Atypical polypoid adenomyoma mixed with endometrioid carcinoma: a case report

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Summary

The following is a description of an extremely rare tumor of the uterus, malignant atypical polypoid adenomyoma (APA), admixed with well-differentiated endometroid carcinoma, in a 29-year-old patient previously treated for sterility in whom, due to the existence of a ten-millimeter sessile tumor on the uterine corpus, verified by transvaginal ultrasonography (TVUS), a hysteroscopic resection of the anomaly was performed. The patient underwent all requisite examinations and was referred to the malignant diseases panel for an examination and a decision on further treatment. As the patient wished to preserve fertility, the authors decided to continue performing regular controls at intervals of two to three months. The first subsequent control called for a TVUS examination or one using another imaging method, with a multiple endometrial biopsy with curettage of the endocervix. The results of the first examination promised that fertility could be preserved. Therapy with medroxyprogesterone acetate (MPA) in daily dosages of 200 to 500 mg was advised, which the patient intentionally did not take. A spontaneous desired pregnancy was verified following the first control.

Key words: Atypical endometrial polipoid adenoma; Hysteroscopic resection; Fertility preservation.

Introduction

Atypical polypoid adenomyoma (APA) is a disease with a low potential for malignancy, first described as such by Mazur in 1981 [1]. Within the tumor there are proliferative endometrial glands and smooth muscle cells [2]. It manifests itself as a sessile form of tumor sized from one to two cm and features increased, irregular, and profuse uterine bleeding in premenopausal patients or is present together with infertility in patients of reproductive age. It is very difficult to diagnostically differentiate between APA and atypical endometrial hyperplasia, as well as adenocarcinoma, adenofibroma, adenosarcoma, and carcinosarcoma [3]. In any case, a definite diagnosis is determined after dilatation and explorative curettage procedure of the uterine cavity or a hysteroscopic resection of the uterine corpus, with a histopathological examination of the material obtained.

A study evaluating the risk factor of a parallel development of a carcinoma and malignant transformation of APA, is required in order to establish indications for preserving fertility [4].

The locations where APA appears most frequently include: the fundus of the uterus, the lower parts of the uterus isthmus, and the cervix. The diagnostic methods, besides transvaginal ultrasonography (TVUS) are: computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography-CT (PET-CT) imaging, as well as hysteroscopy [5]. Its incidence is higher in nulliparous women who have undergone sterility treatment, aged around 40 years, although it can also appear in perimenopausal patients [6]. No clear medical consensus exists with respect to the evolution and concurrence of APA with carcinoma of the uterine corpus, as well as the form therapy should take if fertility preservation is desired. Even more uncertainty exists, when a pregnancy does occur, regarding how to follow it through until delivery, and what procedure to implement after birth – continuing intensive controls or performing a hysterectomy [3].

Case Report

During TVUS examination of a 29-year-old patient in connection with sterility, a sessile tumor of a size of about ten mm was detected on the uterine corpus. Blood-type O Rh+, biochemical, and laboratory parameter analyses showed no deviations outside normal reference values. Colposcopy findings included: ectocervix covered with stratified squamous epithelium, SCH +, PA II group. US examination of the abdomen confirmed a liver homogeneous without lesions, a cholecyst with no pathological content, a homogenous pancreas, no enlarged paraaortic lymph nodes, a homogenous and properly sized spleen, and both kidneys with hypotonia of the pharmacokinetic (PK) system. TVUS exam revealed a uterus in anteversion/flexion (AVF), hyperechogenicity in cavity, dilated by five mm in the isthmic region with hyperechogenic change in a part of the fundus up to ten mm in size. Chest X-ray showed no signs of active pathological changes or secondary deposits in parenchyma of the lungs. Hilar structure was normal and filtration coefficient (KF) sinuses were unobstructed.

Hysteroscopic resection of the anomaly in the uterine fundus was performed under general IV anaesthesia. Following the usual procedure of cervical canal dilatation, the cervical canal and uterine cavity were hysteroscopically examined. The canal and the tube openings were observed and had conventional morphological characteristics, with a sessile tumor generally white in appearance present in the fundus, positioned somewhat laterally to the right. A resection was performed and the anomaly was completely removed and sent for histopathological analysis. Hemostasis control was performed with a bipolar thermal cauteriser, and surgery was then completed. Postoperative recovery period was uneventful.

Pathologist's report included APA, with a low potential for malignancy – a polypoid structure dominated by an epithelial component, over a smooth-muscle component. Glandular epithelium showed signs of atypia and the presence of squamous morules;

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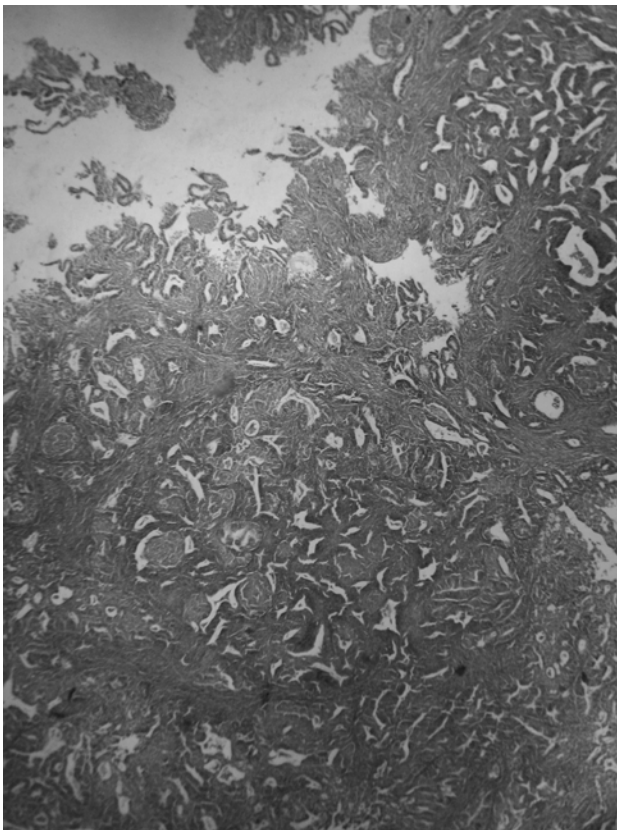

Figure 1. — Atypical polypoid adenomyoma with low-malignant potential with endometrial carcinoma.

cribriform structures were focally present as seen in well-differentiated endometrioid adenocarcinoma. The anomaly was completely removed with negative recession margins (Figure 1).

Abdominal multislice computed tomography (MSCT) and pelvis minor findings two weeks after the surgery showed a uterus dextraposed in AVF, size 93 x 80 x 67 mm, with a cavum width of up to 20 mm without focal lesions and without changes in the area surrounding the uterus. Follicles were ≤ 15 mm in size in both ovaries. No abnormalities were seen in the vagina. The abdominal findings showed no signs of spread or presence of the disease.

The patient and all documentation were presented to the malignant diseases panel. As preservation of fertility does exist among patients, the decision was taken to conduct intensive controls and regular TVUS examinations, as well as multiple biopsies of the uterine cavity. Therapy with medroxyprogesterone acetate (MPA) in daily dosages of from 200 to 500 mg was advised, until further notice.

At the next control after three months, a TVUS examination and exploratory curettage of the uterine cavity were performed. The patient had declined to apply the recommended therapy.

TVUS examination revealed a uterus in AVF, with a size of 90 x 76 x 60 mm, endometrium of 12 mm, and the adnexal findings were normal. Exploratory curettage of the uterine corpus and cervical canal performed under general IV anaesthesia and passed without complications. Pathologist's report included an APA, with a low potential for malignancy, with proliferative endometrium of standard characteristics. Endocervical mucosa were without significant changes and included squamous morules.

At the next control, a spontaneous physiological pregnancy was confirmed in the patient.

Discussion

APA is a very rare disease reported over the past 30 years and histologically characterized by proliferative endometrial glands and smooth muscle cells. The patient presented an APA, with benign changes with a low potential for malignancy; there were also histological changes representative of a well-differentiated endometroid carcinoma. It is very difficult to differentiate between APA and atypical hyperplasia, because it is unclear whether APA is a precancerous lesion for endometrioid carcinoma of the uterine corpus, or if it is a completely separate entity whose histogenesis is not sufficiently understood. Quite often it is difficult to determine the correct diagnosis, as histological forms which are detected can also be seen in malignant diseases [4]. Several cases have been reported of admixed well-differentiated endometroid carcinoma and APA, the admixture being unclear, pointing to the conclusion that a timely diagnosis and recognition of the disease must be the priority [4, 7]. There are also reports of serial changes from endometrium to carcinoma in patients without child-bearing data, which is the main reason for enhanced monitoring of patients, as the speed and progress of changes in this condition are not clear [3].

Immunohistochemical research indicates that actin, desmin, Ki67, and more recently also CD10, can provide much help in differentiating between APA and malignant diseases [8, 9]. The presence of a malignant disease and APA are based at a global level in individual cases. It is easier to set a definite diagnosis on material obtained by a hysterectomy [10]. It occurs both in women of reproductive age and older. The average patient's age is 40 years, the age range reported so far being between 25 and 73 years. The majority are women of reproductive age, and 14 out of 16 patients wish to preserve fertility [11]. The average survival time is 25.2 months; in a sample of 29 patients the range was from one to 112 months. The authors have presented a 29-year-old nulliparous patient, in whom during preparations for an artificial insemination (AI) procedure, an ultrasound examination determined the existence of a sessile tumor on the uterine corpus, without the presence of the appropriate symptomatology.

Methods for resolving this clinically-represented sessile form of tumor are hysteroscopic resection, in younger patients desiring to preserve fertility, and where symptomatology may not necessarily be present, and a more radical approach – hysterectomy, in older patients where there is also bleeding. In this patient after the requisite preparations, the anomaly was completely removed hysteroscopically and submitted for histopathological analysis. Hysteroscopic resections are proposed in four steps: the polyp is removed, the tissue surrounding the polyp is removed, as is the tissue under the polyp, and multiple biopsies are taken, in order to confirm the disease [12]. Repeated polypectomies as a part of exploratory curettages are one of the methods that can

prove a possible germinal invasion of the myometrium, although false-negative results are present in materials obtained by curettage. There are reports stating that in repeated polypectomies, in 29 cases, the disease was confirmed in 45% of all cases, 33% having a low malignant potential, and around 60% with a high potential. Some recidivation following conservative treatment has also been reported [3].

A higher APA incidence has been observed in patients subjected to estrogen therapy for longer periods, as well as in persons with Turner syndrome in whose treatment estrogen was used [13]. Hyperprolactinemia and resultant changes in hormonal status can also lead to this disease [14]. In women desiring to preserve fertility, within preparations for AI, as was the case with our patient, it is necessary to focus attention on the endometrium, together with an anamnesis of the menstrual cycle, because obvious anovulation is a factor leading to this disease [15].

APA develops in the fundus, the lower segments, and the cervix of the uterine corpus, in sizes not exceeding two cm. There are studies, based on just five presentations, where the mean value is about 3.12 cm [8].

Admixture with carcinoma and a differential diagnosis with well-differentiated endometroid carcinoma has been reported in some cases [16, 17]. Statistical analyses, based on the presentations, show that the risk of the occurrence of endometroid carcinoma in APA is 8.8% [18]. In the material obtained by a repeated curettage after resection of the polyp, the authors did not histopathologically verify the existence of endometroid carcinoma. Diagnostic methods are TVUS, where the APA is observed as a hyperechogenic sessile swelling of the interior uterine wall, and MRI, which shows a characteristic mixture of hyper- and hypoechogenicity with an irregular contrast distribution [5]. There have been reports of pregnancies in patients with this disease, but only in individual cases, and the objective is to determine the manner of control, the delivery, and postnatal treatment intended to reduce the risk of disease progression [16]. The authors have presented a patient with APA who became pregnant following resection surgery, gave birth, and for three years has been free of the disease and subject to a strict follow-up regimen [19-21]. Preserving fertility in patients of this kind certainly represents a certain risk which must be made known to them, which the authors had done with the patient presented.

Conclusion

A very rare disease whose histogenesis is not known, occurs in younger people at an average age of 40 years with sizes up to 3.12 cm. Long-term exposure to estrogen leads to the disease, and careful observation of the endometrium is required. A disease in whose treatment has no established opinions, as experiences are based on individual cases. Pregnancies and preservation of fertility are possible, while more work needs to be done in connection with the manner of delivery and postnatal control. In a period when the number of endometroid malignancies is rising, even more cases of this kind can be expected to occur.

References

[1] Iori K., Kouji B., Megumi Y., Yusuke K., Arisa U., Asuka O. *et al*.: "Atipical polipoid adenomyoma (APAM) of the uterine-relationship with endometrial cancer". *J. Cancer Therapy*, 2011, *2*, 458.

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

[3] Fukuda M., Sakurai N., Yamamoto Y., Taoka H., Asakawa Y., Kurasaki A. *et al*.: "Case of atypical polypoid adenomyoma that possibly underwent a serial progression from endometrial hyperplasia to carcinoma". *J. Obstet. Gynaecol. Res.,* 2011, *37,* 468.

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

[5] Maeda T., Tateishi U., Sasajima Y., Hasegawa T., Daisaki H., Arai Y., Sugimura K.: "Atypical polypoid adenomyoma of the uterus-appearance on F-FDG PET/MRI Fused images". *Am. J. Roentgenol*., 2006, *186*, 320.

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

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

[8] Terada T.: "Atypical polypoid adenomyoma of the uterus: an immunohistochemical study on 5 cases". *Ann. Diagn. Pathol.,* 2011, *15,* 338.

[9] Horita A., Kurata A., Maeda D., Fukayama M., Sakamoto A.: "Immunohistochemical characteristics of atypical polypoid adenomyoma with special reference to H-caldesmon". *Int. J. Gynecol. Pathol.,* 2011, *30*, 64.

[10] Horita A., Kurata A., Komatsu K., Yajima M., Sakamoto A.: "Coexistent atypical polypoid adenomyoma and complex atypical endometrial hyperplasia in the uterus". *Diagn. Cytopathol*., 2010, *38*, 527.

[11] Longacre T. A., Chung 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, *20*, 1.

[12] Di Spiezio Sardo A., Mazzon I., Gargano V., Di Carlo C., Guida M., Mignona C. *et al*.: "Hysteroscopic treatment of atypical polypoid adenomyoma diagnosed incidentally in young infertile woman". *Fertil. Steril*., 2008, *89,* 456. Epub 2007, Aug. 13.

[13] 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 with Turner's Syndrome". *Int. J. Gynecol. Pathol*., 1987, *6,* 104.

[14] Nasu K., Miyazaki T., Takai N., Miyakawa I.: "Atypical polypoid adenomyoma in patinet with hyperprolactinemia". *Int. Gynecol. Cancer,* 2001, *11,* 326.

[15] Burke C., Kelehan P., Wingfield M.: "Unsuspected endometrial pathology in subfertile woman". *Ir. Med. J*., 2007, *100*, 466.

[16] 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.

[17] Baschinsky D., Keyhani-Rofagha S., Hameed A.: "Exfoliative cytology of atypical polypoid adenomyoma, a case report". *Acta Cytologica*, 1999, *43*, 637.

[18] Dinas K., Daniilidis A., Drizis E., Zarabouks T., Tzafettas J.: "Incidental diagnosis of atypical polypoid adenomyoma in young infertile woman". *Eur. J. Gynaecol. Oncol*., 2009, *30,* 701.

[19] Yahata T., Nonaka T., Watanabe A., Sekine M., Tanaka K.: "Complete hysterosopic resection of large atypical polypoid adenomyoma, followed by a successful pregnancy". *Fertil. Steril*., 2011, *95,* 2435.

[20] Clouqueur E., Lucot J.P., Collinet P., Farine M.O., Kedraon O., Poncelet E.: "Atypical polypoid adenomyoma". *Gynecol. Obstet. Fertil.,* 2012, epub a head of print.

[21] Wong A.Y., Chan K.S., Lau W.L.,Tang L.C.: "Pregnancy outcome of patient with atypicalpolypoid adenomyoma". *Fertil. Steril*., 2007, *88,* 7.

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