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Case Report

Fertility-Preserving Transcervical Complete Resection of Progestin-Treated Atypical Polypoid Adenomyoma: A Case Report

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Abstract

Atypical polypoid adenomyoma (APAM) is a rare benign uterine tumor, mostly arising in premenopausal women. Because the tumor can cause hypermenorrhea or infertility and sometimes endometrial carcinoma is detected with APAM, surgical removal is essential treatment. We experienced 26-year-old woman with APAM, which could be completely removed by trans-cervical excision after remarkable size reduction by treatment of progestin, dienogest.

Keywords: Atypical polypoid adenomyoma; Progestin therapy; Dienogest; Fertility-sparing

Introduction

Atypical polypoid adenomyoma (APAM), first reported by Mazur in 1981, is a rare benign tumor of the uterus [1]. Most patients with APAM are premenopausal and complain of abnormal uterine bleeding and/or hypermenorrhea or may be diagnosed during infertility investigations [2,3]. Histologically, APAM is characterized by a polypoid lesion composed of atypical endometrioid-type glands within a myofibromatous stroma [4], without endometrial stroma. Since recurrence after polypectomy is common and the prevalence of coexistent endometrial carcinoma is reportedly 8.8%, hysterectomy is preferable in patients who do not desire pregnancy [5]. However, standard treatments remain to be developed for patients wishing to preserve their fertility.

Progestin is an ovarian hormone with an antiproliferative effect on the endometrium and is used for the treatment of endometrial cancer [6]. In benign tumors other than those associated with endometriosis, the antitumor activity of progestin remains unclear.

We report a case of a young patient with APAM managed by transcervical complete resection (TCR) after remarkable size reduction with dienogest, a fourth-generation progestin drug.

Case Presentation

A 26-year-old woman (height, 166 cm; weight, 59.2 kg; body mass index, 21.5 kg/m2) having severe hypermenorrhea and dysmenorrhea with endometrial hypertrophy was referred to our hospital. She had a 35–40-day long menstrual cycle and no history of intercourse. She had no relevant past medical or family history. Physical examination revealed no remarkable findings. Her hemoglobin level was low (8.0 g/dL). Transrectal ultrasonography revealed a high echoic lesion in the endometrium measuring

51 × 27 mm, suspected to be an endometrial tumor, presenting diminished diffusion capacity on magnetic resonance imaging. None of the tumor markers were elevated (CA125, 23 U/L; CA19-9 23 U/L; CEA 0.9 U/L). Because vaginal examination was difficult, we collected cervical and endometrial cytology samples and performed endometrial curette biopsy under general anesthesia. Papanicolaou smears of the cervix and endometrium did not show any atypical cells. The condition was diagnosed as APAM based on the curette biopsy results. TCR was planned for fertility preservation and was preceded by progestin treatment with dienogest for suspected endometriosis-related dysmenorrhea for almost 2 months.

Since the tumor diminished remarkably in size to 40 × 15 mm with dienogest treatment (Figure 1), complete resection was achieved with TCR. The tumor was composed of estrogen receptor (ER)-positive atypical glands and smooth muscle actin-positive stromal cells (Figure 2). The dienogest treatment significantly decreased the number of epithelial cells (Figure 3). A final diagnosis of APAM was made. The patient experienced relief from hypermenorrhea and dysmenorrhea, and no tumor recurrence was reported.

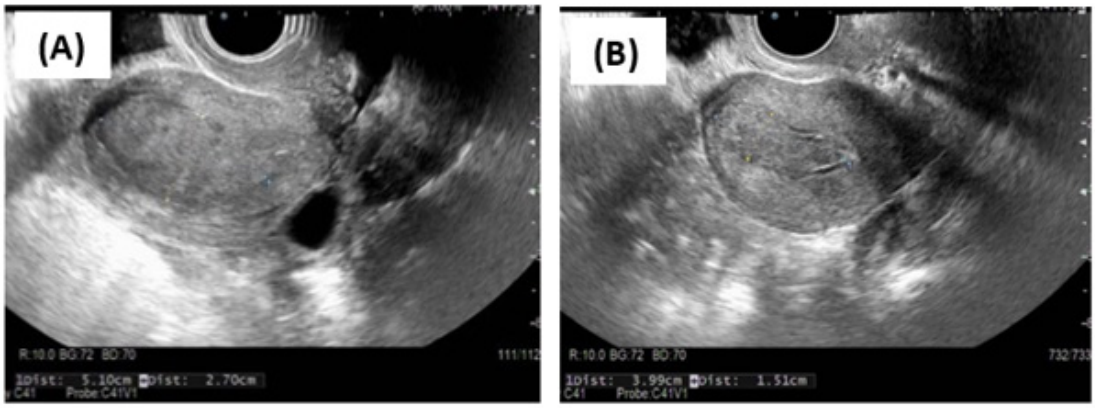

Figure 1: Transrectal ultrasonography during the first visit revealed a tumor measuring 51 x 27 mm in the uterus body (A). After almost 2 months of dienogest treatment, the size diminished to 45 x 15 mm (B).

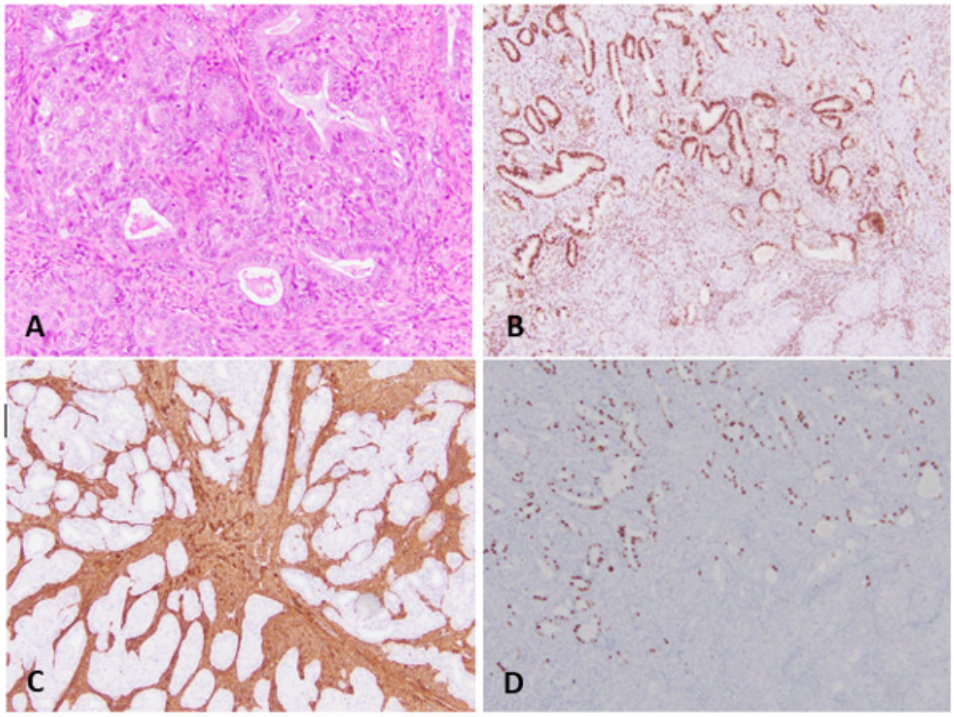

Figure 2: Proliferating atypical endometrial glands with round enlarged nuclei forming morules are seen in the stroma of the spindle-shape cells (A). The atypical glands tested positive for estrogen receptors (B). The stromal spindle cells tested positive for smooth muscle actin (C). Ki-67 positivity was 15% in the glands and less than 1% in the spindle cells (D).

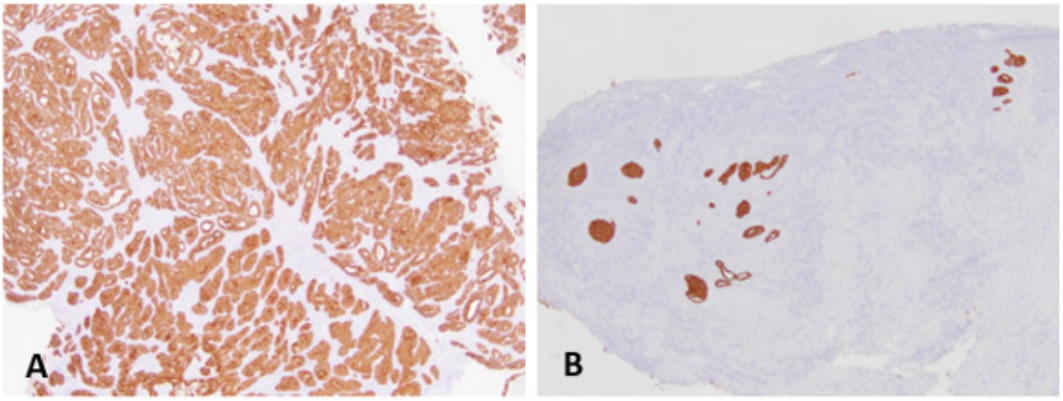

Figure 3: Dienogest treatment reduced the proportion of the glands to that of the stroma, as shown with cytokeratin AE1/AE3 immunohistochemical staining (A: pre-treatment, B: post-treatment).

Discussion

According to the World Health Organization classification, APAM is classified as a mixed epithelial and mesenchymal tumor of the uterine corpus [7]. Although Mazur, who proposed the term APAM, suggested that it could be managed conservatively in premenopausal women without the need for hysterectomy [1], success with conservative tumor management methods remains uncertain. APAM includes uterine adenofibromatous lesions with a broad range of adenomatous atypia. Longacre et al. proposed and described details of APAM of low malignant potential that have marked architectural complexity in the glands. They recur more frequently than APAM with mild gland atypia after local excision [2]. In fact, among the 29 cases managed with polypectomy or complete curettage, 13 cases showed persistence or recurrence. Moreover, he reported a case showing recurrence as many as five times after local excision. Our patient was retrospectively diagnosed with APAM with mild atypical glands.

APAM is a rare disease that mostly affects premenopausal women. TCR followed by diligent follow-up is one of the most effective strategies for tumor management. However, there is limited knowledge regarding the hormonal treatments for APAM for both post-excision maintenance and pre-operative treatment. To the best of our knowledge, this is the first case of an APAM tumor that diminished remarkably in size with pre-operative treatment using dienogest, a fourth-generation progestin. There is a previous report of recurrent APAM treated with high-dose medroxyprogesterone acetate (MPA) followed by maintenance therapy with dienogest [8]. Another study reported a case of recurrent APAM in a patient with and adjuvant progestin-releasing intrauterine device, who later delivered a baby [9]. Although it is a proof-of-concept that the usual-dose progestin can treat APAM, a benign, ER-positive, progesterone receptor-positive tumor related to unopposed estrogen [3,10], some other authors prefer high-dose MPA for maintenance. This is probably because of the risk of or coexistence of atypical endometrial hyperplasia (AEH) or endometrial carcinoma [11].

Progestins are commonly used not only for contraception or hormone replacement therapy, but also for the treatment of dysmenorrhea and endometriosis. Among the synthetic progestins, MPA is known for its antitumor effect on uterine tumors, especially malignant tumors [12,13]. High-dose MPA is typically limited to patients with malignancies such as endometrial carcinoma or AEH because of side effects, such as edema, nausea, and risk of venous thromboembolism. For benign tumors, such as uterine fibroids and APAM, there is limited evidence to determine the type and quantity of progestin to be used.

Dienogest is a fourth-generation progestin that can be used as hormonal therapy for endometriosis and exhibits long-term safety. It prevents ovulation, lowers estrogen levels, and demonstrates direct antiproliferative effect on the endometrial cells [14]. The antitumor activity of dienogest has been previously reported in tumor cell lines and in a patient with adenosarcoma [15]. In Japan, dienogest is currently approved for the treatment of endometriosis-associated pain. In our case, 1 mg of dienogest was administered twice a day orally and could be continued without any side effects, except for slight atypical genital bleeding. The tumor showed a significant reduction in size in this case.

Conclusion

In conclusion, we encountered a young patient with an APAM tumor that significantly diminished in size with dienogest treatment before complete TCR. Since APAM is a rare tumor presenting mostly in premenopausal women, worldwide clinical outcomes of the combination treatment of dienogest and TCR for pregnancy-preserving management of APAM are awaited. A precise management strategy is necessary for APAM patients, as they are at a high risk of endometrial carcinoma.

Acknowledgement

None.

Conflict of Interest

The authors declare no competing interests.

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