Atypical polypoid adenomyoma of the uterus. A case report and a review of the literature

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Summary

Atypical polypoid adenomyoma (APA) is a rare, benign lesion. The tumor occurs in nulliparous women aged 22-48 years (average 33 years) and it has been suggested as being related to prolonged estrogenic stimulation. We describe a case of a 72-year-old woman who presented at our hospital with persistent, worsening urinary incontinence and pelvic pain. Physical examination and pelvic ultrasound disclosed uterine enlargement, a mass in the endometrial cavity and multiple small myomas. Total hysterectomy with bilateral salpingo-oophorectomy was performed. The histological diagnosis for the mass of the endometrial cavity was atypical polypoid adenomyoma. APA should be distinguished from endometrial carcinoma and other malignant uterine neoplasms such as adenofibroma, adenosarcoma and malignant mixed mullerian tumor. The immunohistochemical panel which usually includes alpha smooth muscle actin, desmin, Ki67 and recently CD10 is often helpful in establishing the diagnosis. The treatment may vary depending on the patient's age, her desire to preserve fertility, and the severity of her symptoms.

Key words: Uterus; Atypical polypoid adenomyoma; Endometrial stromal cells; Immunohistochemistry.

Introduction

The term atypical polypoid adenomyoma (APA) was first described by Mazur in 1981 [1]. This entity is a rare, benign, polypoid tumor of the uterus and it is composed of endometrial glands admixed with a stromal component of interlacing bundles of smooth muscle [2]. The tumor occurs in premenopausal women, usually in their fourth and fifth decades, and rarely after menopause. In adittion APA has been seen in patients with Turner syndrome [3]. Although the lesion is benign, it should be distinguished from hyperplasia, endometrial carcinomas and other malignant uterine neoplasms with which it is often confused, particularly in curettage specimens [4, 5]. The published series indicate an average risk of endometrial carcinoma of 8.8% in women with a history of polypoid adenomyoma [6]. We report a case of APA of the uterus in a postmenopausal woman, discuss the histogenesis of this tumor, and review the English literature.

Case Report

A 72-year-old woman, gravida 2, para 2, presented with a 4-month history of lower abdominal pain and abnormal uterine bleeding of about three weeks duration. She had completed menopause at the age of 53. Gynecological and medical history were uneventful. On physical examination an enlarged, irregular uterus was found. No other masses were detected anywhere else. Laboratory findings were within normal limits, including tumor markers CEA and CA125. Pelvic ultrasound (US) disclosed uterine enlargement, a mass in the endometrial cavity and multiple myomas. A total hysterectomy with bilateral salpingo-oophorectomy was performed. On gross examination, the uterus weighed 1200 g and was lobulated. The endometrium contained a well circumscribed polypoid tumor 12 x 3 x 2 cm in size and which arose from the uterine fundus and extended down to the endocervical canal. The cut surface was moderately firm, uniform, and without cystic degeneration. Many multiple intramural and subserosal tumors were also identified. On histologic examination the tumor was composed of widely spaced proliferative glands with slightly irregular spaces which were lined by atypical cells showing occasional mitoses (Figure 1). The stroma was composed of short interlacing bundles of smooth muscle cells which appeared benign (Figure 2). Mitoses were rare. Foci of adenomyosis were seen at the margins of the tumor. In some areas the glands were back to back (Figure 3), whereas in other areas smooth muscle was present among the glands. The tumor did not invade the myometrium. The uninvolved endometrium was atrophic.

Immunohistochemistry the myofibromatous mesenchymal cells were strongly positive for SMA (Figure 4) weakly positive for desmin and negative for CD10, oestrogen, progesterone. The Ki67 proliferative antigen was low (Figure 5). The tumors in the myometrium were leiomyomata.

Discussion

The term APA of the uterus was first described in 1981 by Mazur [1] and approximately less than 200 cases in the uterus have been reported in the English literature ever since. He defined it as an uncommon focal polypoid lesion of the uterus featuring the proliferation of irregular endometrial glands with squamous metaplasia embedded within a prominent cellular smooth-muscle stroma.

APA is an unconmon endometrial tumor that typically occurs in women of reproductive age. Average age of occurence is 39 years, but ages have ranged from 21 to 73 years. Rarely, affected patients are postmenopausal [7]. In addition, APA has been seen in patients with Turner syndrome, possibly representing a complication of long-term estrogen therapy in these patients [3]. The

Revised manuscript accepted for publication March 16, 2011

Fig. 1

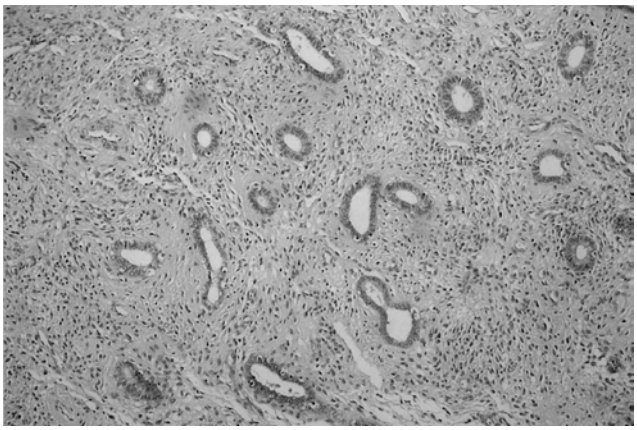

Fig. 2

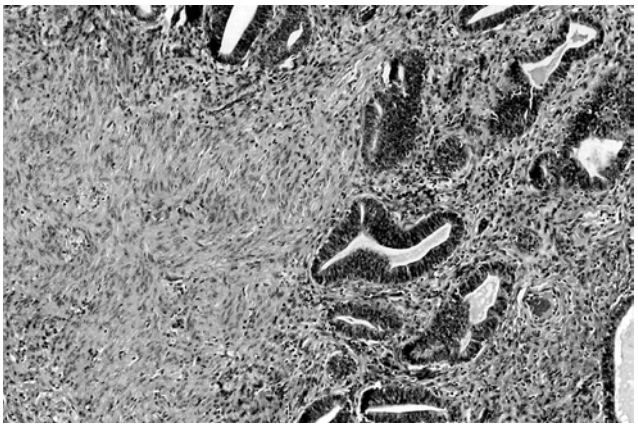

Fig. 3

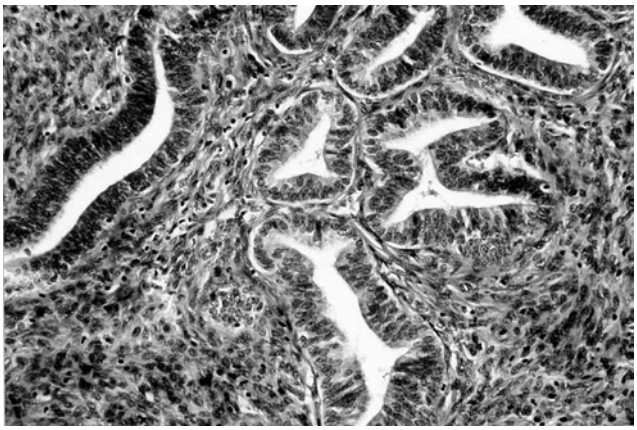

Fig. 4

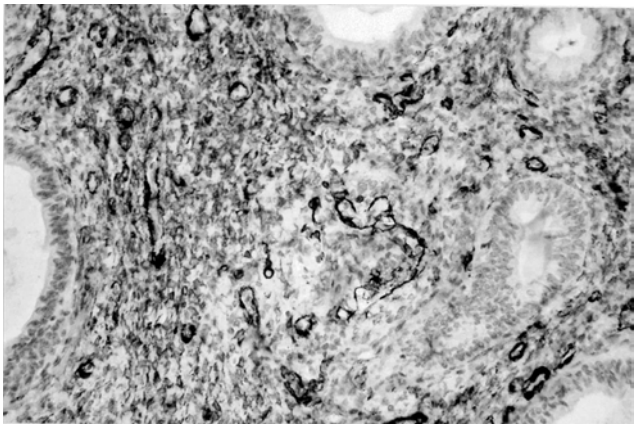

Fig. 5

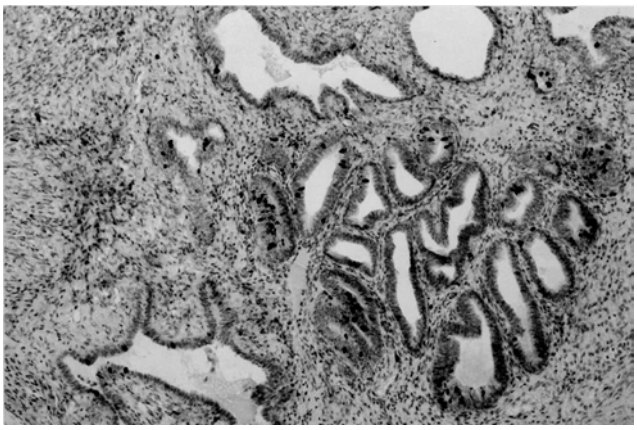

Figure 1. — Atypical polypoid adenomyoma (H&E x 100).

Figure 2. — Cellular smooth muscle component (H&E x 200).

Figure 3. — Atypical endometrial glands are back to back with atypia (H&E x 200).

Figure 4. — The myofibromatous component is strongly positive for SMA (SMA x 200).

Figure 5. — Ki67 scattered positive nuclei in tumor glands (Ki67 x 200).

main clinical symptom is abnormal uterine bleeding. Vaginal discharge, pelvic pain or postcoital spotting may be seen [8-10]. Most lesions are detected on endometrial biopsy specimens or dilation and curettage specimens obtained for workup of the abnormal bleeding. However, APA has been discovered incidentally during routine hysteroscopy and biopsy for infertility or, when the uterus is removed for other reasons, such as leiomyomata [2, 5, 9]. It arises most frequently in the lower uterine segments but has also been reported to involve the uterine fundus, as in our case, or endocervical canal. Grossly APA presents as a pedunculated or sessile polypoid mass with bulging, lobulated or bosselated, firm or rubbery sectioned surfaces. The greatest dimension ranges from 0.1 to 6 cm [9-11]. The size of the tumor in the present case was 12 cm in the longest diameter.

Microscopically APA is a biphasic tumor, consisting of atypical endometrial glands separated by intersecting fascicles of smooth muscle cells.

The glands vary considerably in size and frequently have irregular shapes and are lined by cuboidal to low columnar to pseudostratified columnar epithelium with varying degrees of cytologic atypia and mitoses [2, 6, 8, 9].

Longacre *et al*. reported that if the APA contains markedly complex glands and glandular proliferation, the lesion should be designated as "APA of low malignant potential" [10].

The glandular components may be focally obliterated by the metaplastic squamous elements. In some cases the squamous elements seem to blend almost imperceptibly with the stroma [2]. Foci of mucinous metaplasia are occasionally seen and an Arias-Stella-like change may be evident in pregnant patients [11] .

The stromal component, typically appears benign and predominantly consists of intrelacing bundles of smooth muscle. The stroma of APA differs from normal myometrium by exhibiting increased cellularity, short interlacing fascicles rather than elongated muscle bundles and a minor component of fibrous tissue [2, 11]. Hyalinization may be present. The uninvolved endometrium is typically benign and rarely the adjacent endometrium may be secretory or hyperplastic [2]. Minor foci of superficial adenomyosis may be seen in the tumor. Longacre *et al*. proposed an alternative term "atypical polypoid adenofibroma", as they demonstrated that the stroma in these lesions contained a mixture of smooth-muscle cells, fibrous tissue and endometrial stromal cells [10]. The differential diagnosis of APA includes endometrial carcinoma with invasion of the myometrium [12, 13], adenofibroma, adenosarcoma and malignant mullerian mixed tumor [1, 2].

The young age of patients with APA (average 39 years), should be a clue to the diagnosis because adenofibroma, adenosarcoma and malignant mullerian mixed tumor (MMMT) all typically occur in postmenopausal women. On gross examination small, solid, polypoid, well circumscribed, lobulated APA differs in appearance from large exophytic masses seen in most adenosarcomas and MMMTs.

In addition APA differs from tumors in the adenofibroma-adenosarcoma category in the muscular nature of its stromal component. The latter category almost always resembles that of endometrial stroma and its fibrous stroma. The stromal component of adenosarcomas often forms periglandular cuffs.

Distinction between APA and MMMT should not be difficult because both the glandular and stromal components of the latter are highly malignant [2].

The most important differential diagnostic problem presented by APA is exclusion of well differentiated endometrial carcinoma invading the endometrium [12-14]. Although APA architecturally may resemble endometrial adenocarcinoma it lacks stromal desmoplasia and usually affects young women. The distinction between them is very important but sometimes very difficult. In these cases the immunohistochemical panel, which usually includes alpha smooth-muscle actin and desmin [14, 15], and recently CD10 is often helpful in establishing the diagnosis [16].

It is acknowledged in the field of gynecologic pathology that CD10 is a sensitive and diagnostically useful marker of neoplastic and non neoplastic endometrial stromal cells [15]. According to recent studies CD10-immunostaining pattern demonstrated a significant difference in the stromal components between microinvasive carcinoma and APA. The microfibromatous stromal component of APA is completely negative for CD10 in most cases, whereas mesenchymal cells immediately surrounding the myoinvasive carcinoma were positive (fringe-like staining pattern) [16-19].

Immunohistochemical studies for Ki67 have demonstrated that proliferative activity of the glands in APA is lower when compared with glands of usual endometrial adenocarcinoma.

A few molecular studies for DNA ploidy analysis demonstrated that APA had a diploid DNA content and that the S phase fraction was relatively low [20].

The histogenesis of APA remains uncertain. The intimate relation between its glands and the myofibromatous stromal component suggests that the myofibromatous stromal component of APA may be explained by the histogenesis of the "myofibromatous metaplasia" of the endometrial stromal cells [18]. Moreover, Clement and Young believe that the estrogen-related factor may play an important role in the development of atypical polypoid adenomyoma due to the fact that the lesion mainly occurs in premenopausal patients and the uninvolved endometrium exhibits an estrogen phase appearance [3].

Since APA generally occurs in premenopausal women and as conserving fertility potential may be an important consideration, hysteroscopic resection of such tumors may be a therapeutic option in women who wish to retain their uterus or who would be at high medical risk for hysterectomy [21] .

In conclusion APA is a rare benign tumor of the uterus that could appear in postemopausal women. The fact that in our case the uninvolved endometrium was atrophic shows that this tumor was not related to estrogenic conditions.

References

[1] Mazur M.T.: "Atypical polypoid adenomyomas of the endometrium". *Am. J. Surg. Pathol*., 1981, *5*, 473.

[2] Young R.H., Treger T., Scully R.E.: "Atypical polypoid adenomyomas of the uterus. A report of 27 cases". *Am. J. Clin. Pathol*., 1986, *86,* 139.

[3] Clement P.B., Young R.H.: "Atypical polypoid adenomyoma of the uterus associated with Turner's syndrome. A report of three cases, including a review of "estrogen-associated" endometrial neoplasms and neoplasms associated with Turner's syndrome". *Int. J. Gynecol. Pathol*., 1987, *6,* 104.

[4] Lee K.R.: "Atypical polypoid adenomyoma of the endometrium associated with adenomyomatosis and adenocarcinoma". *Gynecol. Oncol*., 1993, *51,* 416.

[5] Savelli L., De Iaco P., Santini D., Rosati F., Ghi T., Pignotti E., Bovicelli L.: "Histopathologic features and risk factors for benignity, hyperplasia and cancer in endometrial polyps". *Am. J. Obstet. Gynecol*., 2003, *188*, 927.

[6] Fukunaga M., Endo Y., Ushigome S., Ishikawa E.: "Atypical polypoid adenomyomas of the uterus". *Histopathology*, 1995, *27,* 35.

[7] Kuwashima Y., Uehara T., Kurosumi M., Kishi K., Ohno H., Maruyama M., Takayama S.: "Atypical polypoid adenomyoma of the uterus in a very old woman: a report of a case with immunohistochemical characterization of its stromal components and proliferative status". *Eur. J. Gynaecol. Oncol*., 1995, *16,* 115.

[8] Heatley M.K.: "Atypical polypoid adenomyoma: A systematic review of the English literature". *Histopathology*, 2006, *48,* 609.

[9] Rollason T.P., Redman C.W.: "Atypical polypoid adenomyoma - clinical, histological and immunohistochemical findings". *Eur. J Gynecol. Oncol*., 1988, *9*, 444.

[10] Longacre T.A., Chung M.H., Rouse R.V., Hendrickson M.R.: "Atypical polypoid adenomyofibromas (atypical polypoid adenomyomas) of the uterus: a clinicopathologic study of 55 cases". *Am. J. Surg. Pathol*., 1996, *201*, 1.
[11] Wong A.Y., Chan K.S., Law W.L., Tang L.C.: "Pregnancy outcome of a patient with atypical polypoid adenomyoma". *Fertil. Steril*., 2007, *88,* 1438.e7.
[12] Sugiyama T., Ohta S., Nishida T., Okura N., Tanabe K., Yakushiji M.: "Two cases of endometrial adenocarcinoma arising from atypical polypoid adenomyoma". *Gynecol. Oncol*., 1998, *71,* 141.
[13] Mittal K.R., Peng X.C., Wallach R.C., Demopoulos R.I.: "Coexistent atypical polypoid adenomyoma and endometrial adenocarcinoma". *Hum. Pathol*., 1995, *26*, 574.
[14] Soslow R.A., Chung M.H., Rouse R.V., Hendrickson M.R., Longacre T.A.: "Atypical polypoid adenofibroma/APA versus well-diffentiated endometrial carcinoma with prominent stromal matrix: an immunohistochemical study". *Int. J. Gynecol. Pathol.,* 1996, *15,* 209.
[15] Di Palma S., Santini D., Martinelli G.: "Atypical polypoid adenomyoma of the uterus. An immunohistochemical study of a case". *Tumori,* 1989, *75*, 292.
[16] McCluggage W.G., Sumathi V.P., Maxwell P.: "CD10 is a sensitive and diagnostically useful immunohistochemical marker of normal endometrial stroma and of endometrial stromal neoplasms". *Histopathology*, 2001, *39,* 273.
[17] Srodon M., Klein W.M., Kurman R.J.: "CD10 imunostaining does not distinguish endometrial carcinoma invading myometrium from carcinoma involving adenomyosis". *Am. J. Surg. Pathol.,* 2003, *27,* 786.
[18] Ohishi Y., Kaku T., Kobayashi H., Aishima S., Umekita Y., Wake N. *et al*.: "CD10 immunostaining distinguishes atypical polypoid adenomyofibroma (atypical polypoid adenomyoma) from endometrial carcinoma invading the myometrium". *Hum. Pathol.,* 2008, *39,* 1446.
[19] Nascimento A.F., Hirsch M.S., Cviko A., Quade B.J., Nucci M.R.: "The role of CD10 staining in distinguishing invasive endometrial adenocarcinoma from adenocarcinoma involving adenomyosis". *Mod. Pathol*., 2003, *16*, 22.
[20] Ota S., Catasus L., Matias-Guiu X., Bussaglia E., Lagarda H., Pons C. *et al*.: "Molecular pathology of atypical polypoid adenomyoma of the uterus". *Hum. Pathol*., 2003, *34*, 784.
[21] Vilos G.A., Ettler H.C.: "Atypical polypoid adenomyoma and hysteroscopic endometrial ablation". *J. Obstet. Gynaecol. Can*., 2003, *25,* 760.

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