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Case report

Endometrial carcinoma in a 14-year-old: A case report

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1. Introduction

Endometrial carcinoma (EC) has been increasing in Japan. Various reasons have been offered for this change, including late marriage accompanying women's social advancement, more women who forego having children, and increased obesity and diabetes due to Westernization of diet (Sugawara et al., 2018). EC accounts for more than half of gynecological malignancies among women in their 50s and 60s but has shown an increase in occurrence in women of reproductive age, among whom its incidence rate is about 5%–25% (Crissman et al., 1981; Gallup and Stock, 1984; Kaku et al., 1993). In the report of the Gynecologic Malignancy Committee of the Japanese Association of Obstetrics and Gynecology, EC among reproductive-age women roughly tripled, from 161 cases (5.8%) in 1999 to 507 cases (4.5%) in 2016. Standard treatment of low-risk EC (such as grade 1–2 endometrioid adenocarcinoma and cancer limited to endometrium) is surgical staging with total hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node evaluation. The 5-year survival rate of low risk EC is 90% or more, which is a very good prognosis. However, for reproductive-aged women who wish to preserve fertility, fertility-sparing therapy is needed. Progestin therapy is a common approach for low-risk EC in women who wish to preserve fertility (Ushijima et al., 2007; Qin et al., 2016).

Here, we present a case of juvenile EC in a 14-year-old girl, who was successfully treated with medroxyprogesterone acetate (MPA).

2. Case presentation

This patient was a 14-year-old girl. She was not sexually active. Her menarche occurred at the age of 10 and her menstrual cycle was regular. She was 153 cm tall, and weighed 52.3 kg (body mass index: 22.3). Her family had no known history of EC. Because of abnormal uterine bleeding, she visited a nearby gynecological clinic. As abdominal ultrasonography showed highly thickened endometrium, she was directed to a larger hospital for review and treatment. At the time of consultation, she was found to be severely anemic (Hemoglobin: 7.7 g/dL) because of sustained vaginal bleeding, and was admitted to the hospital for examination and treatment. Pelvic magnetic resonance imaging (MRI) confirmed a thickened endometrium; lesions were not observed in the muscle layer, but a solid portion with a contrast effect was found in the thickened endometrium. The diffusion-weighted image showed a high signal and decreased apparent diffusion coefficient (ADC), so endometrial hyperplasia and partial malignancy were diagnosed (Fig. 1). She underwent a diagnostic endometrial curettage under anesthesia. Pathology of the endometrium showed atypical hyperplasia in most of the tissues, but some of them exhibited a back-to-back structure with high linear density and very narrow interstitium. It was diagnosed as endometrial adenocarcinoma, Grade 1 (Fig. 2). Immunostaining status of mismatch repair proteins (MLH1, PMS2, MSH6 and MSH2) did not indicate germline mutations. No accumulation suggestive of distant metastasis or lymph node metastasis was observed in positron emission tomography-computed tomography (PET-CT). Based on the above findings, she was diagnosed with endometrioid adenocarcinoma Grade 1, International Federation of Gynecology and Obstetrics (FIGO) stage

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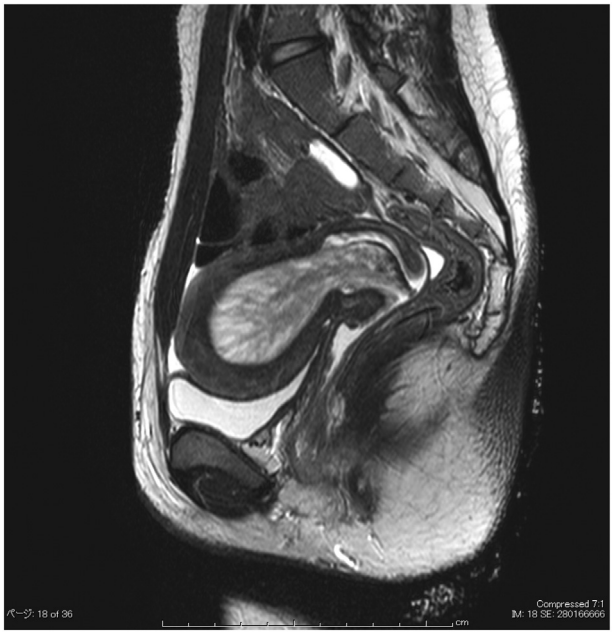

Fig. 1. Pelvic MRI(T2-weighted sagittal image) shows that myometrial invasion did not occur in the uterus.

IA, cT1aN0M0, and brought to our department for further treatment. The recommended treatment for early EC is total hysterectomy and bilateral salpingo-oophorectomy, but as this patient was 14 years old, hormone therapy for fertility preservation was chosen. Her and her parents' informed consent included the possibility that she would require a hysterectomy if preservative treatment were not successful, and she started hormonal therapy with MPA. For treatment, MPA (Hysron-H Tab, 600 mg/ day) was administered daily for 26 weeks. Over this time, she also underwent dilation and curettage three times during hormone therapy (at 7, 15 and 26 weeks after starting treatment). Histology from an endometrial scratch biopsy at 7 weeks after starting treatment revealed an atypical endometrial hyperplasia, so the MPA was judged to have therapeutic effect. The result of the tissue examination after 15 weeks was benign endometrium. Finally, a hysteroscopy performed at the end of the MPA course confirmed that no obvious proliferative lesion was found in the uterus (Fig. 3). The patient developed pelvic inflammatory disease after curettage at 7 weeks after starting treatment and was prescribed antibiotic treatment. After confirming the disappearance of disease, she was prescribed low-dose estrogen-progestin, and periodically underwent estimation of the endometrium with abdominal ultrasonography. As an office endometrial biopsy was difficult for her, endometrial curettage was performed under anesthesia every 4 months.

Currently, at 47 weeks after the end of MPA therapy, pathological examination and CT imaging have not shown any disease recurrence.

3. Discussion

Although most cases of EC occur after menopause, it has been reported in women of reproductive age, with 4% of cases occurring in women aged 40 years or younger (Lee et al., 2007). Here, we report an extremely rare case of a juvenile woman with EC, despite having no risk factors such as obesity or family history. However, despite the absence of a positive family history, hereditary factors must be considered in the face of development of EC in such a young woman. We therefore performed immunohistochemical analysis of mismatch repair protein, this being the optimal means of screening for Lynch syndrome, the false negative rate being 5%–10% in individuals with colorectal carcinoma (Hampel et al., 2005; Shia, 2008). Normal staining of mismatch repair protein was found in our patients; however, this does not entirely exclude Lynch syndrome. Because the patient and her family opted for no further evaluation of germline mutations associated with Lynch syndrome, we did not perform germline testing on her.

Although the most common cause of abnormal uterine bleeding in young adolescents is anovulatory bleeding associated with an immature hypothalamic–pituitary–ovarian axis, severe anovulatory uterine bleeding combined with a low hemoglobin concentration (< 10 g/dL) suggests a diagnosis of a coagulopathy or other serious problems (including hepatic failure) and, rarely, malignancy. (ACOG Committee Opinion, 2015) Our patient had continuous uterine bleeding and a low hemoglobin concentration of 7.7 g/dL with normal hemostatic function. We consider that the finding of heavy thickened endometrium by abdominal ultrasonography and MRI in young adolescents with such symptoms justifies investigation of the possibility of malignant disease by performing endometrial curettage under anesthesia.

The standard treatment for early-stage EC is total hysterectomy and bilateral salpingo-oophorectomy with pelvic lymph node evaluation. However, for young women who desire fertility preservation, progestin therapy is an acceptable treatment option. A meta-analysis has reported that the rate of remissions by progestin therapy is 82.4% (Qin et al., 2016). In Japan, MPA is the only available oral form of progestin. It has latent side effects, such as thrombus formation, dysthymia, headache, weight gain, chest pain and the like. We treated this patient with MPA at a dose of 600 mg/day, and aspirin at 100 mg/day to prevent thrombus formation. Progestin-releasing IUD is another option for progestin therapy in worldwide and, along with oral progestin agents, they are associated with an overall complete remission (CR) rate of 87.5% (Kim et al., 2013). Progestin-releasing IUDs combined with oral progestin is expected both to improve the CR rate, and to provide strong therapeutic choice for patients who do not desire immediately to conceive a pregnancy. In particular, in very young patients who need long-term treatment to avoid recurrence, progestin-releasing IUD is an adequate maintenance treatment with low risk of adverse effects. In Japan, progestin-releasing IUD (levonorgestrel IUD) can be used for women who complain of hypermenorrhea or dysmenorrhea. We hope that a progestin-releasing IUD is immediately approved as continuing therapy in Japan for young EC patients who receive fertility-sparing therapy and achieve CR. The KGOG study group demonstrated that, after achieving CR, the recurrence rate is 30.4% for patients with stage IA, grade 1 EC (Park et al., 2013). Women who have achieved CR are recommended to receive long-term follow-up by endometrial evaluation and imaging, such as MRI or CT. In this case, the patient is a virgin, for whom office endometrial biopsies are difficult. Therefore, she receives endometrial curettage under anesthesia every 4 months. Frequent endometrial curettage carries a risk of inducing endometrial adhesion and consequent infertility. We intend to perform minimum endometrial curettages after confirming the absence of EC recurrence after one year.

4. Conclusion

We present a case of juvenile patient with EC who desired fertility preservation. She was treated by progestin therapy for 26 weeks and achieve CR. Although juvenile EC is extremely rare, it should be considered among juveniles with sustained abnormal uterine bleeding, even if they have no risk factors. Furthermore, fertility preservation in juvenile patients (who presumably do not want to become pregnant for many years) requires a longer time frame than for older patients; during this time, maintenance treatments that avoid EC recurrence with low adverse effects are needed after achieving CR of disease.

Ethics approval and consent to participate and consent for publication

Written informed consent was obtained from the patient and

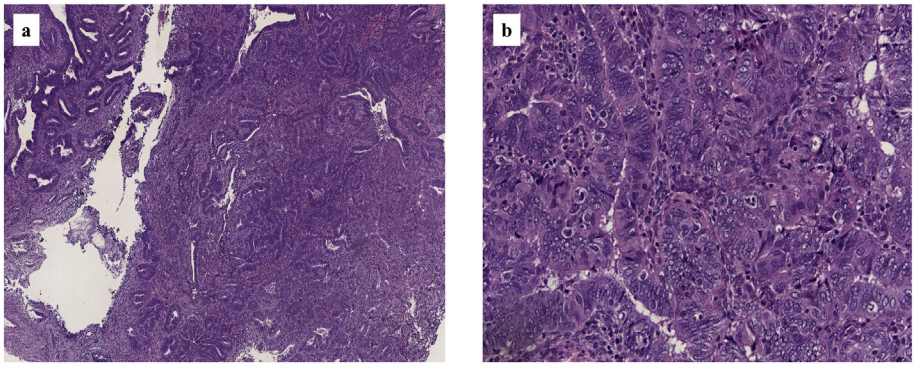

Fig. 2. Histological findings of endometrial specimen. (a) Tumor cells show atypical hyperplasia. (hematoxylin and eosin, ×40). (b) Cellular and structural atypia in an endometrioid adenocarcinoma, grade 1 (hematoxylin and eosin, ×200).

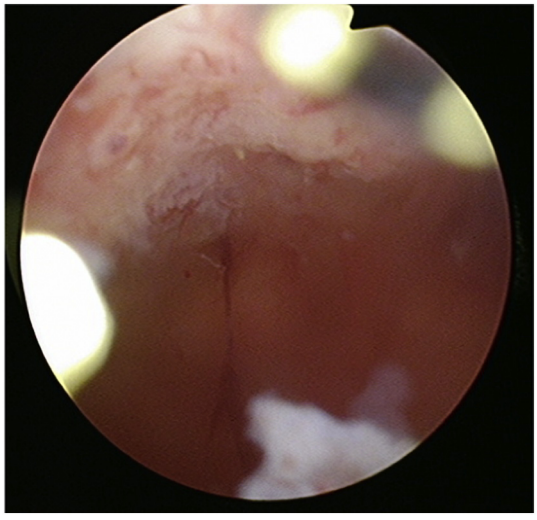

Fig. 3. Hysteroscopy found no obvious proliferative lesion in the patient's uterus.

parents, and this case report was approved by the Institutional Review Board of Hyogo Cancer Center according to the ethical standards laid down in the Declaration of Helsinki.

Conflict of interests

The authors declare no conflicts of interest.

Author contribution

HU and MK wrote the main manuscript body. HU, MK and AK were in charge of the presented patient and treated her endometrial cancer with conservative management. AK and TS were responsible for evaluation in pathology. SN and SY read the article and gave the first author suggestions to improve the manuscript.

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References

ACOG Committee Opinion No.651, 2015. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Obstet. Gynecol. 126, e143.
Crissman, J.D., Azoury, R.S., Barnes, A.E., et al., 1981. Endometrial carcinoma in women 40 years of age or younger. Obstet. Gynecol. 57, 699–704.
Gallup, D.G., Stock, R.J., 1984. Adenocarcinoma of the endometrium in women 40 years of age or younger. Obstet. Gynecol. 64, 417–420.
Hampel, H., Frankel, W.L., Martin, E., et al., 2005. Screening for the lynch syndrome (hereditary nonpolyposis colorectal cancer). N. Engl. J. Med. 352, 1851–1860.
Kaku, T., Matsuo, K., Tsukamoto, N., et al., 1993. Endometrial carcinoma in women aged 40 years or younger: a Japanese experience. Int. J. Gynecol. Cancer 3, 147–153.
Kim, M.K., Seong, S.J., Kim, Y.S., et al., 2013. Combined medroxyprogesterone acetate/levonorgestrel-intrauterine system treatment in young women with early-stage endometrial cancer. Am. J. Obstet. Gynecol. 209 (358.e1-4).
Lee, N.K., Cheung, M.K., Shin, J.Y., et al., 2007. Prognostic factors for uterine cancer in reproductive-aged women. Obstet. Gynecol. 109 (3), 655.
Park, J.Y., Kim, D.Y., Kim, J.H., et al., 2013. Long-term oncologic outcomes after fertility-sparing management using oral progestin for young women with endometrial cancer (KGOG 2002). Eur. J. Cancer 49, 868–874.
Qin, Y., Yu, Z., Yang, J., et al., 2016. Oral progestin treatment for early-stage endometrial cancer: a systematic review and meta-analysis. Int. J. Gynecol. Cancer 26, 1081–1091.
Shia, J., 2008. Immunohistochemistry versus microsatellite instability testing for screening colorectal cancer patients at risk for hereditary nonpolyposis colorectal cancer syndrome. Part I. The utility of immunohistochemistry. J. Mol. Diagn. 10, 293–300.
Sugawara, Y., Sugiyama, K., Tomata, Y., et al., 2018. Age at first birth and the risk of endometrial cancer incidence: a pooled analysis of two prospective cohort studies among Japanese women. J. Cancer 9 (23), 4422–4429.
Ushijima, K., Yahata, H., Yoshikawa, H., et al., 2007. Multicenter phase II study of fertility-sparing treatment with medroxyprogesterone acetate for endometrial carcinoma and atypical hyperplasia in young women. J. Clin. Oncol. 25, 2798–2803.