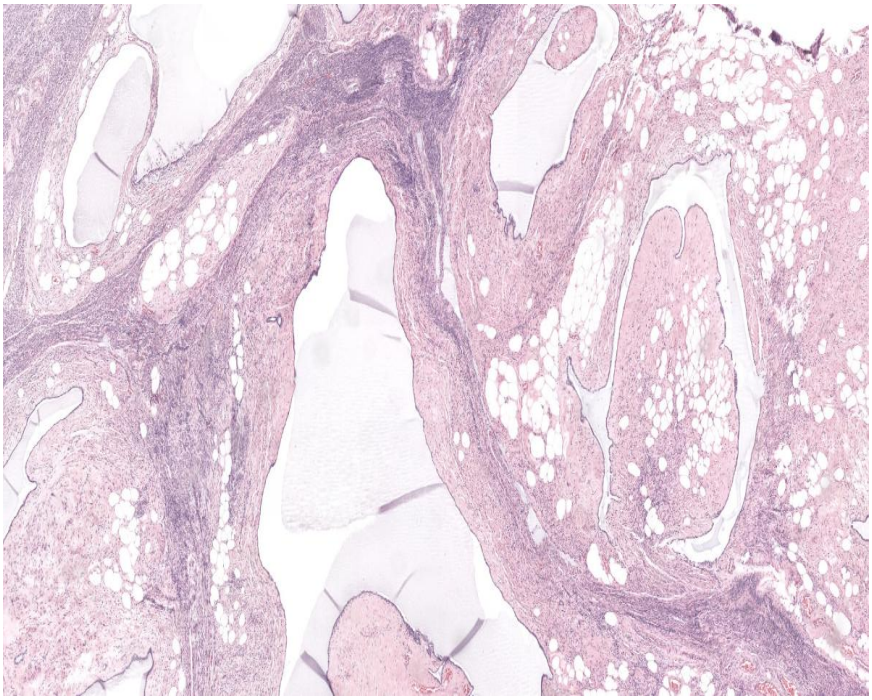

Figure 1: Lower-power view of the tumor of the uterine corpus. Cystic spaces and large clefts are seen (haematoxylin-eosin, original magnification x100).

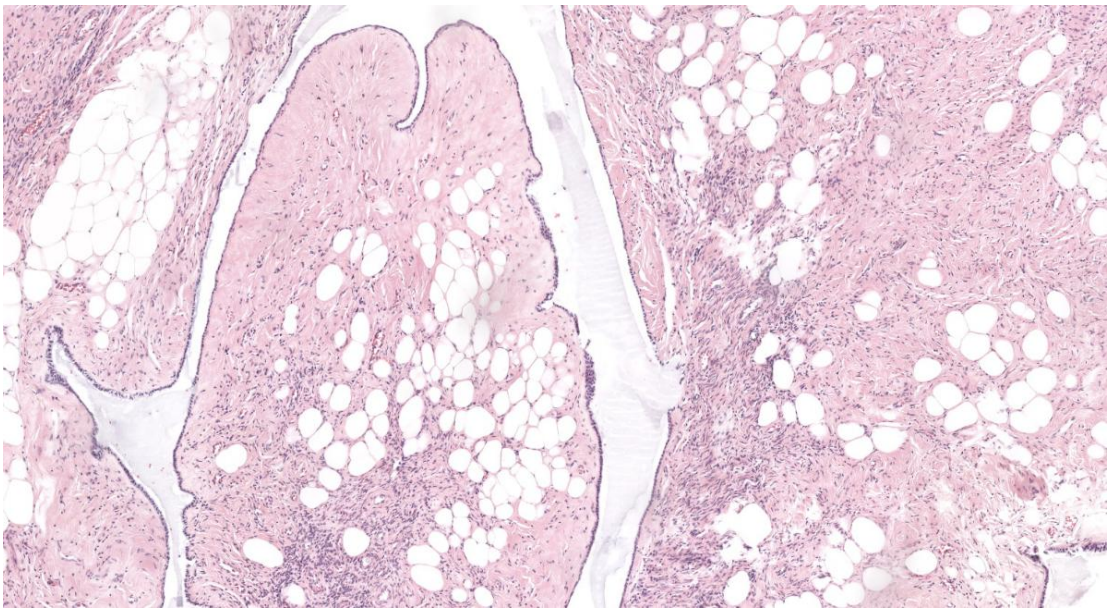

Figure 2: The stromal component is made up of fibroblasts and abundant mature fat cells around the epithelial component (haematoxylin-eosin, original magnification x200).

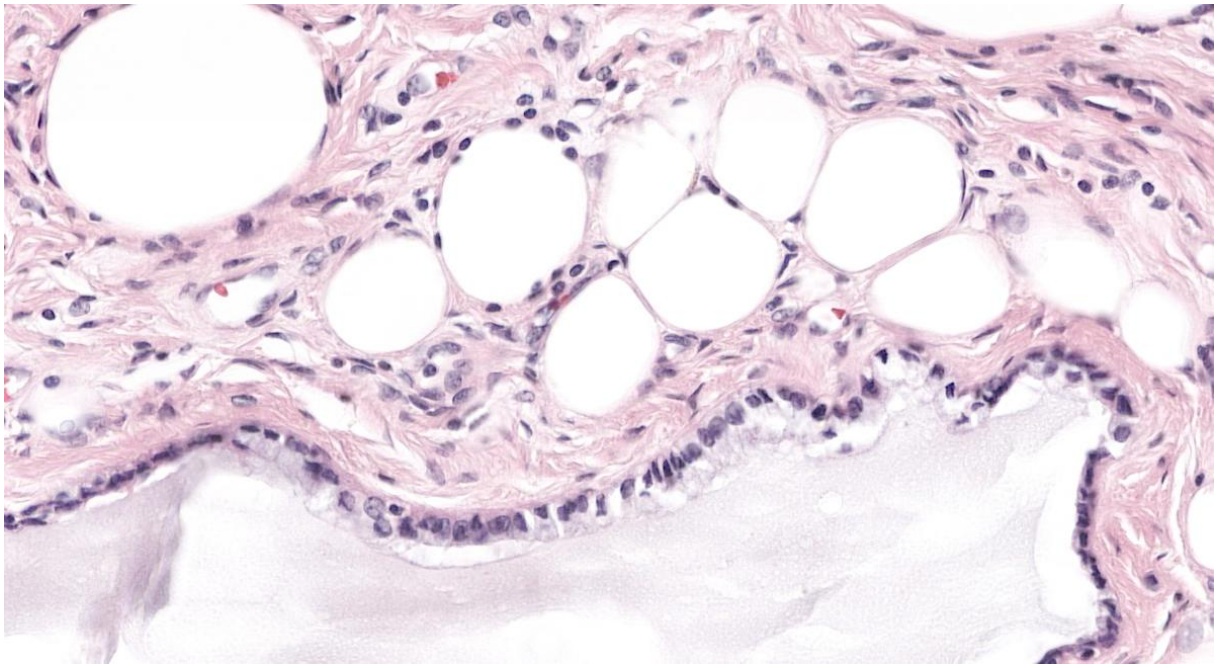

Figure 3: Mature fibro-lipomatous tissue and small vessels around endometrial cystic glands. Epithelium is cuboïdal to columnar and the epithelial cells are endometrial type (haematoxylin-eosin, original magnification x400).

The remaining histological findings include a glandular-cystic endometrial polyp and an atrophic endometrium. The other sixteen nodules were classic leiomyomas. The ovaries contain epithelial inclusion cysts and no residual tumor. Peritubal mesonephric cysts are present. In the epiploic tissue, there is no residual ovarian serous carcinoma. Finally, a 2 cm lymph node metastasis in the right pelvic curage is noted. The final pathological stage according to the 2017 edition of the American Joint Committee on Cancer (AJCC) is ypT0 pN1b.

Discussion

The adipose tissue is not usual to the myometrial and endometrial tissue. This adipose mesenchymal component is mainly found in gynecological lesions such as lipoleiomyoma, lipoma **[4],** adenolipoleiomyoma, adenosarcoma or carcinosarcoma. The presence of fat is a rare phenomenon in adenofibroma. In the literature there is a lesion called "lipoadenofibroma" **[2,3],** which is an adenofibroma with a fat component.

Described by Ober in 1959, uterine adenofibroma is a mixed, benign müllerian tumor with epithelial and fibroblastic stromal elements **[5].** Adenofibroma occurs at any age of life, however, is more frequent in the postmenopausal period. This lesion develops more often from the endometrium, with a preponderance of 10% in the endocervical area **[1,6-7].** It presents usually as a broad-based polypoid mass, with villous and a spongy cross-sectional surface and cystic spaces or clefts surrounded by firm tissue **[6].** Its consistence varies from soft to firm. Its color may differ, from beige to brown and its size from 1 to 20 cm long axis. In our present case, the small tumor measures 1.2 cm in its longest axis and it was difficult to differentiate this nodule from other leiomyomatous nodules macroscopically.

The most common presenting symptom of adenofibroma is abnormal vaginal bleeding. Our nodule was discovered incidentally and no low gynecologic bleeding was reported.

Histological differential diagnoses of adenofibroma include benign lesions such as endometrial polyp, endometrial hyperplasia, submucosal lipoleiomyoma, adenomyoma, adenolipoleiomyoma and malignant lesions such as adenosarcoma and carcinosarcoma. It can be difficult to distinguish between endometrial hyperplasia with several cysts and adenofibroma. The endometrial polyp has well-developed vessels in its stroma, with sometimes dilated glands, instead of adenofibroma lacks proeminent central vasculature **[8]** but can rarely contain smooth muscle and adipose tissue such called adenolipoleiomyoma **[9].** Lipoleiomyoma has a purely mesenchymal component made up of smooth muscle cells interspersed with mature adipose tissue, without endometrial glands **[10].** Adenomyoma has endometrial glands and endometrial blue stroma deep in the myometrium **[11].**

The benign fatty tissue in our lesion differs from the cellularity or sarcomatoid appearance of adenosarcoma and carcinosarcoma. In the context of intrauterine biopsy or curettage, analysis of this lipomatous component requires particularly careful attention because heterologous component- as fat, cartilage, bone or muscle- is mainly found in uterine adenosarcomas or carcinosarcomas, which are mixed müllerian malignant tumours **[1,6,12].** The main elements to be assessed to attest the malignancy of the lesion are: a phyllode-like glandular architecture, rigid cystic dilatation, periglandular stromal condensation, marked stromal cytonuclear atypia, mitotic activity greater than or equal to 2 mitoses per 10 fields at high magnification. With a benign glandular component, two or more of the above criteria are sufficient to make the diagnosis of adenosarcoma. Usual homologous malignant mesenchyme in adenosarcoma is composed of smooth muscle, endometrial stroma or fibroblasts. The heterologous spectrum is made of skeletal muscle, cartilage, bone and fat **[1,6].** Our lesion was benign because it doesn't have any of the above quoted malignant characteristics. However, benign lipomatous differentiation has been described in an adenofibroma in two cases reports, defining the term of lipoadenofibroma **[2,3, Table 1].** The main diagnoses of lipoadenofibroma are summarized below **[Table 2].**

Table 1: Clinical and pathological features of the current tumor and uterine lipoadenofibromas reported in the literature.

Authors	Age (year)	Presentation	Known concomitant malignancy	Tumor location	Tumor largest diameter (cm)	Histology	Therapy	Outcome, Follow-up
Horie and al. (1995)	67	Lower abdominal pain	None	Sub-mucosal uterine mass	6	✓ Fibrous stroma ✓ Cystic spaces lined by endometrioid-type proliferative epithelium ✓ Foci of mature adipose tissue ✓ Focally fascicular bundles of smooth muscle	Hysterectomy and bilateral salpingo-oophorectomy	No evidence of disease 12 months
Akbulut and al. (2008)	60	Incidental (bleeding and pelvic pain)	Squamous cell carcinoma of cervix	Sub-mucosal, fundus of uterine corpus	1,5	✓ Collagenated fibrous stroma ✓ Cystic spaces lined by endometrioid-type proliferative epithelium ✓ Foci of mature adipose tissue ✓ No smooth muscle	Hysterectomy and bilateral salpingo-oophorectomy	No evidence of disease 24 months
Current case	73	Incidental (Lower abdominal pain)	High grade serous carcinoma of the ovaries	Intra-mural uterine mass	1,2	✓ Collagenated fibrous stroma ✓ Cystic spaces lined by endometrioid-type non-active epithelium ✓ Foci of mature adipose tissue ✓ No smooth muscle	1st: Chimiotherapy 2nd: Hysterectomy and bilateral salpingo-oophorectomy	No evidence of disease 24 months

Table 2: The main differential diagnoses of uterine lipoadenofibroma. (*Abbrevation: yr=year*).

Lesions	Average age	Tumor location	Average size (cm)	Macroscopy	Histology	Malignancy
Lipoadenofibroma	Post-menopausal 60-73 yr	Uterine corpus Sub-mucosal / Intra-mural	1,2-6	Mass or polypoïd Grey to white, focally yellow Cystic spaces or clefts	✓ **Mature adipose tissue** ✓ Fibrous stroma ✓ No smooth muscle fascicles or focally	Benign
Endometrial polyp	Peak incidence in the 5th decade	Anywhere in the uterine cavity	0.3-12	Polypoïd usually Grey to white Soft or firm Bosselated Possibly cystic	✓ **No adipose tissue** ✓ Reduced collagenated fibrous stroma ✓ Thick hyalinised vessels +/- ✓ Oedema or myxoid change ✓ Endometrial glands +/- cystic	Benign
Adenolipoleiomyoma	19-55 yr with mean age in 45.8 yr	Endometrium Intramural / Sub-serosal / Intra-luminal in uterine corpus	2,5-43	Polypoïd possibility Fibrous, firm White, fasciculated focally yellow	✓ **Mature adipose tissue** ✓ Endometrioïd-type glands ✓ **Smooth muscle fascicles**	Benign (but one described case had an aggressive behaviour)
Adenosarcoma	Young female median age of 37-39 yr	Uterine corpus > cervix > ovary/pelvis	Variable focal mass	Broad based or sessile polypoïd mass Heterogeneous color Solid Numerous cysts or clefts	✓ Benign endometrial leaf-like glands ✓ **Malignant condensed periglandular stroma** with **atypia and mitotic activity** (included **fatty malignant changes**)	Malignant

Horie et al. report a lipoadenofibroma in a 67-year-old woman who was presented with lower abdominal pain and an elevated serum CA125 levels, without concomitant malignant tumour. The intrauterine mass is a submucosal tumor of 6 cm in long axis **[2].** Akbulut et al. report a polypoid lipoadenofibroma in a 60-year-old woman, measuring 1.5 cm and found incidentally during a hysterectomy for a squamous cell carcinoma of the cervix **[3].** Our case completes the observation of this rare lesion in the setting of post-menopausal.

We consider that lipoadenofibroma is not a hamartoma. By histological definition, a harmatoma is a benign nodular proliferation comprising the same histological constituents as the normal parenchyma of the organ, but in which these constituents are arranged in a less ordered manner and are found in very variable proportions. Adipose tissue is not a constituent of the endometrium, nor of the myometrium. Furthermore, it is referred that müllerian stromal cells have the ability to transform into mesenchymal-like cells **[13].** Some eventual neoplasms have contained heterologous tissue such as skeletal muscle or fat, especially in the cervix **[13,14].** Lipoadenofibroma represents a particular type of müllerian tumor with a benign lipomatous component.

In conclusion, we reported a case of uterine lipoadenofibroma presenting cystic dilatation of the epithelial structures and stromal fibrosis, with abundant foci of mature adipose tissue. This lesion is benign and has no implication in the concomitant ovarian carcinoma process. Other differential diagnose to be considered is mainly malignant mesenchymal neoplasia of the endometrium such as adenosarcoma. Assessment on biopsy specimen should be more careful to look for a malignant component in the mesenchyme, as adenosarcoma. We suggest that uterine adenofibroma with a lipomatous component is a rare variant of the uterine adenofibroma family (benign mixed müllerian tumour) of the uterine corpus.

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Reprints requests

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