Uterine Lipoleiomyoma: Review of literature and Two Case Reports✍

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Lipoleiomyoma is uncommon mesenchymal neoplasm which contains mature adipose tissue and smooth muscle components. Its prevalence among all uterine leiomyomas varies between 0,03-0,2% . In the current study, we present two lipoleiomyoma cases alongside clinical and histopathological data as well as information on etiopathogenesis.

The first case was a 59-year-old female patient presented with postmenopausal hemorrhage and she was subjected to hysterectomy upon clinical diagnosis of myoma uteri. Second case was a 45-year-old woman who presented with postcoital hemorrhage. Polypoid lesion which had a uterine cervix localization was excised.

Histopathological examination of the operation materials belonging to these two cases, revealed intramural (first case) and submucosal (second case) lipoleiomyoma, both of which had a varying degree of adipose tissue and smooth muscle components.

In leiomyoma cases, detection of other heterologous components alongside smooth muscle cells, is an uncommon event. Presence of an adipose tissue higher than 10%, should indicate lipoleiomyoma.

Key Words: Lipoleiomyoma, Leiomyoma, Uterus, Pathology

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Introduction

In leiomyomas, the presence of other heterologous components alongside smooth muscle cells is a rare, yet well described entity. Other components that can be observed in leiomyomas are mature fat cells, brown adipose tissue, striated muscle tissue, cartilage cells, and hematopoietic cells.[1] Lipoleiomyoma is an uncommon mesenchymal tumor of uterus that contains varying amounts of mature adipose tissue. Although there are no definitive data on its biological behavior, it is recognized to show benign behavior[2-5] Discrimination of lipoleiomyoma from other lipomatous tumors of uterus with regard to clinical, pathological, and radiological aspects, bears importance due to its different behavioral patterns and treatment options.[4-7] Another notable point is the ongoing discussions over the histogenesis of lipoleiomyomas.[7-11] Recently, lipoleiomyomas have been found to have cytogenetic abnormalities[8] While some investigators advocate the leading role of the degeneration of smooth muscle cells in development of the adipose component, others underscore the importance of metaplasia process.[5,8-10] The latest studies propose that adipose component is generated as a result of the transdifferentiation of the stem cells in the adult uterus.[11]

In the current study, two uterine lipoleiomyoma cases were clinically and pathologically discussed due to their uncommon nature. Moreover, literature data concerning histogenesis of the lesions were reviewed, as well.

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Case 1

Clinical characteristics: A 59-year-old female patient presented to the Gynecology and Obstetrics Department due to postmenopausal hemorrhage, and her eventual pelvic examination revealed a uterus larger than normal. Ultrasonographic examination showed a solid mass with a regular margin, filling the endometrial cavity. She has undergone dilatation and curettage (D&C). Histologic study revealed atrophic endometrium. Papanicolau (PAP) smear, no abnormality was observed.

Total abdominal hysterectomy and bilateral salpingoophorectomy were performed on the patient prediagnosed as myoma uteri. She had no remarkable event in her personal

and familial medical history. No pathology was observed with the routine laboratory techniques.

Macroscopical Characteristics: The examination of the hysterectomy material displayed an submucous nodular mass of 12x10x10 size which was filling the entire cavity. The section of the lesion was of fibrillar appearance showing patchy bright yellow areas (Figure 1). No pathological appearance was observed in other structures of the uterus and uterine adnexa.

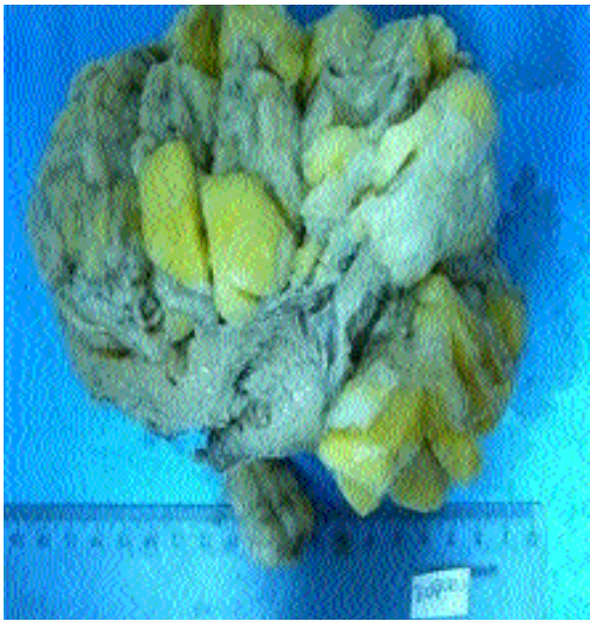

Figure 1: Macroscopic view of uterine lipoleiomyoma.The section of the solid tumoral lesion exhibiting bright yellow areas and filling the entire uterine cavity.

Histopathological Characteristics: Adipose tissue with honeycomb-like appearance was observed among the spindle-cells forming bundles on the sections (Figure 2A). Collagenized stroma had capillary vascular structures and sparse lymphoplasmocyte inflammatory cells. Adipose component showed a homogeneous distribution in the tumor tissue which was comprising approximately 80% of the lesion. There was no atypia, pleomorphism, or mitosis in the spindle-cells. Adipose component was of mature characteristics and no lipoblast was determined.

Histochemical and immunohistochemical results: Histochemical examination was performed with Masson's Trichrome (MT) dye and spindle-cells showed positive staining in favor of muscles. Immunohistochemical examination demonstrated a positive reaction with smooth muscle actin (SMA) in the spindle-cells, and with S-100 in the adipose component. In light of the histopathological data, the lesion was evaluated as "submucous lipoleiomyoma". The follow-up at 12 months after the operation showed no recurrence or metastatic spread in the patient.

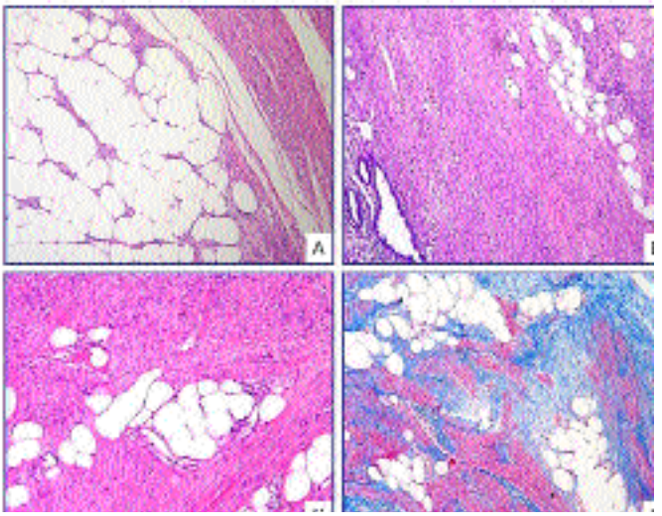

Figure 2. Microscopic views of lipoleiomyoma cases. (A) In sections of the first case, most of the nodular lesion is comprised of mature adipose component with a honeycomb appearance. In this case, tumor tissue shows an intramural localization (H&E, X200). In section of the second case, tumoral tissue is composed of spindle-cells over a large area while fat cells display an irregular distribution in small clusters. Tumor tissue in this case shows a submucosal localization (H&E, B; X100, C; 400). (C) Histochemically, spindle-cells forming the lipoleiomyoma show staining in favor of muscles (D; Mason Trikrom, X200).

Case 2

Clinical Characteristics: A 45-year-old female patient presented with postcoital hemorrhage and her eventual pelvic examination showed a polypoid formation in the cervix. The patient had normal personal and familial medical history, and the routine laboratory results were within normal range.

A polypoid lesion filling the endocervical canal and protruding through ectocervix was identified in ultrasonographic examination. Other uterine areas and adnexa, and pelvic structures exhibited no pathological finding. The results of PAP smear was normal (benign cellular changes). Polypectomy was performed under the clinical diagnosis of endocervical polyp.

Macroscopic Characteristics: The surface of the polypoid lesion of 2x1.5x1.5 cm size, was covered with an ulcerated mucosal tissue. The section of the lesion was of solid character and tan color, while showing patchy bright yellow areas.

Histopathological Characteristics: Microscopic examination revealed a nodular lesion with bundles and fascicles formed by the spindle-cells under the mucosa and comprised of endometrial stroma and glands on the surface (Figure 2B). Adipose component was of mature characteristics with irregular distribution (Figure 2C). Approximately 25% of the entire tumor area was comprised of adipose components. No findings consistent with malignancy was determined in the components making up the tumor.

Histochemical and immunohistochemical results: MT histochemical staining showed positivity for muscles in the spindle-cells forming the lesion (Figure 2D). Immunohistochemical examination demonstrated reaction with SMA in the spindle-cells (Figure 3A), and with S-100 in the adipose component (Figure 3B).

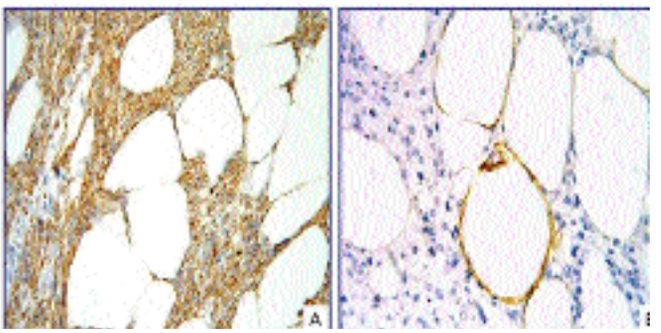

Figure 3: Positive immunoreaction with SMA in spindle cells, and with S-100 in the adipose component (ACE- DAB, A;X200, B;X400).

These histopathological findings disclosed the case as having a 'submucosal uterine lipoleiomyoma' originating from the endometrial cavity prolapsing into the endocervical canal. In light of the histopathological findings, the case was diagnosed as 'submucosal uterine lipoleiomyoma'. No recurrence was determined in the follow-up performed at six weeks postoperatively.

Discussion

Uterine lipoleiomyoma is an uncommon, benign mesenchymal tumor that contains smooth muscle and fat tissue.[1] Its incidence among the entire uterine leiomyomas varies between 0.35-2.1%.[2-5] Since they are rare, there are no definitive data on their clinical importance and treatment options.[2-4] Majority of the lipoleiomyomas are seen in postmenopausal patients as solitary lesions. Approximately 90% of the lesions are localized in the uterine corpus, while, on rare occasions, they may arise from the endocervical canal, as well. They may mimic leiomyomas clinically and liposarcomas radiologically.[1-8,12]

Clinically, discrimination of lipoleiomyoma from a well-differentiated liposarcoma bears importance. In the literature, 60-70% of lipoleiomyoma cases have been preoperatively diagnosed as well-differentiated liposarcomas.[4,12] Establishing an accurate preoperative diagnosis is important with regard to prevention of unnecessary surgical procedures. Liposarcomas are treated surgically. Asymptomatic lipoleiomyomas can be followed-up clinically and radiologically.[2-7] In the literature, only one liposarcoma case originating from lipoleiomyoma has been reported.[13] In a series including 50 lipoleiomyoma cases, no malignant transformation has been detected.[4] Those data support the view that lipoleiomyomas show benign behavior. Since lipoleiomyomas are commonly seen in postmenopausal patients and because 10% of cases are found to be among patients above age of 80, a detailed risk analysis should be carried out prior to proceeding with surgery.[2-4]

Radiologically, a definitive criteria for distinction of lipoleiomyomas and liposarcomas have not yet been described due to rarity of both of the lesions.[6,12] Magnetic resonance imaging (MRI) modality shows high sensitivity because of clear visualization of fat density, detection of the lesion's location, and demonstration of the lesion's relationship with its surrounding tissues. Performing a needle biopsy under guidance of radiological imaging modalities, contributes significantly to the preoperative diagnostic process.[6-7]

In histopathological differential diagnosis, uterine lesions involving spindle-cells and fat tissue, should be considered.[1] Spindle-cell lipoma, angiolipoma, angiomyolipoma, leiomyoma showing fatty degeneration, atypical lipoma, and well-differentiated liposarcoma may present with findings similar to those of lipoleiomyoma.[2-5,7,8] Maturity of the adipose component, lack of lipoblasts, absence of atypia and pleomorphism, and absence of infiltration to the peripheral tissues are important indicators in differentiating them from malignancies. Unlike leiomyomas showing fatty degeneration, necrosis and other degenerative changes are not observed. Histochemical and immunohistochemical examinations contribute significantly to the histopathological differentiative diagnosis.[1-8]

In the present study, since both of our cases were symptomatic and at postmenopausal period, surgical removal was performed. First case was localized submucous in the uterine fundus. The case was operated on with the prediagnosis of myoma uteri. Second case was localized submucosally in the lower uterine segment. Excisional biopsy was performed due to prediagnosis of cervical polyp due to extension of the lesion to the cervical canal. Both lesions were solitary. Since there was no clinical or radiological sign of malignancy, preoperative diagnostic intervention was not applied. Histomorphologically and immunohistochemically, lesions had the characteristics of a lipoleiomyoma. No recurrence or metastasis developed after the operation.

Histogenesis of uterine lipoleiomyoma is not known. Several authors suggest that uterine smooth muscle cells may undergo adipose degeneration, metaplasia, or transdifferentiation.[8-11,14-17] Because they are rare tumors and many studies focus on clinical and histopathological properties, data concerning the pathogenesis of those lesions are limited. WNT gene family, which involves in the signal transmission, has an influence over Mullerian development. The products of this gene regulate the antenatal and postnatal development of uterus through beta-catenin. Myogenic progenitor cells originating from the mesenchyma of the Mullerian ductus, normally differentiate towards smooth muscle, however, in absence of beta-catenin, they transdifferentiate into adipocytes.

This process may be generated as a result of the activation of adipogenic transcription factors and/or inhibition of MyoD which plays a critical role in myogenesis.[14-17] Those data obtained from in vitro studies, have been supported in vivo by the study of Arango and colleagues.[11] Arango et al. advocated the presence of a possible genetic mechanism for lipoleiomyomas behind the specific deletion in the uterus. They reported a similar morphology for uterine lipoleiomyoma and the myometrial layer of mice having beta catenin mutation.[11]

In conclusion, adult myometrium is not stable. As in the skeletal muscle, it can regenerate itself through differentiation from myogenic precursor cells. The results of the previous studies show that genetic mutations occurring in the uterine precursor cells during formation of leiomyomas, may lead to development of lipoleiomyomas. In the present study, in light of our two cases, we discussed the clinical and histopathological characteristics of uterine lipoleiomyomas as well as data on their histogenesis. Future studies comprising larger series and molecular techniques, will shed light on the effects of myogenic stem cells over other physiological and pathological events as well as lipoleiomyomas.

Uterin Lipoleiomyom: Literatürün Gözden Geçirilmesi ve İki Olgu Sunumu

Lipoleiomyom, matür adipöz doku ve düz kas komponenti içeren, nadir görülen mezenkimal bir neoplazmdır. Tüm uterin leiomyomlar içerisinde görülme sıklığı %0,03-0,2 arasında değişmektedir. Bu çalışmada iki lipoleiomyom olgusu klinik, histopatolojik ve etiyopatogeneze yönelik bilgiler eşliğinde sunulmuştur.

İlk olgu 59 yaşında, postmenopozal kanama yakınması ile başvuran kadın hasta olup, myoma uteri klinik tanısı ile histerektomi operasyonu uygulanmıştır. İkinci olgu, postkoital kanama yakınması ile başvuran 45 yaşında kadın hastadır. Uterin serviks yerleşimli polipoid lezyon eksize edilmiştir.

Her iki olguya ait operasyon materyallerinin histopatolojik incelemesinde değişen oranlarda adipöz doku ve düz kas komponenti içeren, ilk olguda intramural, ikinci olguda submukozal yerleşimli lipoleiomyom saptanmıştır.

Leiomyomlarda düz kas hücreleri yanı sıra diğer heterolog elemanların görülmesi nadirdir. Adipöz dokunun %10'dan fazla olması lipoleiomyom tanısını akla getirmelidir.

Anahtar Kelimeler: Lipoleiomyom, Leiomyom, Uterus, Patoloji.

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