ORIGINAL ARTICLE

Concurrent Endometrial Carcinoma in Endometrial Hyperplasia with Atypia

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Abstract

Background: Endometrium that lies within the uterus may develop hyperplasia, due to various causes, of which unopposed estrogen exposure is the most common one. Endometrial hyperplasia may well mask an underlying malignancy and should be followed upon by further procedures to rule out underlying malignancy.

Materials and methods: This is a prospective observational study, from June 2017 to June 2019, at a tertiary care level teaching institution. Seventy patients who underwent hysterectomy following a diagnosis of endometrial hyperplasia with atypia were included.

Results: 95.7% were in multiparous group, 67.14 % were in perimenopausal, 30% in postmenopausal and 2.85% in reproductive age groups, 52.8% presented with abnormal uterine bleeding, 34.28% with postmenopausal bleeding and 12.85% were asymptomatic, 35.41% had diabetes mellitus, 22.91% had hypertension and 30.20% had obesity as comorbid factors. Positive family history for malignancy was noted in 3.1%. MRI findings suggested endometrial carcinoma in 27.2%. In cases in which MRI suggested non malignancy, 82.4% turned out to be malignant in the final histopathology report. Of the 70 patients, 40% had endometrial carcinoma (not otherwise specified), 30% had adenocarcinoma, 10% had serous carcinoma, 5.7% had papillary serous carcinoma and carcinosarcoma in 1.4%. 12.9% were declared to be nonmalignant by final histopathology reports. Except for two patients, all others had grade 1 well differentiated carcinomas.

Conclusion: This study demonstrates that endometrial carcinoma may be coexisting with endometrial hyperplasia with atypia, in majority of cases and available imaging modalities are not foolproof to rule out malignancy. Hence where appropriate hysterectomy may be suggested as the treatment option.

Keywords: Abnormal uterine bleeding, Carcinoma endometrium, Endometrial biopsy, Endometrial cancer, Endometrial thickness, Malignancy, Posmenopausal bleeding, Trans vaginal sonogram.

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Introduction

Carcinoma endometrium happens to be the fourth most common malignancy of women in the world and the sixth leading cause of death in women. Older and obese women, women with chronic ovulatory dysfunction, unopposed estrogen, diabetes mellitus, hypertension, and those with family history of Lynch syndrome (increased genetic risk) are at high risk of developing endometrial carcinoma.

Endometrial atypical hyperplasia is a precursor of carcinoma endometrium, with 25–45% ultimately developing malignancy. Atypical hyperplasia consists of glands that are crowded (>50% gland to stromal ration) and appear disorganized and have luminal outpouching with mitosis.

The World Health Organization Classification of 2014 has two categories for endometrial hyperplasia, which are hyperplasia without atypia (non-neoplastic) and atypical hyperplasia (endometrial intraepithelial neoplasm).

The Endometrial Intraepithelial Neoplasia Classification proposed in 2000 defines two classes of endometrial changes being benign endometrial hyperplasia (non-neoplastic) and endometrial intraepithelial neoplasia (EIN). Studies show that EIN and WHO classification system were similarly effective for prediction of progression of hyperplasia to endometrial carcinoma.[1,2]

Using the WHO classification, the presence of nuclear atypia in endometrial hyperplasia is the most important indicator for the risk of coexisting carcinoma.[3]

Hence, women with atypical endometrial hyperplasia on endometrial biopsy require further evaluation and intervention.

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Aim and Objective

To analyze the prevalence of concurrent carcinoma in patients identified with endometrial hyperplasia with atypia in our institute.

Materials and Methods

This is a prospective observational study undertaken in the Department of Obstetrics and Gynecology at Sri Ramachandra Medical Centre, Sri Ramachandra Institute of Higher Education and Research.

About 70 patients identified with "hyperplasia with atypia," diagnosed through endometrial aspiration or hysteroscopic-guided biopsy for various menstrual-related complaints, such as abnormal uterine bleeding, postmenopausal bleeding, and thickened endometrium inappropriate for age identified on pelvic scan were observed from June 2017 to June 2019.

Age, BMI, parity, comorbid conditions, medical history, clinical symptoms, and trans vaginal sonogram (TVS) reports were collected of these 70 patients in a set pro forma. Patients were advised MRI abdomen, pelvis, and subsequently hysterectomy with bilateral salpingo-oophorectomy with or without staging laparotomy and the final histopathology report analyzed to identify the incidence of concurrent malignancy (Tables 1 to 11).

Results

In our institute, we observed that majority of patients (59, 84%) were in the menopausal age. Total 3 of 70 (4.3%) were nulliparous and 95.7% (67) were multiparous. Abnormal uterine bleeding was the most common symptom in the reproductive and perimenopausal age group (52.8%), with postmenopausal bleeding being the presenting symptom in the postmenopausal age group (34.28%).

Table 1: Age of patients with hyperplasia with atypia

Age	*Number*	*Percentage*
36–40	2	2.9
41–45	9	12.9
46–50	10	14.2
51–55	21	30
56–60	11	15.7
61–65	6	8.5
66–70	5	7
>70	6	8.5

Table 2: Parity in patients with hyperplasia with atypia

Parity	*Number*	*Percentage*
Nulliparous	3	4.3
Multiparous	67	95.7

Table 3: BMI in patients with hyperplasia with atypia

BMI	*Number*	*Percentage*
<18.5	1	1.4
18.5–24.9	6	8.5
25–29.9	34	48.5
30–34.9	24	34.2
35–39.9	3	4.3
>40	2	2.8

Table 4: Clinical symptoms in patients with hyperplasia with atypia

Clinical symptoms	*Number*	*Percentage*
Abnormal uterine bleeding	37	52.8
Postmenopausal bleeding	24	34.28
Asymptomatic	9	12.85

Table 5: Menstrual status in patients with hyperplasia with atypia

Menstrual status	*Number*	*Percentage*
Reproductive	2	2.85
Perimenopausal	47	67.14
Postmenopausal	21	30

Table 6: Associated risk factors in patients with hyperplasia with atypia

Risk factors	*Number*	*Percentage*
Diabetes mellitus	34	35.41
Hypertension	22	22.91
Hypercholesterolemia	8	8.3
Obesity	29	30.20
Family history	3	3.1

Table 7: Investigations for diagnosis in patients with hyperplasia with atypia

Investigations	*Number*	*Percentage*
Endometrial aspiration	54	77
Hysteroscopic-guided biopsy	11	15.7
Endometrial curettage	5	7.1

Table 8: MRI findings in patients with hyperplasia with atypia

MRI findings	*Number*	*Percentage*
Nonmalignant	51	72.8
Ca endometrium stage IA	7	10
Ca endometrium stage IB	5	7.1
Ca endometrium stage IIA	3	4.3
Ca endometrium stage IIB	2	2.8
Ca endometrium stage III	1	1.4
Ca endometrium stage IV	1	1.4

Table 9: Correlation of nonmalignant MRI report showing concurrent malignancy in final histopathology in patients with hyperplasia with atypia

Histopathology grading	*Number (51)*	*Percentage*
Ca endometrium stage IA	19	37.2
Ca endometrium stage IB	14	27.4
Ca endometrium stage IIA	7	13.7
Ca endometrium stage IIB	2	3.9
Ca endometrium stage III	–	–
Ca endometrium stage IV	–	–
Remains nonmalignant	9	17.6

Table 10: Surgery performed in patients with hyperplasia with atypia

Surgery performed	*Number*	*Percentage*
TAH with BSO	1	1.4
Staging laparotomy	68	97.1
Palliative care	1	1.4

Table 11: Final histopathology results in patients with hyperplasia with atypia

Histopathology reports	*Number*	*Percentage*
Endometrial Ca (NOS)	28	40
Endometrioid adeno-Ca	21	30
Serous Ca	7	10
Papillary serous Ca	4	5.7
Carcinosarcoma	1	1.4
Downgraded to non-neoplasia	9	12.9

Out of the 70 patients, 1 patient opted for observant management in view of advanced age with multiple associated comorbid conditions. Of the 69, who underwent surgery for hyperplasia with atypia, 68 (97.1%) had staging laparotomy, whereas 1 patient (1.4%) underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy.

The final histopathology was reported according to FIGO staging, which showed endometrial carcinoma (not otherwise specified) in 28 patients (40%) and endometrial endometrioid adenocarcinoma in 21 patients (30%). Seven patients had serous carcinoma (10%). Only one (1.4%) patient had carcinosarcoma and four patients had papillary serous-type carcinoma (5.7%). The remaining nine (12.9%) patients who had hyperplasia with atypia were downgraded to other non-neoplastic lesions in the final histopathology report.

Of the four patients with papillary serous carcinoma, two patients had concurrent Ca ovary with histopathology showing papillary serous carcinoma of ovary.

One patient with serous carcinoma of endometrium had additional lymphovascular extension and one patient with endometrial endometrioid adenocarcinoma showed positive for microvascular residual tumor.

Of the 28 patients with endometrial carcinoma—not otherwise specified—14 (50%), had FIGO stage IA, well-differentiated carcinoma, with 8 (28.5%) patients having FIGO stage IB. Seven patients (25%) had FIGO stage II, and two (7%) had FIGO stage III.

In 21 patients with final histopathology report of endometrial endometrioid adenocarcinoma, 17 (81%) had FIGO stage I and 4 (19%) FIGO stage II.

Except for two patients, all other patients had grade I well-differentiated carcinomas.

Discussion

Endometrial carcinoma is most commonly seen in the 40–60 age group and we found a similar result in our study. Though it is reported to be two to four times more common in nulliparous women, or in women with unopposed estrogen, in our study majority of the patients were multiparas.[4–6]

Endometrial carcinoma risk is increased 1.5 times in overweight patients and 2.5 times in obese patients and in our study we found most of the patients were in overweight and obese group accounting to 30.2 and 48.5%.[7]

Diabetes mellitus is associated with a modest increase in endometrial cancer risk and in our study we found that 35.41% patients were diabetic.[8]

Though there is inconclusive evidence between familial association between breast and endometrial cancer,[9] we observed 2 patients of 70 (2.85%) with first-degree relatives with breast cancer and 1 patient of 70 (1.42%) with family history of colorectal cancer in first-degree relative.

About 3–5% endometrial cancers can be attributed to Lynch syndrome.[10] In our study, we found two patients having concurrent ovarian malignancy, but genetic workup of the patients was not done.

Worldwide, the risk of an underlying malignancy ranges from 25 to 43% in a patient identified with hyperplasia with atypia.[11] In our study, we observed that the incidence of underlying malignancy in patients with endometrial hyperplasia with atypia was 88.4%, which is twice the rate prevalent worldwide. The associated risk factors such as diabetes, hypertension, and obesity could be attributed to this increased progression in our study population.

The prognosis for stage IA, grade I is good.[12] In our study population, we found majority of women to have stage I carcinoma (60.5%).

Trimble et al. in his study observed that endometrial adenocarcinoma was the most common underlying malignancy in patients identified with hyperplasia with atypia. However, in our study population we observed that endometrial carcinoma (not otherwise specified) is slightly more common that adenocarcinoma endometrium.[3]

Conclusion

Hyperplasia with atypia, when diagnosed, should be evaluated further with higher imaging modalities so that concurrent counseling regarding appropriate surgery can be given.

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