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Case Report

Atypical polypoid adenomyoma of the endometrium: diagnosis and treatment. A case report

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Summary
Atypical polypoid adenomyoma (APA) is a rare uterine lesion that commonly recurs after local excision and is occasionally associated with or anticipates the development of atypical hyperplasia or endometrioid adenocarcinoma. We report a case of a 45-year-old woman affected by APA treated with local resection.

Key words: atypical polypoid adenomyoma, differential diagnosis, myoinvasive endometrioid carcinoma, uterus, immunoistochemistry

Introduction

Atypical polypoid uterine adenomyoma (APA) is an uncommon lesion first described in 1981 [1]. It retains the same definition in WHO classification of mixed epithelial and mesenchymal tumors of the uterine corpus [2]. It usually occurs in premenopausal women and most commonly involves the endometrium of the lower uterine tract or the upper endocervix and appears as a polypoid mass. APA is a biphasic lesion that is composed of atypical endometrial glands and fibromuscular stroma. Because the glandular component shows endometrioid features with irregular architecture and cytologic atypia, pathologists sometimes have difficulties in differentiating APA from myoinvasive adenocarcinoma [3]. This distinction is crucial and influences the clinical management of patients, allowing fertility preservation for patients with APA [1-6]. Specifically, patients affected by APA can be treated with local resection, possibly repeated in case of recurrence of the lesion, while women with myoinvasive adenocarcinoma should undergo surgery (5,6). To discriminate between these cases, some immunoistochemical markers are needed. Previous studies investigated the expression of muscular and endometrial stromal markers in APA [3,7-12].

Case report

A 45-year-old woman with abnormal uterine bleeding (recurrent hypermenorrea, abnormal bleeding other than menstrual), since November 2019 developed secondary anemia and underwent operative hysteroscopy on February 28th of the following year. The date of the last menstruation was February 19th. The patient was nulliparous and underwent

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Conflict of interest
The Authors declare no conflict of interest.

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3 cycles of hormonal therapy due to infertility in 2016. At hysteroscopy a peduncolated polypoid lesion extended from the last segment of the uterine body to the upper endocervix was detected and removed. The lesion was removed by piecemeal hysteroscopic transcervical resection.

Pathological findings

At macroscopic examination many polypoid fragments of different size were encountered. They were grey and firm and the largest piece showed a short pedicle. All the fragments were formalin fixed and paraffin embedded for histological examination.

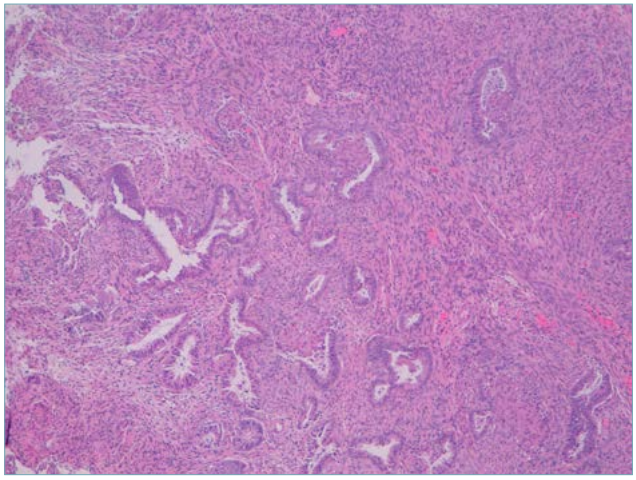

Figure 1. H&E Atypical endometrial glands haphazardly distributed in smooth muscle with irregular contours and shapes, occasionally clustered together, but generally evenly distributed.

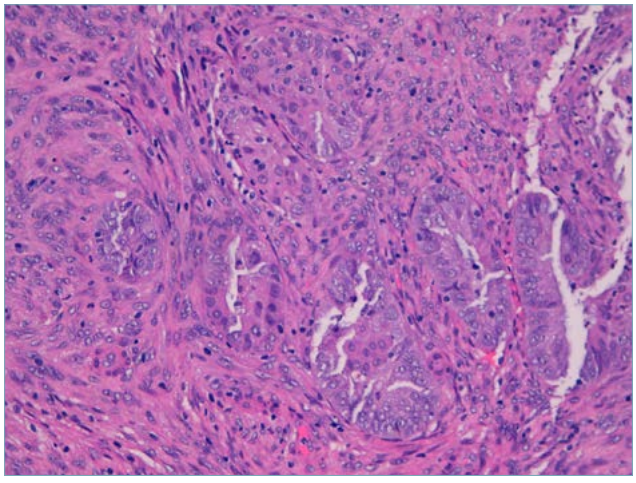

Figure 2. H&E Enlarged nuclei with irregular thickened nuclear membranes and prominent nucleoli. Cytoplasm may be sometimes eosinophilic and cells show loss of nuclear polarization. Some mitoses are present in the epithelial component.

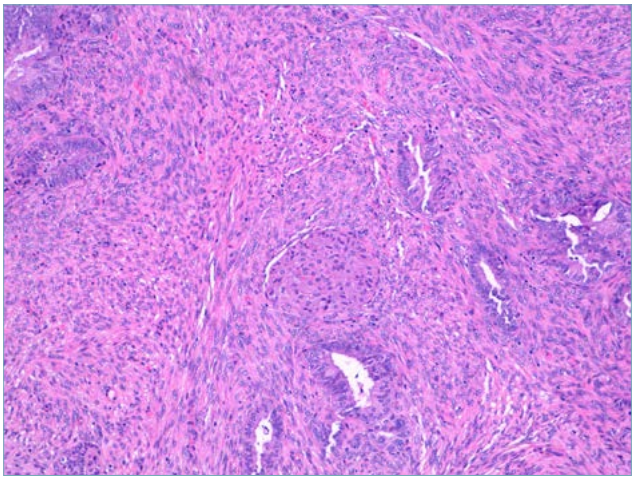

Figure 3. H&E Nodular structures of squamous nonkeratinzing metaplasia (morular metaplasia) in the context of endometrial glands.

Microscopically, the lesion was characterized by atypical endometrial glands aphazardly distributed in smooth muscle with irregular contours and shapes. The glands occasionally clustered together, but generally they were evenly distributed (Fig. 1). The cytologic atypia included enlarged nuclei with irregular thickened nuclear membranes and prominent nucleoli (Fig. 2). The cells showed a loss of nuclear polarization and, in some fields, the cytoplasm was eosinophilic. Mitotic figures were frequent in the epithelium of glands. Squamous nonkeratinzing metaplasia (morular metaplasia) was diffusely present (Fig. 3). The glands were encompassed by interlacing fascicles of elongated smooth muscle cells which showed features of smooth muscle. The surface glandular epithelium did not show cytoarchitectural atypia.

Immunohistochemical analysis

The stromal component was diffusely and intensively positive with smooth muscle actin (Fig. 4) and focally and slightly positive with p16 (Fig. 5). Morules were negative for progesterone receptors (Fig. 6) and had beta-catenin positive nuclei. On the contrary, the remaining epithelium showed a regular membranous expression of beta-catenin (Fig. 7). Moreover, morules revealed strongly positive membranous CD10 positivity,while no “fringe-like CD10 periglandular staining pattern” [10] was observed (Fig. 8). A retained

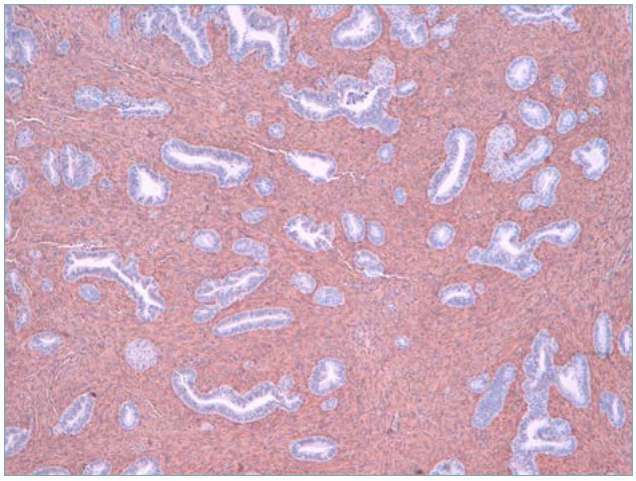

Figure 4. Stromal positivity with smooth muscle actin (act-L).

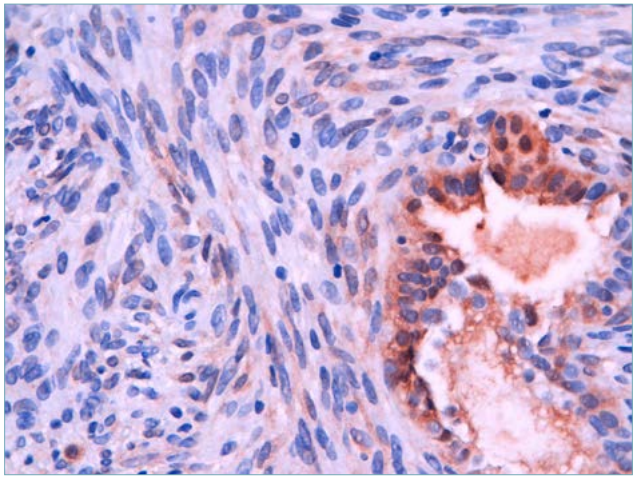

Figure 5. Focal and slight p16 positivity in the stromal cells. This findig suggests APA myoinvasive carcinoma [4].

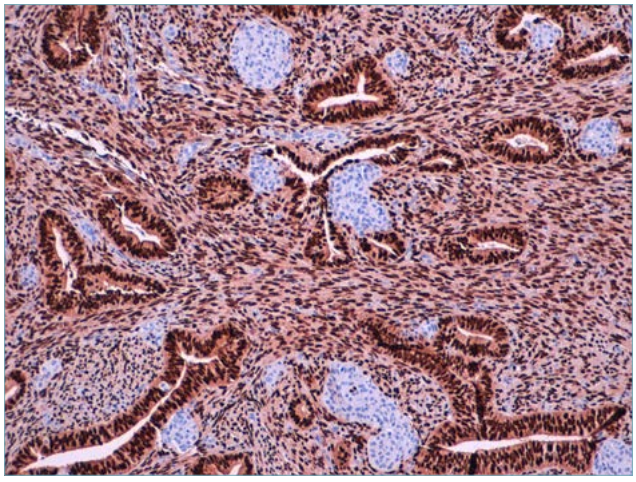

Figure 6. Morules are negative for progesteron receptors in contrast with the stromal and glandular endometrial component.

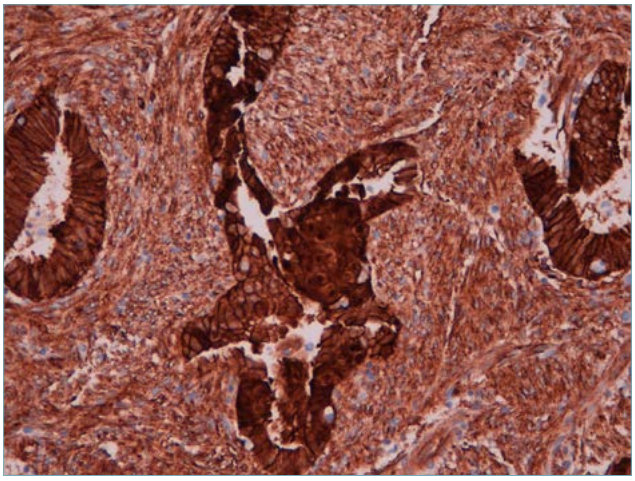

Figure 7. Morules show beta-catenin nuclear positivity, while glands retain membranous staining

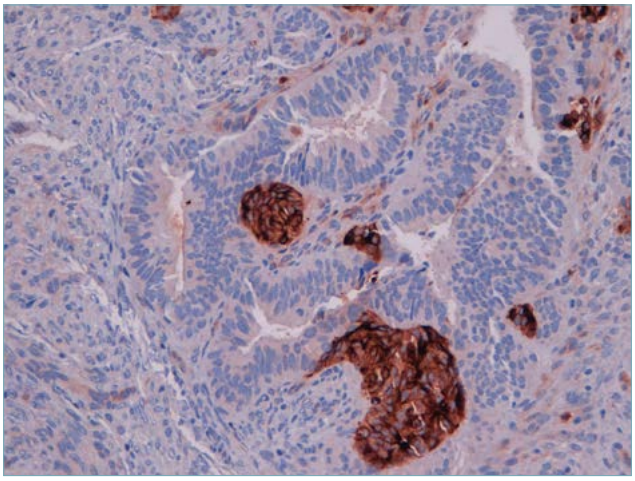

Figure 8. Morules reveal strongly positive membranous CD10 staining, lacking "fringe-like CD10 periglandular staining pattern", a finding suggesting of myoinvasive carcinoma [3,7,10].

expression of the mismatch-repair (MMR) proteins MLH-1, PMS-2, MSH-2, MSH-6 was detected; p53 protein was not over-expressed and did not show a complete lack of expression.

Discussion

Clinical presentation and histological findings were consistent with the diagnosis of atypical polypoid adenomyoma (APA) of the uterus. However, as clinical characteristics are not specific, the differentiation between APA and myoinvasive endometrioid adenocarcinoma depends on the pathological findings [1,3].

Differential diagnosis is based on glands crowding with back-to back arrangement and cribriform pattern that is typical of endometrial carcinoma. Although it is still important to recognize differences in glandular density and architectural complexity between APA and carcinoma, we need to identify useful markers for differential diagnosis. Among them, CD10 is useful to discriminate between the two different lesions as it is expressed around the neoplastic glands ("fringe-like staining pattern") [10] in myoinvasive carcinoma. The CD10 "fringe-like staining pattern" is absent in APA [3,7]. Unfortunately, the absence of CD10 "fringe-like staining pattern" does not exclude myoinvasive carcinoma; therefore further markers are needed [4].

The p16 protein can be variously expressed in different gynecological lesions. It is usually absent in endometrial carcinoma, while it is usually present in the stromal component of APA [4]. Moreover, typical and constant immunohistochemical findings of APA are the intense nuclear beta-catenin positivity of morules and their negativity for estrogen and progesterone receptors.

In previous studies, some molecular alterations were described in APA cases such as mutations in K-RAS and CTNNB1, deletions of PTEN and MLH-1 promoter methylation. However, these alterations do not distinguish APA from endometrial carcinoma because they can be found in both lesions [3,4].

Microscopically, the absence of cytoarchitectural atypia of the surface epithelium is typical of APA, differentiating it from atypical glandular hyperplasia and well differentiated endometrioid adenocarcinoma [1].

Atypical polypoid adenomyoma of the uterus affects premenopausal women in most cases and shows high recurrence rate if conservatively treated. Moreover, atypical glandular hyperplasia and endometrioid carcinoma can coexist.The majority of the patients are nulliparous; the most frequent symptom is abnormal uterine bleeding (hypermenorrea in almost all cases, but also irregular menses and abnormal bleeding other than menstrual). Transcervical resection showed significantly higher initial response rates than any other treatment and, when hormonal therapy is added, lower progression rates are observed. To date, the management of patients is based on low quality evidence and is not standardized. However, follow-up biopsies are advisable.When fertility preservation is not required, hysterectomy might be advisable [5,6].

The quantitative systematic review Raffone et al. shows 11 retrospective studies with 237 patients; 85.5% of patients were premenopausal and 62.9% were nulliparous. Atypical polypoid adenomyoma coexisted with atypical hyperplasia in 5.5% of cases and with endometrial cancer in 5.9%. Fertility-sparing treatments included hormonal therapy with or without maintenance, hysteroscopic transcervical resection, dilation and curettage, and hormonal therapy combined with transcervical resection or dilation and curettage [6]. Decision on treatments also depends on age, desire to bear children, and the individual circumstances, but if the patient is postmenopausal and clinical management by polypectomy or dilatation and curettage is not effective, simple hysterectomy is also an option [13].

Conclusion

In conclusion, a case of APA affecting a 45-years-old woman is reported. The patient was treated recently with a local excision of the lesion by TCR (hysteroscopic transcervical resection). TCR is a recommended diagnostic and treatment option for patients who desire to preserve fertility and follow-up with biopsies is advisable. When fertility preservation is not required, hysterectomy might be suitable.

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