Recurrent Endometrial Intraepithelial Neoplasia in a Patient Desiring Fertility: The Importance of Surveillance and Fertility-Sparing Management

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INTRODUCTION

Endometrial Hyperplasia results from excessive proliferation of endometrial glands, most commonly due to prolonged unopposed estrogen exposure. In addition to increasing the risk of endometrial cancer, abnormal endometrial proliferation may impair endometrial receptivity and fertility. This case highlights the combined impact of PCOS, obesity, and a CHEK2 mutation as hormonal, metabolic, and genetic risk factors for endometrial pathology.

PCOS causes chronic anovulation and unopposed estrogen exposure, while obesity (BMI > 40 kg/m^2) increases peripheral estrogen production in adipose tissue. CHEK2 mutations have also been associated with increased endometrial cancer risk, creating a potentially high-risk environment for recurrence and progression.

For patients desiring fertility preservation, progestin therapy provides a conservative treatment option. However, ACOG recommends endometrial biopsy every 3 months until two consecutive negative biopsies are obtained. Inadequate surveillance or loss to follow-up may increase the risk of recurrence, malignancy, and further compromise fertility.

OBJECTIVE

- To highlight the development and recurrence risk of endometrial hyperplasia in patients with multiple compounding risk factors.
- To emphasize the importance of fertility-preserving management when clinically appropriate.
- To emphasize the importance of continued surveillance and preventative care in the long-term management of endometrial hyperplasia.
- To emphasize the role of consistent follow-up, risk-factor recognition, and patient-centered care in reducing recurrence and preventing long-term complications.

CASE PRESENTATION

37-year-old nulliparous female, BMI 47.55 kg/m^2

PMH: PCOS

2017: CHEK2 mutation identified.

2021: Presented with menorrhagia. Transvaginal ultrasound revealed 12-mm endometrial thickening, biopsy demonstrated complex endometrial hyperplasia. Given her desire for future fertility, she underwent hysteroscopy and two rounds medroxyprogesterone therapy, with subsequent biopsy showing a normal endometrial lining. She was referred to REI for fertility treatment.

Following unsuccessful fertility treatment, the patient was lost to follow-up, with no documented surveillance of her endometrial lining after October 2021.

2026: Returned with severe menorrhagia and ongoing concerns regarding fertility. Hemoglobin was 8.6 g/dL, despite a recent transfusion. Transvaginal ultrasound demonstrated marked progression of endometrial thickening to 23-mm.

Repeat biopsy revealed complex endometrial hyperplasia with atypia/endometrial intraepithelial neoplasia (EIN), representing recurrence and progression of her prior hyperplasia.

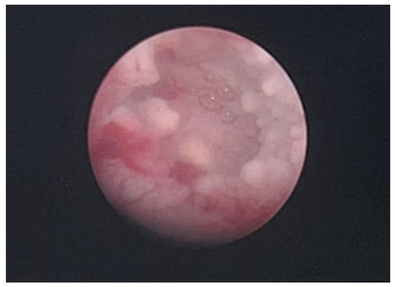

Fig 1. Polypoid endometrial tissue

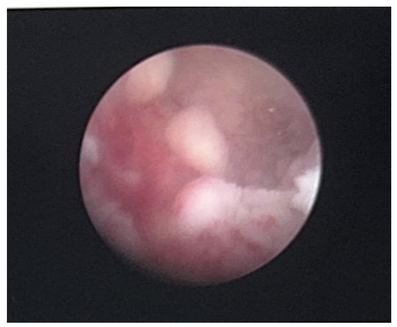

Fig 2. Polypoid endometrial tissue

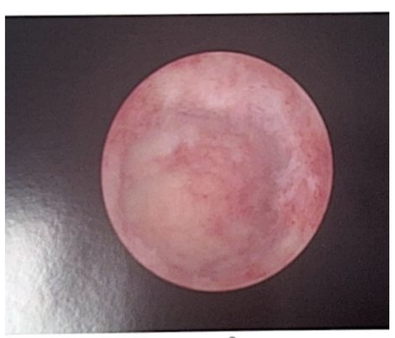

Fig 3. Post-polypectomy and curettage removal of abnormal tissue

INTERVENTION

- A fertility-preserving multidisciplinary approach was pursued while addressing the risk of progression to malignancy.
- AMH testing to assess ovarian reserve, followed by hysteroscopy with endometrial sampling to evaluate for malignancy and remove abnormal tissue.
- A levonorgestrel-releasing IUD was placed for conservative treatment of EIN and suppression of endometrial proliferation, with REI referral.
- Treatment was guided by the patient's goals, CHEK2 mutation, and family history. She agreed to three potential management pathways based on hysteroscopic findings and ovarian reserve:
  - **If malignancy is identified:** Referral to gynecologic oncology for definitive surgical management.
  - **If no malignancy is identified and low AMH:** Consideration of hysterectomy and alternative family-planning options.
  - **If no malignancy is identified and adequate AMH:** Continued conservative management with IUD and fertility treatment through REI.

RESULTS

- AMH: 2.4, indicating possible preserved ovarian reserve and potential for future fertility treatment.
- Hysteroscopic polypectomy and curettage revealed diffuse polypoid endometrial tissue; the uterus sounded to 9-cm (Figures 1 and 2).
- Post-resection hysteroscopy demonstrated a smooth, uniform endometrial cavity without residual visible lesions (Figure 3).
- Pathology: Complex adenomatous hyperplasia with partial endometrial polyp involvement, without evidence of malignancy.
- Absence of malignancy allowed for continued conservative management and preservation of future fertility options.
- Patient elected to defer REI consultation for approximately 6 months with continued OB/GYN surveillance and repeat endometrial assessments to monitor treatment response and reduce the risk of recurrence or progression.

DISCUSSION

This case demonstrates that regression of EIN/endometrial hyperplasia does not eliminate recurrence risk, especially when underlying risk factors persist. Long-term surveillance with endometrial assessment every 3-6 months until two consecutive negative biopsies is essential.

Fertility preservation requires balancing definitive treatment with reproductive goals. Although AMH suggested preserved ovarian reserve, PCOS and chronic anovulation may impair reproductive function independently.

Effective management should combine continued endometrial surveillance, fertility-sparing therapy, and modification of underlying risk factors, including obesity and chronic anovulation, to reduce recurrence and malignant progression while supporting fertility goals.

American College of Obstetricians and Gynecologists. (2023). *Management of endometrial intraepithelial neoplasia or atypical endometrial hyperplasia*. https://www.acog.org/clinical/clinical-guidance/clinical-consensus/articles/2023/09/management-of-endometrial-intraepithelial-neoplasia-or-atypical-endometrial-hyperplasia; An, H., Li, T., Huang, K., Shi, H., Wang, C., Chu, T., & Zhai, J. (2024). Pregnancy outcomes in infertile patients with endometrial hyperplasia with or without atypia undergoing in vitro fertilization: The early-follicular long protocol is superior to midluteal long protocol. *Frontiers in Endocrinology, 15*, 1314432. https://doi.org/10.3389/fendo.2024.1314432; Butt, M. S., Saleem, J., Aiman, S., Zakar, R., Sadique, I., & Fischer, F. (2022). Serum anti-Müllerian hormone as a predictor of polycystic ovarian syndrome among women of reproductive age. *BMC Women's Health, 22*(1), 199. https://doi.org/10.1186/s12905-022-01782-2; Fernandez-Montoli, M. E., Sabadell, J., Contreras Perez, N. A., Verdaguer Menéndez-Arango, P., Julia Torres, C., & Lleberia, J. (2025). Fertility-sparing treatment for atypical endometrial hyperplasia and endometrial cancer. *Cochrane Database of Systematic Reviews, 7*(7), CD013111. https://doi.org/10.1002/14651858.CD013111.pub2; Işçi Bostanci, E., Durmuş, Y., Duru Çöteli, A. S., Kayikçioğlu, F., & Boran, N. (2021). Outcomes of the conservative management of the patients with endometrial intraepithelial neoplasia/endometrial cancer: Wait or treat! *Turkish Journal of Medical Sciences, 51*(4), 2066–2072. https://doi.org/10.3906/sag-2012-207; Lin, C., Jing, M., Zhu, W., Tu, X., Chen, Q., Wang, X., Zheng, Y., & Zhang, R. (2021). The value of anti-Müllerian hormone in the prediction of spontaneous pregnancy: A systematic review and meta-analysis. *Frontiers in Endocrinology, 12*, 695157. https://doi.org/10.3389/fendo.2021.695157; Meczekalski, B., Rasi, M., Battipaglia, C., Fidecicchi, T., Bala, G., Szeliga, A., Luisi, S., & Genazzani, A. (2025). PCOS and obesity: Contraception challenges. *Open Access Journal of Contraception, 16*, 43–58. https://doi.org/10.2147/OAJC.S501434; Ørbo, A., Arnes, M., Vereide, A. B., & Straume, B. (2016). Relapse risk of endometrial hyperplasia after treatment with the levonorgestrel-impregnated intrauterine system or oral progestogens. *BJOG: An International Journal of Obstetrics & Gynaecology, 123*(9), 1512–1519. https://doi.org/10.1111/1471-0528.13763; Wise, M. R., Jordan, V., Lagas, A., Showell, M., Wong, N., Lensen, S., & Farquhar, C. M. (2016). Obesity and endometrial hyperplasia and cancer in premenopausal women: A systematic review. *American Journal of Obstetrics and Gynecology, 214*(6), 689.e1–689.e17. https://doi.org/10.1016/j.ajog.2016.01.175; Xue, Z., Li, J., Feng, J., Han, H., Zhao, J., Zhang, J., Han, Y., Wu, X., & Zhang, Y. (2021). Research progress on the mechanism between polycystic ovary syndrome and abnormal endometrium. *Frontiers in Physiology, 12*, 788772. https://doi.org/10.3389/fphys.2021.788772