Adenomyosis: Is It A Confounder Or An Innocent Companion In Patients With Endometrial Hyperplasia?

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Abstract

Purpose: To evaluate the effect of adenomyosis on the discordance of pathologic findings in patients with endometrial hyperplasia (EH) before hysterectomy.

Methods: Two hundred seventeen patients who were diagnosed as having EH via endometrial sampling and underwent hysterectomy within 3 months were included in this retrospective study. The patients' preoperative and postoperative pathologic findings were compared and discordant results were defined as overdiagnosed and underdiagnosed.

Results: The rate of concurrent endometrial carcinoma (EC) among all EH was 22.11%, whereas this rate was 41.4% in EH with atypia. There was no difference between EH subtypes in terms of demographic characteristics and coexisting myometrial lesions. The discordance between preoperative endometrial sampling and final hysterectomy specimen results was evaluated, and patients with underdiagnosis were older (60.5 years, $p<0.001$), had a higher BMI (30.84 kg/m^2, $p<0.001$), were mostly postmenopausal ($p<0.001$), had lower parity numbers (median=2, $p=0.002$), and had a lower rate of co-existing adenomyosis ($p=0.009$). The rates of co-existing leiomyomas between the groups were not different. No effect of other demographic characteristics was observed in the multivariate regression analysis; however, the presence of adenomyosis was a significant independent risk factor affecting a 5.8-fold increase in overdiagnosis (-1.50; OR: 0.17 (0.05-0.50) $p=0.002$) and 4.5-fold increase in underdiagnosis (-1.50; $p=0.005$).

Conclusion: Co-existing adenomyosis could lead to discordance of the pathologic findings in women with EH diagnoses before hysterectomy.

Introduction

Endometrial hyperplasia (EH) is an abnormal proliferation of endometrial glands and stroma [1]. In 1994, the World Health Organization (WHO) divided EH into four groups according to cytologic nuclear atypia and glandular complexity: simple hyperplasia without atypia, complex hyperplasia without atypia, simple hyperplasia with atypia, complex hyperplasia with atypia [2]. In 2014, the WHO revised EH classification into two groups based on only nuclear atypia: non-atypical EHs (NAEH) are defined as benign, and atypical EHs (AEH), which are similar to endometrial intraepithelial neoplasia (EIN), are considered as precursors of endometrial cancer (EC) [3]. The clinical significance of atypical hyperplasia, in particular, is that these patients have an up to 40% probability of having concomitant EC detected in the final pathologic examination of hysterectomy specimens [4, 5].

It may not be easy to distinguish EC precursor AEH from well-differentiated EC[6]. Therefore, studies have focused on identifying patients with concurrent EC and evaluating factors that contribute to the discrepancy between endometrial sampling results and final pathologic findings of hysterectomy specimens. The most studied subject has been the effect of different endometrial sampling methods.

The effect of patient-related factors such as age, body mass index (BMI), chronic diseases, and nulliparity on the coexistence of EC with AEH has also been evaluated [7–9].

Adenomyosis and leiomyoma, which are benign myometrial lesions, are frequently found in pathologic specimens of hysterectomies performed with benign indications at rates of 20–30% and 40–60%, respectively [10–11]. High rates of coexistence of these benign myometrial lesions with EC have also been reported (adenomyosis 18.9–22.6%; leiomyoma 27%) [12–14].

Therefore, in this study, we aimed to evaluate the effect of myometrial lesions such as adenomyosis and leiomyoma on the discordance of pathologic findings in patients who were diagnosed as having EH before undergoing hysterectomy.

Material And Methods

This retrospective observational study was performed in a university-affiliated hospital in Turkey. Institutional review board approval was obtained. The study complied with the principles of the Declaration of Helsinki. All patients signed informed consent forms before undergoing surgery, allowing their medical records to be used for research purposes.

Patients who were diagnosed as having EH through endometrial sampling and underwent hysterectomy within 3 months after this diagnosis between May 2016 and May 2021 were reviewed. The medical records of 217 patients were evaluated.

Endometrial sampling was performed under local anesthesia using an Endosampler® device. Patients who underwent dilatation and curettage (D&C) for endometrial pathologic evaluation under general anesthesia, and those in the postmenopausal period who underwent pipelle aspiration biopsy were excluded from the study. Endometrial sampling and hysterectomy specimens of patients were reviewed by gynecologic pathologists in our institution. Women with NAEH (simple and complex) and AEH (simple and complex) according to their endometrial sampling and who underwent hysterectomy as first-line treatment were included. Patients whose pathology specimens were evaluated in another center, who received progestin treatment before hysterectomy, using tamoxifen or hormone replacement therapy, and those whose duration between EH diagnosis and hysterectomy was longer than 3 months were excluded.

The presence of myometrial lesion was concluded according to preoperative ultrasonography reports and pathologic examination results after hysterectomy. Final hysterectomy pathology results reported as ‘no residual disease,’ ‘secretory endometrium,’ and ‘proliferative endometrium’ were considered normal.

The patients were evaluated in three groups according to the consistency of endometrial sampling and final hysterectomy pathology results: overdiagnosis, underdiagnosis, and concordance. Among patients with preoperative diagnoses of NAEH (n = 106), those with normal final pathologic findings were defined as overdiagnosis, those with AEH and EC in final pathologic examinations were defined as underdiagnosis, and patients with NAEH in the final examination were defined as concordance. Among

patients with preoperative diagnoses of AEH (n = 111), those who were normal and had NAEH in the final pathologic examination were defined as overdiagnosis, those with EC in the final pathological examination were defined as underdiagnosis, and patients with AEH in the final examination were defined as concordance. Patients with EC were staged according to the revised 2009 International Federation of Gynecology and Obstetrics (FIGO) staging system [15].

The SPSS version 20.0 software package (SPSS Inc., Chicago, IL, USA) was used for the data storage and statistical analysis. The Shapiro-Wilk test was used for detecting the distribution pattern of variables. The Kruskal-Wallis and Chi-square tests were used for comparing continuous and categorical variables among groups. Multivariate logistic regression was performed to detect the independent effects of variables on discordant results. P-values of < 0.05 were considered statistically significant.

Results

A total of 217 patients who were diagnosed as having EH before undergoing hysterectomy and met the inclusion criteria were retrospectively evaluated regarding their hysterectomy histopathology results.

The histologic results of endometrial samples were 40.55% simple NAEH, 8.29% complex NEAH, 10.01% simple AEH, and 41.01% complex AEH. The final pathologic results from the hysterectomy specimens were 36.4% normal, 16.1% simple NAEH, 4.6% complex NAEH, 4.6% simple AEH, 16.1% complex AEH, and 22.11% EC (Table 1).

Table 1
Endometrial Sampling and Final Hysterectomy Histopathology Results.

Final Hysterectomy findings								
		Normal	NAEH		AEH		EC	Total
Endometrial Sampling Results			Simple	Complex	Simple	Complex		
NAEH	Simple	53	25	2	3	3	2	88 (40.55)
	Complex	6	5	3	-	4	-	18 (8.29)
AEH	Simple	10	2	-	2	3	6 (22)*	22 (10.01)
	Complex	10	3	5	5	25	42 (46.06)+	89 (41.01)
Total		79 (36.4)	35 (16.10)	10 (4.60)	10 (4.60)	35 (16.10)	48 (22.11)	217

NAEH: Non-atypical endometrial hyperplasia, AEH: atypical endometrial hyperplasia. Values are given n (%).

*One was carcinosarcoma + One was adenosquamous carcinoma

According to the endometrial sampling results, among the four EH groups, the patients in the complex AEH group had a higher BMI than others, and the patients in the simple NAEH group had a higher rate of co-existing leiomyoma than the others. There was no difference between the groups in terms of other demographic data (Table 2).

Table 2. Demographic Characteristics of the Groups According to the Endometrial Sampling Results

	Simple NAEH n=88	Complex NAEH n=18	Simple AEH n=22	Complex AEH n=89	p
Age (years)	52 (40-84)	49.5 (41-70)	51.5 (41-79)	54 (36-77)	0.433
BMI (kg/m^2)	27.3 (21.80-35.16)	28.99 (22.5-33.98)	27.1 (22.06-34.61)	30.11 (21.56-39.11)	<0.001
Parity	3 (0-10)	3 (1-5)	3 (1-7)	3 (0-7)	0.724
Menopause status, n (%)					
Premenopausal (n=88)	39 (44.3)	9 (10.2)	10 (11.4)	30 (34.1)	0.367*
Postmenopausal (n=129)	49 (38.3)	9 (7%)	12 (9.3)	59 (45.7)	
Myometrial lesions, n (%)					
Adenomyosis (n=64)	27 (42.2)	6 (9.4)	6 (9.4)	25 (39.1)	0.951*
Leiomyoma (n=98)	46 (46.9)	10 (10.2)	16 (16.3)	26 (26.5)	<0.001*

BMI: Body Mass Index, NAEH: Non-atypical endometrial hyperplasia, AEH: atypical endometrial hyperplasia.

Values are given as median (range) unless stated. P<0.05 was significant.

*Chi-square test was used.

The overall diagnostic concordance between the endometrial sampling results and the final hysterectomy pathologic findings was 41.47%; 22.11% of patients were underdiagnosed and 36.40% were overdiagnosed.

Those with underdiagnoses had significantly higher BMI (30.84 kg/m^2, $p < 0.001$), were older (60.5 years, $p < 0.001$), postmenopausal ($p < 0.001$), and their median parity number was significantly lower (median = 2, $p = 0.002$). Co-existing adenomyosis was significantly less frequent in the underdiagnosis group ($p = 0.009$). There was no difference between groups in terms of co-existing leiomyoma rates (Table 3).

Table 3. Comparison of groups according to endometrial sampling and final hysterectomy pathological results compatibility.

	Overdiagnosis (n=79)	Underdiagnosis (n=48)	Concordance (n=90)	p
Age (years)	51 (38-72)	60.5 (37-79)*	52 (36-84)	0.001
BMI (kg/m^2)	27.58 (21.80-35.16)	30.84 (21.56-38.04)*	28.12 (21.90-39.11)	<0.001
Parity	3 (0-10)	2 (0-6)*	3 (1-7)	0.002
Menopause status[a]				
Pre- (n=88)	41 (46.6)	9 (10.2)*	38 (43.2)	0.001
Post- (n=129)	38 (29.5)	39 (30.2)*	52 (40.3)	
EH diagnosis to surgery interval (days)	45 (16-82)	38 (18-84)	41.5 (20-88)	0.321
Adenomyosis[a]				
Yes (n=64)	28 (43.8)	6 (9.4)*	30 (46.9)	0.009
No (n=153)	51 (33.3)	42 (27.5)*	60 (39.2)	
Leiomyoma[a]				
Yes (n=98)	42 (42.9)	17 (17,.3)	39 (39.8)	0.142
No (n=119)	37 (31.1)	31 (26.1)	51 (42.9)	

BMI: Body mass index EH: endometrial hyperplasia. Values are given as median (range); the Kruskal-Wallis test was used unless stated.

*The group that differs from others.

[a] chi- square test was used. values are given n(%).

The rate of co-existing adenomyosis was 29.49% among all EH cases, and the rate of co-existing adenomyosis was 13% in patients with a preoperative diagnosis of AEH and a final pathologic diagnosis of EC. In multivariate logistic regression analysis, no significant independent effects of age, BMI, parity, menopausal status, and presence of fibroids on discordant results were observed. The presence of adenomyosis was found to be a significant independent risk factor in obtaining discordant pathologic results. Overdiagnosis was found to be 5.8 times more likely in the presence of adenomyosis, regardless of age (B= -1.76; OR: 0.17 (0.05–0.50) p = 0.002). The presence of adenomyosis was also found to increase the probability of underdiagnosis by 4.5 times (B= -1.50; OR: 0.22 (0.07–0.63), p = 0.005).

Discussion

To the best of our knowledge, the current study is the first to report the effect of myometrial lesions such as adenomyosis and leiomyoma on the discordance of pathologic findings in patients who were diagnosed as having EH before undergoing hysterectomy. We retrospectively evaluated patients who underwent hysterectomy and their pre-post operative endometrial pathology results. We calculated the discordance rate of these results as 58.52%; 22.11% of patients were underdiagnosed and 36.40% were overdiagnosed. Patients who were classified as underdiagnosed were found to be older and had higher BMI than the others. It was also concluded that discordance rates were higher in patients with adenomyosis.

Adenomyosis is described as the presence of the endometrial glands and stroma within the myometrium. Microscopically, adenomyosis consists of non-neoplastic ectopic endometrial stroma and glands surrounded by hypertophic and hyperplastic myometrium [16]. Although traditionally the diagnosis is made through histopathologic examination, preoperative diagnosis can be made using transvaginal ultrasonography (TVUSG) or magnetic resonance imaging (MRI) due to the developments in imaging techniques [17]. Adenomyosis is found incidentally in 20–25% of benign hysterectomy specimens [18]. The relation between the diagnosis of EH and adenomyosis cannot be demonstrated with the available data. Existing literature focused on EC developing in the presence of adenomyosis. Although the results of studies related to adenomyosis co-existence with EC are contradictory, a 22.6% pooled prevalence of adenomyosis in EC has been reported in recent studies and it has been shown that this rate is not different from co-existence in benign conditions [13]. In our data, the co-existence rate of adenomyosis and EC was 12.5% (6 of 48). Although the underlying disorder is hyperestrogenism, the known etiologic factors of EC and adenomyosis are polar opposites. Multiparity and oral contraceptive use are associated with increased risk of adenomyosis, and these are also associated with a reduced risk of EC [14]. This could suggest that the coexistence of these two pathologies may be related to a high incidence of adenomyosis in peri and postmenopausal patients, rather than a common etiologic cause or direct cause-effect relationship.

In the current study, none of the concurrent ECs originated from adenomyotic foci. Thirty-nine of the ECs were stage 1 and nine were stage 2. None of the stage 2 ECs had co-existing adenomyosis. Although the adenomyosis co-existence rate did not differ between EH subtypes, it was observed that adenomyosis accompanied fewer cases in those who were underdiagnosed in the final pathologic evaluation.

When the presence of myometrial lesions is not taken into account, there are several studies identifying patients with EH who are likely to be underdiagnosed, to avoid possible suboptimal surgery, especially in AEH cases in which concurrent EC rates are reported up to 40% [4]. Vetter et al. evaluated 169 patients with complex AEH and reported that the concurrent EC rate was 48.5% and that the risk of concurrent EC was increased in patients with a preoperative endometrial thickness of more than 2 cm and those aged over 65 years [19]. Erdem et al. reported that age over 50 years, diabetes mellitus, hypertension, and nulliparity were independent risk factors for concurrent EC in AEH [9]. In our study, we found that underdiagnosed patients were significantly older and postmenopausal. In the underdiagnosis group, patients had higher BMI and lower parity. Consistent with our results, Hui et al. examined occult AEH and

EC risk factors in NAEH cases and stated that patients with higher grades in the final pathology had significantly lower median parity and higher BMI [20]. A recent study that evaluated risk factors for occult AEH and EC in women diagnosed as having NAEH in endometrial biopsy found that patients aged ≥ 51 years with complex NAEH subtype had a high risk for underdiagnosis [21]. According to the results of the mentioned studies [20, 21] and our study, it could be concluded that although NAEH was considered as benign by the WHO and the first-line treatment option was conservative, hysterectomy may be an option in the presence of risk factors for underdiagnosis in patients with NAEH.

In addition to the aforementioned risk factors about concurrent EC risk, the preferred endometrial sampling method is also relevant. D&C has been widely used; however, in practice, endometrial aspiration biopsy using a pipelle or Endosampler is the most preferred endometrial sampling method because it can be performed easily in an outpatient setting, does not require general anesthesia, and is as accurate as D&C in the diagnosis of endometrial pathologies [8, 22]. In the current study, the Endosampler was preferred for preoperative diagnosis.

Studies about overdiagnosis in EH are limited. In one study, no characteristic features could be identified that distinguished the overestimated group from the other groups among the clinical parameters and imaging findings [23]. In our study, although the preoperative characteristics of patients with overdiagnosis did not differ from those of concordant patients, we found that the presence of leiomyoma did not affect the results, but the presence of adenomyosis increased the rates of overdiagnosis. The patients in the overdiagnosis group could be candidates for close surveillance, hormonal therapy or even surgery, and they face the risk of overtreatment and increased anxiety.

This novel study investigating the relationship between endometrial pathology discordance and myometrial lesions has a large sample size. Besides that, the use of the same endometrial sampling method in all patients, the evaluation of both pre and postoperative pathology results by the same gynecologic pathologists in the same center are strengths of the study. On the other hand, the retrospective design and the conductance of the study in a referral center that might increase the incidence of occult EC could be considered as limitations of the study.

In conclusion, adenomyosis, which is an incidental and common benign pathology, can cause both overdiagnosis and underdiagnosis in patients with EH. For appropriate diagnostic and therapeutic management of EH, it can be underlined that the possibility of discordant results in the presence of adenomyosis should be considered, and those patients should be carefully evaluated together with their clinical features for treatment options.

Declarations

Author contributions:FN Taşgöz: protocol development, data Collection, manuscript writing, supervision NKender Ertürk: project development, data analysis, manuscript writing, manuscript editing GTanrıverdi Kılıç:protocol development, data Collection GGökçe: data Collection, data management

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Conflict of interest:The authors report no conflict of interest

Consent to participate: All patients signed informed consent forms before undergoing surgery, allowing their medical records to be used for research purposes.

References

1. Kadirogullari P, Atalay CR, Ozdemir O, Sari ME (2015) Prevalence of co-existing endometrial carcinoma in patients with preoperative diagnosis of endometrial hyperplasia. J ClinDiagnRes 9(10):Qc10–Q4. https://doi. org/10.7860/jcdr/2015/12484.6618
2. Sccully RE, BonWglio TA, Kurman RJ et al (1994) Histological typing of female genital tumors: international histological classification of tumors, 2ndedn. Springer, Berlin
3. Sobczuk K, Sobczuk A (2017) New classification system of endometrial hyperplasia WHO 2014 and its clinical implications. PrzegladMenopauzalnyMenopauseRev 16(3):107–111. https://doi.org/10.5114/pm.2017.70589
4. Rakha E, WongSC, Soomro I et al. Clinical outcome of atypical endometrial hyperplasia diagnosed on an endometrial biopsy: Institutional experience and review of literature.(2012) Am J SurgPathol 36: 1683–1690
5. Trimble CL, Kauderer J, Zaino R et al (2006) Concurrent endometrial carcinoma in women with a biopsy diagnosis of atypical endometrial hyperplasia: A GynecologicOncologyGroupstudy. Cancer 106:812–819
6. Kurman RJ, NorrisHJ.(1982)Evaluation of criteria for distinguishing atypical endometrial hyperplasia from well-differentiated carcinoma. Cancer49:2547–59
7. Giannella L, DelliCarpini G, Sopracordevole F, Papiccio M, Serri M, Giorda G, Tsiroglou D, Del Fabro A, Ciavattini A (2020)Atypical Endometrial Hyperplasia and Unexpected Cancers at Final Histology: A Study on Endometrial Sampling Methods and Risk Factors.Diagnostics (Basel).13;10(7):474. doi: 10.3390/diagnostics10070474. PMID: 32668563; PMCID: PMC7400146
8. HwangWY SuhDH, Kim K, No JH, Kim YB.(2021) Aspiration biopsy versus dilatation and curettage for endometrial hyperplasia prior to hysterectomy. DiagnPathol. 14;16(1):7. doi: 10.1186/s13000-020-01065-0. PMID: 33441173; PMCID: PMC7807457
9. Erdem B, Aşıcıoğlu O, Seyhan NA, Peker N, Ülker V, Akbayır Ö (2018) Can concurrent high-risk endometrial carcinoma ocur with atypical endometrial hyperplasia? Int J Surg 53:350–353.

doi:10.1016/j.ijsu.2018.04.019. Epub 2018 Apr 14. PMID: 29665453

10. Garcia L, &Isaacson K (2011) Adenomyosis: review of theliterature.(. J Minim InvasiveGynecol 18:428–437. https://doi.org/10.1016/j.jmig.2011.04.004
11. Pavone D, Clemenza S, Sorbi F, Fambrini M, Petraglia F.(2018) Epidemiology and Risk Factors of Uterine Fibroids. Best PractResClinObstetGynaecol. 46:3–11. doi: 10.1016/j.bpobgyn.2017.09.004. Epub 2017 Oct 1. PMID: 29054502
12. Mao X, Zheng W, Mao W (2017) Malignant changes in adenomyosis in patients with endometrial adenocarcinoma:A case series. Med (Baltim) 96(43):e8336. doi:10.1097/MD.0000000000008336. PMID: 29069006; PMCID: PMC5671839
13. Raffone A, Seracchioli R, Raimondo D, Maletta M, Travaglino A, Raimondo I, Giaquinto I, Orsini B, Insabato L, Pellicano M, Zullo F (2021) Prevalence of adenomyosis in endometrial cancerpatients: a systematic reviewand meta-analysis. ArchGynecolObstet 303(1):47–53. doi:10.1007/s00404-020-05840-8.23. PMID: 33098006; PMCID: PMC7854401
14. Johnatty SE, StewartCJR, Smith D, Nguyen A, O' Dwyer J, O'Mara TA, Webb PM, Spurdle AB. (2020)Co-existence of leiomyomas, adenomyosis and endometriosis in women with endometrial cancer. SciRep.27;10(1):3621. doi: 10.1038/s41598-020-59916-1. PMID: 32108150; PMCID: PMC7046700
15. Pecorelli S (2009) Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet 105(2):103–104. doi:10.1016/j.ijgo.2009.02.012
16. Bird CC, McElinT WandManaloEstrella P (1972) The elusive adenomyosis of the uterusrevisited. Am J ObstetGynecol 112:583593
17. AndresMP BorrelliGM, Ribeiro J, BaracatEC, Abrão MS, KhoRM (2018) Transvaginal Ultrasound for the Diagnosis of Adenomyosis: SystematicReviewand Meta-Analysis. J Minim InvasiveGynecol 25(2):257–264. doi:10.1016/j.jmig.2017.08.653. Epub 2017 Aug 30. PMID: 28864044
18. Aleksandrovych V, Basta P, Gil K (2019) Current facts constituting an understanding of the nature of adenomyosis. AdvClinExpMed. 28(6):839–846. doi: 10.17219/acem/79176. PMID: 30085434
19. VetterMH, Smith B, Benedict J, Hade EM, Bixel K, CopelandLJ, Cohn DE, FowlerJM, O'Malley D, Salani R, BackesFJ. (2020) Preoperative predictors of endometrial cancer at time of hysterectomy for endometrial intraepithelial neoplasia or complex atypical hyperplasia. Am J ObstetGynecol. 222(1):60.e1-60.e7. doi: 10.1016/j.ajog.2019.08.002. Epub 2019 Aug 8. PMID: 31401259; PMCID: PMC7201377
20. Hui LS, ChinSHM, Goh C, Hui LX, Mathur M, KueiTLY XianFCH (2021) Non-atypical endometrial hyperplasia: risk factors for occult endometrial atypia and malignancy in patients managed with hysterectomy. ObstetGynecolSci 64(3):300–308. doi:10.5468/ogs.20294. Epub 2021 Feb 25. PMID: 33631068; PMCID: PMC8138077
21. Lee N, Lee KB, Kim K, Hong JH, Yim GW, SeongSJ, Lee B, Lee JM, Cho J, Lim S, OuhYT, Kim YB (2020) Risk of occult atypical hyperplasia or cancer in women with nonatypical endometrial hyperplasia. J ObstetGynaecolRes.17. doi: 10.1111/jog.14474. Epubahead of print. PMID: 32945047

22. AbdelazimIA, Aboelezz A, Abdulkareem AF (2013) Pipelle endometrial sampling versus conventional dilatation&curettage in patients with abnormal uterine bleeding. J Turkish German Gynecol Assoc 14(1):1–5. https://doi.org/10.5152/jtgga.2013.01
23. Kimura T, Kamiura S, Komoto T, Seino H, Tenma K, Ohta Y, Yamamoto T, Saji F (2003) Clinicalover- and under-estimation in patients who underwent hysterectomy for atypical endometrial hyperplasia diagnosed by endometrial biopsy: the predictive value of clinical parameters and diagnostic imaging. Eur J ObstetGynecolReprodBiol. 10;108(2):213-6. doi: 10.1016/s0301-2115(02)00469-4. PMID: 12781414