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Serous endometrial intraepithelial carcinoma coexistence with atypical polypoid adenomyoma in a young woman: a rare case

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ABSTRACT

Background. Atypical polypoid adenomyoma (APA) is a rare lesion with less than 500 cases reported worldwide (in the literature). It is an unusual tumor of the uterus, first described by Mazur in 1981 that typically develops in young women, which are also associated with infertility. The disease is considered benign, but there is a significant risk of developing an endometrial carcinoma or a risk of recurrence. The most common histological type of associated adenocarcinoma is endometrioid endometrial carcinoma.

Case presentation. In this study we present a case of APA concomitant with a serous endometrial intraepithelial carcinoma (SEIC) in a young woman, an occasion that has not been reported yet.

Conclusions. When a patient is diagnosed as having APA, always an accompanying EC must be carefully searched.

INTRODUCTION

Atypical polypoid adenomyoma (APA) is an unusual uterine tumor first described by Mazur in 1981 as “*irregular atypical endometrial glands with squamous metaplasia and a cellular, smooth muscle mesenchyme*” [1]. It generally develops in young women, which also associated with infertility. Usually, the clinical presentation is an abnormal uterine bleeding. The most typical location of APA is at the cervical / isthmic region, but it

can originate in every uterine level [1-3]. The disease is considered benign, but there is a significant association with coexistence or development of endometrial carcinoma (EC) and a risk of recurrence [2-5]. In a recent report Cheng *et al.* describe a case of APA coexistence with serous adenocarcinoma of endometrium in a post-menopausal woman [6]. In this study we present a case of APA concomitant with a serous endometrial intraepithelial carcinoma (SEIC) in a young woman, an occasion that has not been reported yet.

CASE PRESENTATION

A 35-year-old woman (gravida 0, para 0), with a body mass index of 25,4 kg/m², presented with a pelvic pain and heavy vaginal bleeding not influenced by drug therapy. Her menarche occurred at 13, menstrual cycle was regular every 28 days. Initially dilation and curettage were performed, and the pathology revealed atypical endometrial hyperplasia and EC of mixed type: endometrioid and clear cell carcinoma. A month later the patient underwent radical hysterectomy with total pelvic lymph node dissection and biopsy of the omentum. Macroscopical examination of hysterectomy specimen revealed a uterus 8 cm in length and 3 cm in width with a small polypoid tumor 15 mm in diameter, located at the isthmic part of the uterus, slightly arisen above the endometrial surface. Histological examination

of the polypoid lesion revealed a biphasic tumor composed of slightly irregular endometrial glands with mild cytologic atypia and multiple squamous morules, surrounded by a benign smooth muscle stroma (**Figure 1**). There were areas with highly atypical cells lining focally the surface and some superficial glands of the polypoid formation without invasion in the smooth muscle stroma (**Figure 2**). These epithelial cells had large, atypical nuclei with prominent nucleoli, scant cytoplasm and immunohistochemically revealed p53 strong nuclear overexpression (mutant type) on the background of p53 wild type expression in the rest of the polypoid tumor (**Figure 3**). Ki 67 showed markedly increased proliferative activity on the surface atypical foci in comparison to underlying areas (**Figure 4**). Napsin A and WT1 were negative everywhere.

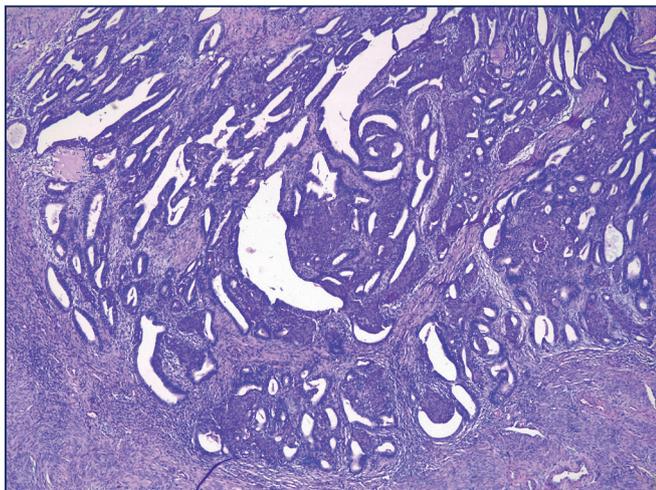


Figure 1. APA with irregular endometrial glands, squamous metaplasia, myomatous stroma and non-invasive base of the lesion (XE x40).

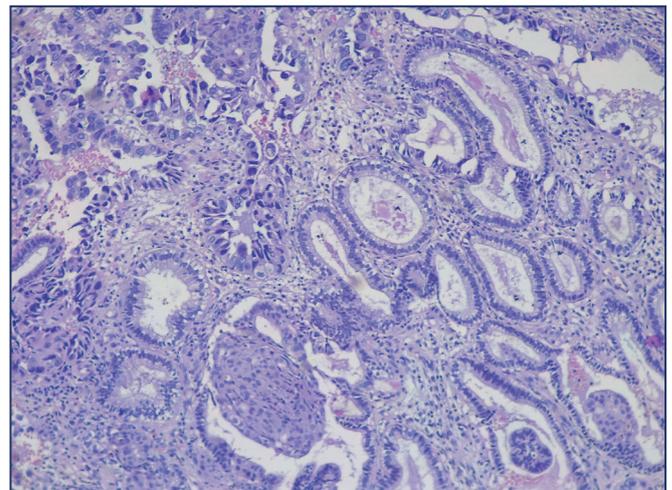


Figure 2. SEIC, presented by areas with highly atypical cells lining focally the surface and some superficial glands (left) of APA (right) (XE x25).

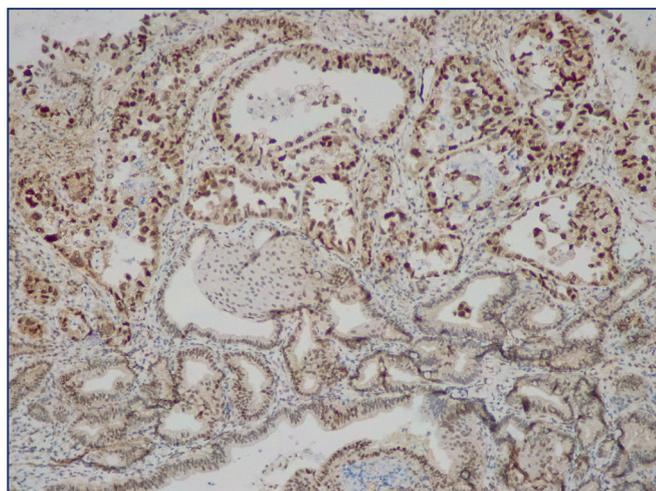


Figure 3. p53 overexpression in SEIC (upper portion) and p53 wild type of expression in APA (lower portion) x25.

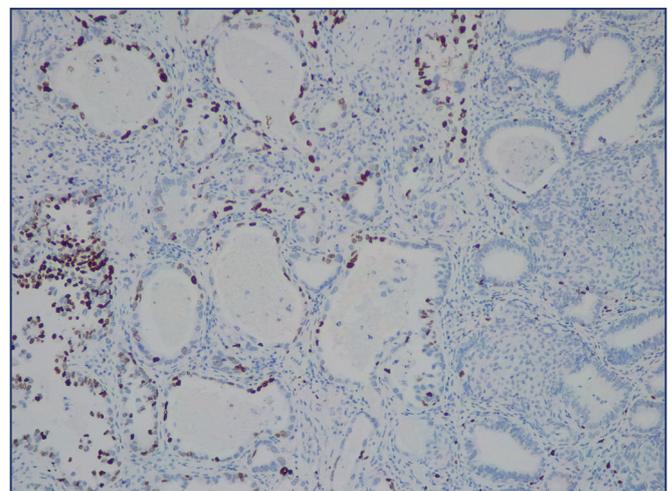


Figure 4. Ki67 high proliferative activity in SEIC (left) and low proliferative activity in APA (right) x25.

The final pathological analysis based on histological findings and immunohistochemistry was that of a SEIC, arising on the surface of APA. The polypoid lesion was located at the isthmic area without an involvement of the endocervix and without stromal invasion. All surgically removed 18 lymph nodes were with sinus histiocytosis. The specimen obtained from the omentum showed no pathological findings. The neoplastic process was staged as FIGO Stage IA. Provided that SEIC can be associated with disseminated disease outside the uterus, despite non-invasive, a consequent brachytherapy was recommended to the patient. No recurrence was observed 15 months postoperatively.

DISCUSSION

APA is a rare lesion with less than 500 cases reported in the literature, often as single cases or small series (less than 5 cases) [4]. It generally develops in women of reproductive ages with common associated infertility [3, 5]. The diagnosis of APA is essentially histological but grossly and clinically it is indistinguishable from endometrial polyp or submucosal leiomyoma [4]. The main histological feature of an APA is the presence of "irregular atypical endometrial glands" [1] and in most of the cases their distinction from an invasive endometrioid endometrial carcinoma (EEC) is a challenge for pathologists. Longacre *et al.* propose that APA with markedly complex glands (high architectural index) be designated "APA of low malignant potential" to emphasize the potential risk for myometrial invasion [2]. Few researches have tried to identify useful immunohistochemical markers for differential diagnosis, but no one has been of essential help [7, 8]. At present APA is histopathologically classified as a benign lesion [9]. In the largest systematic review of the literature that includes 296 cases of APA, reported association with concomitant EC is 11% and development of EC during follow up is 14% [4]. The most common histological type of associating adenocarcinoma is EEC [10-16]. There are only single reports of other histological subtypes of adenocarcinomas, associated with APA: clear cell carcinoma in a young woman with Cowden syndrome [17] and serous carcinoma (SC) in a postmenopausal patient [6]. We could not find any report of APA associated with SEIC. This non-invasive cancer is immediate precursor of invasive uterine SC that is the prototypical Type II EC. All the tu-

mors belonging to Type II EC differ from Type I EC in several features: they are diagnosed at older age; patients are more often multiparous and less often obese than women with EEC; there is no relation to estrogenic stimulation and most cases have p53 mutation [9]. Our patient is very young, nullipara and nulligravida - features which are inconsistent with development of serous type carcinoma.

SEIC usually develops directly on a polyp or in atrophic endometrium and even non-invasive, this carcinoma has a high tendency for extrauterine spread and omentum is the most commonly involved location. In these instances, surgical staging including omentectomy and pelvic-para-aortic lymph node dissection is required [18].

Two steps of managing patients with APA are of special importance: making of correct histological diagnosis and choosing appropriate treatment. In menopausal women, simple hysterectomy is the treatment of choice. Fertility-sparing treatment is the usual choice for the patients which are of reproductive ages and nullipara [12, 15]. It includes: hormonal therapy with or without maintenance, operative hysteroscopy (OH) which present polypectomy, transcervical resection (TCR) and biopsies, dilatation, curettage and polypectomy (DCP), and progestin-based hormonal therapy independently or combined with TCR or DCP [4, 5]. Biasioli *et al.* in their review show that relapses in cases treated with OH and with DCP are 22% and 38%, respectively [4]. Considering the relatively high rates of recurrence and association of APA with EC, it becomes obvious that the therapeutic approach to patients with APA has to be adapted to each one individual case. The association of APA with any type of concomitant EC implies radical surgery (hysterectomy and bilateral salpingo-oophorectomy). In our case, the treatment strategies were based on the aggressiveness of the concomitant carcinoma and possibility of extra-uterine spread. An attempt of fertility-sparing treatment would be a huge risk even with consequent close follow-up. The patient accepted the offered treatment, and no recurrence was observed 15 months postoperatively.

CONCLUSIONS

The precise histological diagnosis is leading in determining the treatment of patients with APA and during their follow-up. So, the close collaboration between pathologists and surgeons is essential for these patients, because their treatment and mainte-

nance are complex and delicate. When a patient is diagnosed as having APA, always an accompanying EC must be carefully searched.

COMPLIANCE WITH ETHICAL STANDARDS

Authors contribution

S.M., M.N.: Conceptualization. M.N.: Methodology. S.M., K.Y.: Formal analysis. S.M., M.N.: Investigation. S.M., K.Y.: Resources. A.Y.: Data curation. S.M., M.N.: Writing—Original & Draft preparation. A.Y.: Writing—Review & editing. M.N.: Visualization. A.Y.: Supervision.

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N/A.

Disclosure of interests

The authors declare that they have no conflict of interests.

Ethical approval

N/A.

Informed consent

The patient signed an informed consent.

Data sharing

Data are available under reasonable request to the corresponding author.

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