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Case Report

Pathology Section

Leiomyoadenomatoid Tumor of the Uterus: Case Report and Literature Review

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ABSTRACT

Adenomatoid tumors are benign neoplasms of mesothelial origin that occur in the genital tracts of both men and women. Adenomatoid tumors are usually located in the subserosa of the cornual myometrium. They are typically small, 0.5-4 cm in diameter, but some larger and cystic adenomatoid tumors have been reported. Macroscopically, they appear as circumscribed masses, but not as sharply defined as in leiomyoma. Microscopically they consist of tubules and cords of varying sizes and shapes that are lined by flat or cuboidal epithelial cells. The microscopic appearance may mimic a malignant tumor due to irregular pseudoinfiltration with tubular formations that suggest presence of an infiltrating carcinoma into a leiomyoma or the myometrium. In this paper we report a very rare case of a leiomyoadenomatoid tumor of the uterus with emphasis on the morphologic and immunohistochemical findings, and discuss the differential diagnosis with review of the recent literature.

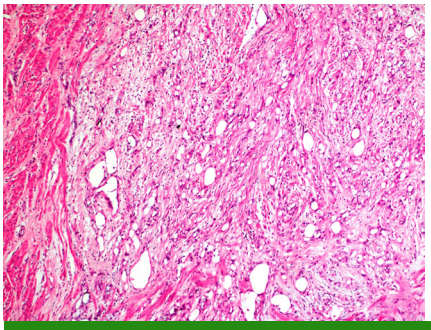
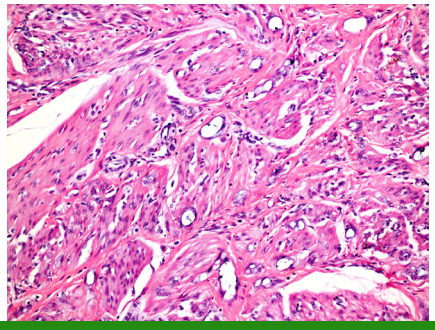
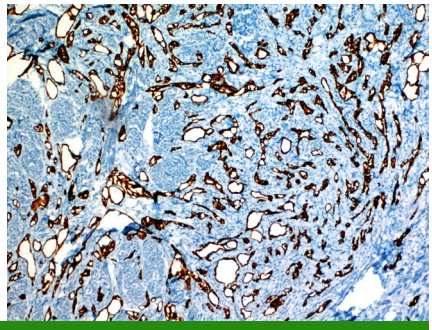
Keywords: Adenomatoid tumor, Immunohistochemistry, Uterus

CASE REPORT

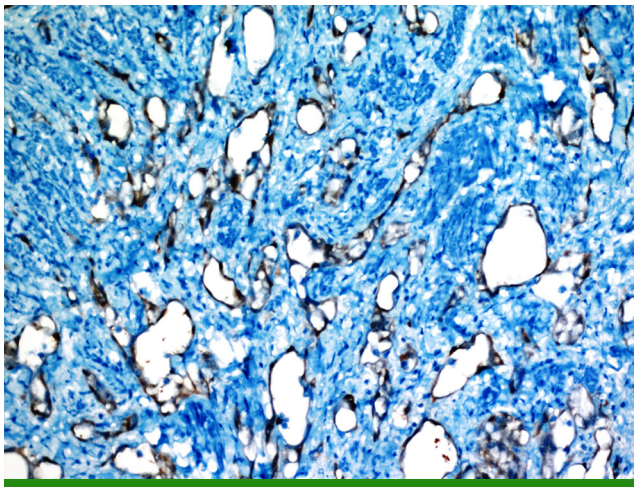
A 51-year-old female (gravid 2, para 1) presented to the gynecology clinic with postmenopausal bleeding and lower abdominal pain. The physical examination revealed that the uterus was larger than normal. Transvaginal ultrasound revealed 2x2 and 1x11.5 cm nodular intramural hypoechoic masses. The patient's fallopian tubes and ovaries were normal. An endometrial biopsy was carried out and showed a proliferative endometrium. The result of the pap smear test was negative. The patient underwent a total abdominal hysterectomy and bilateral salpingo-ooferectomy (TAH+BSO). A 320 gram, 10 x 9 x 5 cm TAH+BSO material was removed. In the sections that were removed intramurally located 2 cm and 1.5 cm, two smooth contoured nodular solid masses were observed. There were no pathological findings in the ovaries and fallopian tubes. The microscopic examination revealed well-defined tubular and clefting cubic and epithelial cells like lined structures within hypertrophic smooth muscle bundles [Table/Fig-1]. Some of these structures had vacuolated cytoplasms similar to signet ring cell tumors [Table/Fig-2]. No pleomorphism, mitosis, inflammation and fibrosis were noted. First, the immunohistochemical investigations were performed to determine whether the lesion is of epithelial or vascular origin. The results showed that the tumor stained positive for pan-cytokeratin (pan-CK), cytokeratin 19 (CK19) and diffusely for cytokeratin 7 (CK7) [Table/Fig-3a] but it was negative for cytokeratin 20 (CK20) and carcinoembriyonic antigen (CEA). The tumor was negative for vascular markers such as CD31 and CD34. The serum CA-125 level was normal. The endometrium and the ovaries were all examined. Since there were no pathological findings the possibility of the presence of an adenocarcinoma metastasis were also considered. Immuno histochemical analysis of breast tumor markers such as estrogen receptor (ER), progesterone receptor (ER) and GCDF-15 was negative. Positron emission tomography (PET) imaging revealed no intake that would suggest the presence of tumors elsewhere in the patient. The analytical focus was shifted to the presence of a primary tumor of the uterus and the case was revised. Additional ımmunohistochemical staining for mesothelial markers such as calretinin [Table/Fig-3b] and Hector Battifora mesothelial cell epitope-1 (HBME-1), were positive [Table/Fig-4a]. In addition, the surrounding stroma was stained positively with smooth muscle actin (SMA) [Table/Fig-4b]. The tumor was graded as low (2%) Ki-67 proliferation index. The case was diagnosed as leiomyoadenomatoid tumor of the uterus based on the histopathological and immunohistochemical findings.

DISCUSSION

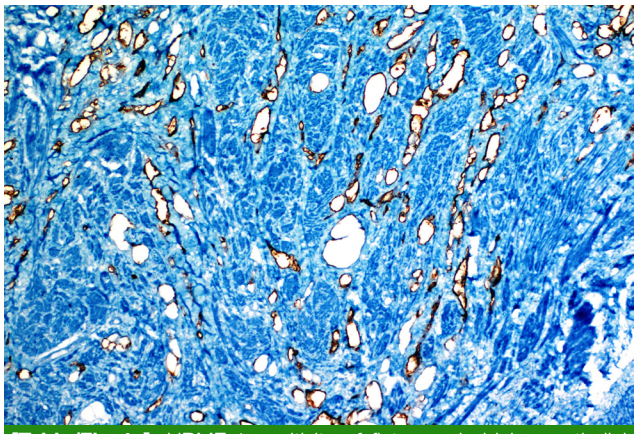
Adenomatoid tumors are benign tumors of mesothelial origin which are often seen in the myometrium and uterine tubes of women and epididymis of men. They are often encountered in the cornual myometrium close to the serosal surface. Smooth muscle hypertrophy often accompanies uterine adenomatoid tumors especially the intramural types and the tumor presents in an infiltrative fashion within the

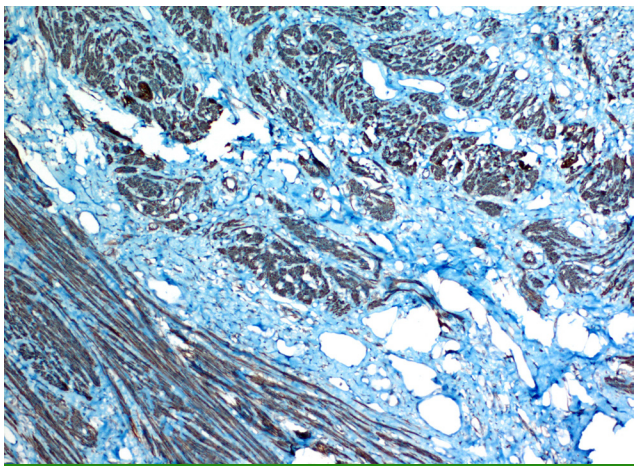
[Table/Fig-1]: Tubular or angiomatoid structures and cords of mesothelial cells infiltrating hypertrophic smooth muscle bundles (H&E stain, x100) **[Table/Fig-2]:** Vacuolated and signet ring cells in tubular formations along with hypertrophied smooth muscle bundles(H&E stain, 200) **[Table/Fig-3a]:** Cytokeratin 7 strong positivity of flat or cuboidal mesothelial cells (immunohistochemistry, x100)



[Table/Fig-3b]: Calretinin positivity of flat or cuboidal mesothelial cells (immunohistochemistry, x200)



[Table/Fig-4a]: HBME-1 positivity of flat or cuboidal mesothelial cells (immunohistochemistry, x100)



[Table/Fig-4b]: SMA is positive only on the smooth muscle bundles , but it is negative in the adenomatoid tumour (immunohistochemistry, x200)

myometrium [1-3]. Adenomatoid tumors may be located within the smooth contoured masses with dominance in the smooth muscle components. These rare types have recently been called leiomyoadenomatoid tumors [1]. Only six cases have been reported to date and one was located within the epididymis, four within the uterine wall and the other in the right ovary [1-6]. In this case report we present a rare case of leioadenomyomatoid tumor in which diagnosis and differential diagnosis were achieved by a morphologic and immunohistochemical investigation.

Adenomatoid tumors are rare; they are generally benign mesothelial neoplasms of the genital system with no propensity for recurrence. Lesions are more common in the male genital system and mostly involve the epididymis, tunica testicularis and the spermatic cord. The incidence in females is 1% and the tumors are mostly located in the uterus, fallopian tubes but rarely in the ovaries and the paraovarian connective tissue. Tumors are often mistakenly identified as leiomyomas and diagnosed incidentally in hysterectomy specimens [7,8].The term adenomatoid tumor was first suggested by Golden and Ash [9] in 1945. Adenomatoid tumors which contain significant smooth muscle components were called mesomyomas by Otis et al., [10] while Ebstein [11] was the first to use the term leiomyoadenomatoid to describe them. Occasionally various degrees of smooth muscle hyperplasia may accompany uterine adenomatoid tumors. This finding is thought to be a reactive response because the Ki-67 proliferation index is higher than the surrounding normal myometrium. However,

Cases	Age	Sex	localization	Immunohistochemical findings
Hong R et al., [1]	24	F	Uterus and left ovary	CK7 (+), CK20(-) calretinin (+), CEA (-), desmin (+), SMA (+)
Amre R et al., [2]	52	F	Uterus	Pan-CK (+)
Amérigo J et al., [3]	55	F	Uterus	Pan-CK (+), CK7 (+), CK20(-), HBME-1(+), calretinin (+), vimentin (+), CD31(-), CD34 (-), CD117(-)
Kausch I et al., [4]	32	M	Epididymis	Not defined
Erra S et al., [5]	44	F	Uterus	Pan-CK(+), CK5/6 (+), calretinin (+), HBME-1(+), vimentin (+), SMA(+), CEA(-), GCDF-15(-), E-cadherin (-), CD31(-), CD34(-),
Dobrosz Z et al., [6]	57	F	Uterus	Pan-CK (+), CK7 (+), CK20(-), HBME-1(+), calretinin (+), vimentin (+), CD31(-), CD34 (-), SMA (+)
Current Case	51	F	Uterus	Pan-CK(+), CK7(+), CK19 (+), CK20 (-), calretinin (+), HBME-1(+), SMA (+), CD31 (-), CD34 (-), CEA(-), EMA (-)

[Table/Fig-5]: Brief summary of leiomyoadenomatoid tumors as reported in the literature

in the adenomatoid components the Ki-67 proliferation index is actually lower than the normal myometrium [3, 12]. These findings are supported by the lack of smooth muscle tissue in adenomatoid tumors located elsewhere; such as in the ovaries, mesentery, adrenal gland and omentum. Some authors describe the lesions as collision tumors because both the leiomyoma and the adenomatoid tumors are neoplastic [13]. In our case the Ki-67 proliferation index was low in the adenomatoid component (2%) but high in the smooth muscle component (5%).

Previously adenomatoid tumor histogenesis was a matter of debate; however, electron microscopic (ultrastructural) and immunohistochemical investigation showed that the tumor is of mesothelial origin [1]. Immunohistochemical studies with widespread panels showed that adenomatoid tumors are positive for pan-CK, CK7, CK8, CK18, CK19, calretinin and D2-40. The ER and PR receptors stained positive in 4 of the 5 cases. The Ki-67 proliferation index was noted as 0.2-3%. The SMA was positive in the surrounding muscle tissue. The CK5/6, CK14, CK20, EMA, HMB45, vimentin, desmin, CD31, CD34, S100, P53 and CD68 were negative [14]. In our case, strong positive staining with epithelial markers such as CK7, CK19 and Pan-CK and positivity with mesothelial markers calretinin and HBME-1 were noted. The CEA, EMA, ER, PR, GCDFP15, CDX2, S100 and vimentin were observed negative. A brief summary of the age, sex, location and immunohistochemical findings of the other cases and the current case are presented in [Table/Fig-5].

Adenomatoid tumors are often encountered in the reproductive period. The most common symptoms are pelvic pain and menorrhagia. Most cases were accompanied by a leiomyoma (56-80%). Infertility, recurrence and metastasis are not among the features of this tumor [7].

Adenomatoid tumors are macroscopically are between 0.5-4 cm in size. The edges are often more irregular compared to leiomyomas and the cut surfaces are more yellowish, white-grayish. Their macroscopic appearance may resemble adenomyosis deposits. This type of tumor are most commonly located in the posterior wall of the uterus especially the cornual region [1,7]. Microscopically they may be adenomatoid, angiomatoid, solid, cystic or sometimes a mixed of more than one. The adenoid type is the most commonly encountered [2,7]. In our case, in addition to small, tubular and cleft like adenoid structures, signet cell like clusters has also infiltrated the myometrium. If the location and the microscopic findings are characteristic, the diagnosis of an adenomatoid tumor is straightforward. However sometimes, the location and infiltration patterns may lead to misdiagnosis particularly if the tubular and signet cell formations infiltrating the smooth muscle tissue of an intramurally located leiomyoma are detected since these may resemble a signet cell adenocarcinoma [1]. During the evaluation intraoperatively, consultation can be confused with metastatic adenocarcinoma because signet ring cell component may mimic signet ring cell carcinoma. The calretinin and HBME-1 mesothelial markers are useful in this identification. In addition, lack of pleomorphism, atypia, mitosis, absence of epithelial mucin, CEA negativity, and low Ki-67 proliferation index are findings in favor of adenomatoid tumor [15].

CONCLUSION

Leiomyoadenomatoid tumor is a variant of adenomatoid tumor, where in the smooth muscle component is predominant. Leiomyoadenomatoid tumor is rare and may mimic primary or metastatic signet ring cell adenocarcinomas due to their infiltrative pattern. Therefore the pathologists should be aware of these tumors for differential diagnosis and the pathologists must use the morphological findings together with mesenchymal originated immunohistochemical markers to avoid from misdiagnosis.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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