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Management of atypical polypoid adenomyomas. A case series☆

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ABSTRACT

Objective: Atypical polypoid adenomyomas (APAs) are endometrial, non-malignant, focal, and non-invasive lesions that are intriguing for their histological resemblence to invasive endometrioid adenocarcinoma or malignant mixed Müllerian tumor. The aim of this study was to present our clinical experience, regarding the reproductive outcome, the recurrence rate, and the association with hyperplasia and cancer, in a small series of patients with APA.
Study design: Retrospective case series of patients treated for APA in a single private hospital setting from 1998 to 2016. All patients underwent diagnostic hysteroscopy and hysteroscopic removal of the lesion. Follow-up was performed annually with endovaginal ultrasonography and hysteroscopy when necessary.
Results: Nine patients (mean age: 37.9 years-old ±8.3 years) were treated because of menorrhagia, infertility, and incidental asymptomatic endometrial lesions with operative hysteroscopy. Mean follow-up was 10.0 years (±5.8 years). Three patients intended for pregnancy and 2 of them had achieved a full term delivery. There were 2 recurrences (22.2%), two cases of atypical endometrial hyperplasia (22.2%), and 2 patients with endometrioid adenocarcinoma (22.2%), all within the first 5 years.
Conclusions: It appears that APAs exhibit a significant recurrence rate and they may be related both to atypical endometrial hyperplasia and endometrial adenocarcinoma; therefore, clinicians should be aware of these lesions in order to individualize treatment according to the patent's age and fertility history.

Introduction

The term Atypical Polypoid Adenomyoma (APA) has been suggested by Mazur et al. to describe endometrial polypoid lesions occurring in premenopausal women characterized by irregular atypical glands with squamous metaplasia and a cellular, smooth muscle stroma [1]. APAs are intriguing lesions, as their histological resemblance to an invasive endometrioid adenocarcinoma or a malignant mixed Müllerian tumor makes the discrimination among these entities sometimes challenging. APAs, which are considered non-malignant, present as focal and noninvasive lesions, and they are characterized by a well-differentiated smooth muscle component [1]. Nevertheless, current literature indicates that these uterine proliferations are occasionally associated with endometrial adenocarcinoma, suggesting that APAs are not a totally benign entity [2,3]. It has been estimated that APAs have a recurrence rate of 30.1%, there is evidence of endometrial hyperplasia on the diagnosis or on follow-up in 8.8% of the cases (background endometrial hyperplasia), while 8.8% of the cases are related with endometrial adenocarcinoma [4].

APAs could be generally classified within the group of adenomyotic lesions. Adenomyosis is characterized by the presence of endometrial tissue (glands and stroma) embedded in the myometrium; heterotopic endometrial tissue foci are related with a variable degree of smooth muscle cell hyperplasia. Adenomyosis can either be diffuse or localized (focal) depending on the degree of myometrial invasion, and adenomyotic lesions may have a histological spectrum from mostly solid to mostly cystic [5]. During the last decades, there is an increasing trend of getting pregnant later in life. Adenomyosis, a disease mostly diagnosed between 30 and 45-years-old, increasingly complicates the fertility potential of these women [6]. Endoscopy techniques and fertility sparing surgery are parallel trends of modern gynecology [7]. Thus, the need for uterus preserving operations

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in women suffering with symptomatic adenomyosis, including APAs, warranted the conservative operative management of the disease.

Treatment of APAs depends on both clinical and microscopic factors of this disease and womens' desire to preserve her fertility. Younger women with a lesion characterized by low architectural index or mild to moderate atypia can be managed conservatively, whereas older women or patients with a lesion characterized by high architectural index or severe atypia consistent with adneocarcinoma in situ should undergo hysterectomy [8]. Nevertheless, the preservation of reproductive capacity can safely be achieved even in the presence of marked glandular atypia or persistent disease [9]. Apparently, hysteroscopic techniques are suitable for the initial excision and the long-term follow-up of the patient with no aggressive features within the lesion and strong desire to preserve her fertility [10]. However, the association of the lesion with endometrial hyperplasia and adenocarcinoma necessitates close postoperative surveillance and consideration of hysterectomy [11].

The aim of this study is to present our experience regarding the association of APAs with hyperplasia and cancer, the recurrence rate, and the reproductive outcome, in a small series of patients.

Patients & methods

This was a retrospective study of a series of patients treated for pre-operatively benign endometrial lesions that turned out to be atypical polypoid adenomyomas in a private hospital and an affiliated university hospital (Geniki Kliniki, Thessaloniki, Greece and 1st Department Obstetrics & Gynecology, Aristotle University of Thessaloniki, Papageorgiou General Hospital, Thessaloniki, Greece) from 1998 to 2016. Ethical approval was obtained by the Research Committee of the affiliated University Hospital. The patients were identified from the histology registry: All the patients diagnosed with APA who were present in the registry were contacted and included in the study. Patients' demographics, medical history, operative details, and postoperative follow-up, were chased after personal communication with these patients.

All patients underwent diagnostic hysteroscopy and subsequent hysteroscopic removal of the lesion under sedation with the use of hysteroscopic scissors. Further use of resectoscope was applied to remove completely the lesion when necessary. All patients had additional endometrial currettage at the end of the procedure.

All surgical specimens were examined by the same pathologist. The specimens were sectioned and stained with hematoxylin and eosin in a standard fashion. The histologic criteria used for the diagnosis of Atypical Polypoid Adenomyoma were: (1) the presence of architecturally and cytologically atypical endometrial gland separated by smooth muscle cells' intersecting fascicles, (2) the stromal component had increased cellularity, and different architecture from that of the normal myometrium, (3) the lesion had a well-delineated, pushing margin with the adjacent endometrium and myometrium [1,8,9], and (4) h-caldesmon immunohistochemistry was used as an adjunct for the differentiation of APAs from myoinvasive endometrioid carcinoma [12].

Annual follow up was available for all the patients including standard bimanual clinical examination, Papanicolaou smear test, and two-dimensional transvaginal sonogram. During sonographic examination, the endometrial cavity was meticulously assessed. Further hysteroscopic evaluation of the cavity and histology was considered: (1) in the presence of abnormal ultrasound findings, (2) in cases with abnormal uterine bleeding (spotting, hypermenorrheoa, etc), (3) in the two patients with backround endometrial hyperplasia.

All data were collected in Microsoft EXCEL spreadsheet. Basic statistics were performed using Microsoft EXCEL.

Results

In total, this study reports the findings from 9 women diagnosed with APA. Mean age was 37.9 years (±8.3 years); one patient, although 43-years-old, was menopausal. Mean parity was 1.0 child (± 1.1 children). Abnormal uterine bleeding was found in 5 patients, infertility and polyps were diagnosed in the rest of patients (Table 1). Mean follow-up was 10.0 years (±5.8 years) (Table 1).

During initial hysteroscopy, all lesions were solitary, measuring <2 cm (Fig. 1). Follow-up hysteroscopy was performed once in patient No5, four times in patient No#6, and three times in patient No7; two of these procedures had positive findings (2/8, 25%), whereas in the other 6 hysteroscopies no lesions were found (6/8, 75%). The additional currettings did not show any extra pathology. In two patients the initial diagnosis included, apart from the APA,

Table 1
Demographic data, follow-up and post-diagnosis clinical behaviour of APAs in the patients of the study.

Case No	Age	Parity	Symptoms	Initial Diagnosis		Follow-up (years)	Recurrence	New Endometrial Pathology		Pregnancy		Comments
				APA	Endometrial Pathology			AEH	EC	Intention	Term pregnacny	
#1	43	2	PV Bleeding	+	–	18	–	–	–	–	–	–
#2	22	0	None	+	–	16	–	–	–	+	6 years later	–
#3	44	1	PV Bleeding	+	–	15	–	–	–	–	–	–
#4	35	0	Infertility	+	–	12	–	–	–	+	1 year later	–
#5	39	2	PV Bleeding	+	–	11	5 years later	–	5 years later	–	–	5 years: TAH + BSO
#6	30	0	Infertility	+	AEH	6	–	–	–	+	–	–
#7	35	0	None	+	AEH	6	5 months later	3 years later	–	–	–	3 years: TAH + BSO
#8	48	1	PV Bleeding	+	–	5	–	–	–	–	–	–
#9	45	3	PV Bleeding	+	EC	1	–	–	–	–	–	TAH + BSO, Menopausal
Mean	37.9	1.0				10.0						

APA: Atypical Polypoid Adenomyoma, PV Bleeding: Per Vagina Bleeding, AEH: Atypical Endometrial Hyperplasia, EC: Endometial Cancer, TAH + BSO: Total Abdominal Hysterectomy + Bilateral Salpino-Oophorectomy, "–": Negative.