Original Article

Utility of Endometrial Aspiration Cytology for Screening Postmenopausal Women for Endometrial Malignancies

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Abstract

Objective: Endometrial aspiration cytology (EAC) is an acceptable and valuable diagnostic procedure for screening the endometrial status. Objective of this study is to know the utility of this procedure as a screening procedure for detection of endometrial malignancies in postmenopausal women with abnormal uterine bleeding (AUB). **Methods:** Endometrial aspiration obtained using 5F infant feeding tube attached to 20cc disposable syringe. Endometrial aspiration material was smeared directly on to three clean glass slides.One smear was wet fixed for papanicolau staining and the remaining slides were air dried for Giemsa stain. Smears were reviewed for cytomorphological findings and were correlated with the histopathological findings. **Results:** 100 postmenopausal women presenting with abnormal uterine bleeding were studied. Age of the patients ranged from 45 to 70 years. In our study, the sensitivity and specificity in diagnosing malignancy on aspiration cytology were 90% and 96.25% respectively. **Conclusions:** Endometrial aspiration is an effective, useful and a minimally invasive procedure. With an experienced cytologist, it can be used rou-tinely for the screening of postmenopausal women with AUB for endometrial malignancies, provided all the points of discrepancies are taken care of.

Keywords: *Endometrial aspiration cytology, endometrial carcinoma, postmenopausal bleeding*

Introduction

Postmenopausal bleeding (PMB) is defined as bleeding that occurs from the genital tract after 1 year of amenorrhea, in a woman who is not receiving hormone replacement therapy (HRT).[1] It may be heavy bleeding, just spotting or just like normal menstruation.[2] With the increase in life expectancy, number of women spending their lives in menopause has also increased, and thus postmenopausal problems are gaining more importance in gynecological clinical practice. PMB accounts for about 5% of gynecology visits.[3] Women with PMB are traditionally investigated with curettage and histology. Thus, dilatation and curettage (D and C) with histopathological examination (HPE) of endometrial curettings (EC) has for long been considered the "gold standard" in the diagnosis of endometrial pathology.[4] One of the most commonly performed gynecological surgeries, it accounts for a large proportion of hospital bed use and operating room time. The cost is significant and carries the complications of anesthesia. For these reasons, there is a need for a simple, accurate, and good outpatient department (OPD) procedure as an alternative to D and C. Endometrial aspiration cytology (EAC) can be used as a safe, minimally invasive and reliable OPD procedure with minimum discomfort to the patient.[5] In this view, we thought it worthwhile to study its diagnostic utility in detection of endometrial malignancies in postmenopausal patients presenting with abnormal uterine bleeding (AUB).

Materials and Methods

A total of 100 cases of PMB attending gynecology and obstetrics OPD were evaluated. We followed a well-set protocol for selecting our patients. All patients having established menopause except those undergone hysterectomy/premature menopause (<40 years)/on HRT/on anticoagulant/having bleeding disorder included in the study. A detailed history was taken, and per vaginal examination was performed to rule out any local or systemic illness as a cause of PMB. The procedure was well-explained to the patients, and

How to cite this article: Mardi K, Rao M, Bhardwaj M, Sharma M. Utility of endometrial aspiration cytology for screening postmenopausal women for endometrial malignancies. Clin Cancer Investig J 2017;6:35-9.

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Access this article online

Website: www.ccij-online.org

DOI: 10.4103/ccij.ccij_151_16

Quick Response Code:

their consent was taken. Under all aseptic conditions, endometrial aspiration was carried out in the OPD or in the operation theater before curettage. Endometrial aspiration obtained using 5F infant feeding tube attached to 20 cc disposable syringe and curettings obtained by blunt end endometrial curette. Endometrial aspiration material was smeared directly onto three clean glass slides. Two air-dried smears were stained using Giemsa stain. One of the slides was immediately fixed in 95% ethyl alcohol and then stained with Papanicolaou stain.

Subsequently, all the patients were subjected to D and C, and then the curettings were fixed in 10% formalin. After tissue processing, sections were obtained and stained with hematoxylin and eosin (H and E) stain. Finally, cytological and histopathological results were compared.

The cytomorphological criteria used in various conditions of the endometrium were as given by An-Foraker *et al*.,[6] Shu and Ikle[7] and Meisels and Jolicoeur[8] The factors of inadequacy were followed as stated by Veneti *et al*.[9] that the reason of histologically and cytologically inadequate material could be old age, uncooperation by the patient or technical errors. Study of composition, architecture, and growth pattern of the large tissue fragments in the cytological samples from the endometrium was done and evaluated using criteria given by Skaarland E[10] and Yanoh *et al*.[11]

Results

Totally, 100 postmenopausal women presenting with AUB were studied. Age of the patients ranged from 45 to 70 years with maximum (35%) patients in the 51–55-year age group [Table 1]. The material was adequate for evaluation in 90% cases of EAC and 86% cases of EC. Various diagnostic categories diagnosed on HPE of these specimens were endometrial atrophy (49% cases), proliferative endometrium (13% cases), secretory endometrium (2 cases), endometritis (4 cases), tuberculous endometritis (1 case), endometrial hyperplasia (6 cases), endometrial carcinoma (9 cases), and Cervical carcinoma (2 cases). 12 cases of endometrial carcinomas were diagnosed on EAC [Table 2]. All the 9 cases of endometrial carcinoma diagnosed on EAC showed cellular material which were "satisfactory for evaluation." In all these smears, cell clumps of various size are collected abundantly. In all these smears, abnormal cell clump rate was more than 70%. Among these 9 cases which were diagnosed as adenocarcinoma on HPE, cell clumps with irregular protrusions were found in 6 cases, whereas a papillary/papillotubular pattern [Figures 1 and 2] was present in 2 of the cases. These smears revealed disorganization of cells in sheets and three dimensional clusters with extreme variation in shape and size of cells, disturbed nuclear polarity, hyperchromasia, increased nuclear chromatin granularity, increased number

Table 1: Age incidence of the cases

Age group (years)	*n* (%)
41-45	3 (3)
46-50	15 (15)
51-55	35 (35)
56-60	19 (19)
61-65	13 (13)
>65	15 (15)
Total	100 (100)

Table 2: Endometrial patterns obtained by endometrial curettings and endometrial aspiration cytology

Histopathological diagnosis	Number of cases on HPE	Number of cases on EAC
Hyperplasia	6	4
Endometrial carcinoma	9	12
Atrophic	49	47
Proliferative	13	16
Secretory	2	2
Endometritis	4	6
Tuberculous endometritis	1	1
Carcinoma of the cervix	2	2

EAC: Endometrial aspiration cytology, HPE: Histopathological examination

Table 3: Statistical analysis of detection of endometrial malignancies by endometrial aspiration cytology

Parameter	Value
Number of cases diagnosed on HPE	9
Number of cases diagnosed on EAC	12
Sensitivity (%)	90
Specificity (%)	96.25
Positive predictive value (%)	75
Negative predictive value (%)	98.72
Accuracy (%)	95

EAC: Endometrial aspiration cytology, HPE: Histopathological examination

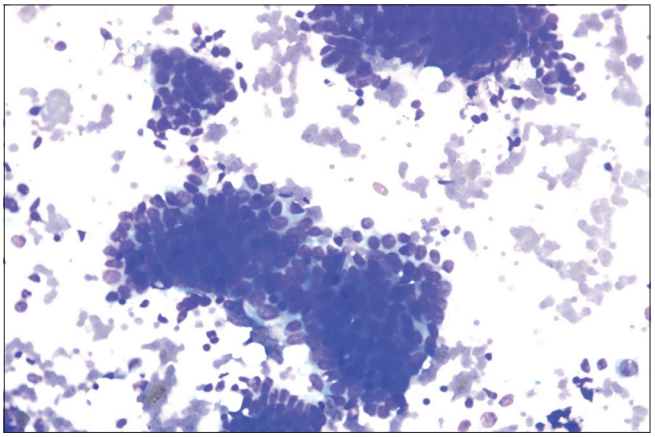

Figure 1: Endometrial carcinoma showing irregular clusters with nuclear overlapping and focal papillary projections (Giemsa, ×20)

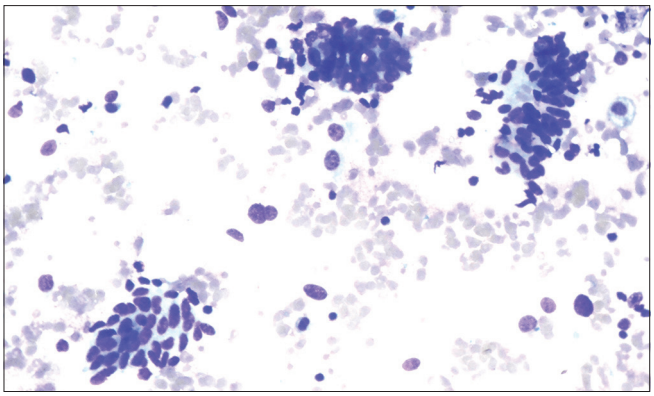

Figure 2: Endometrial aspiration cytology smears revealing well-differentiated endometrial carcinoma (Giemsa, ×40)

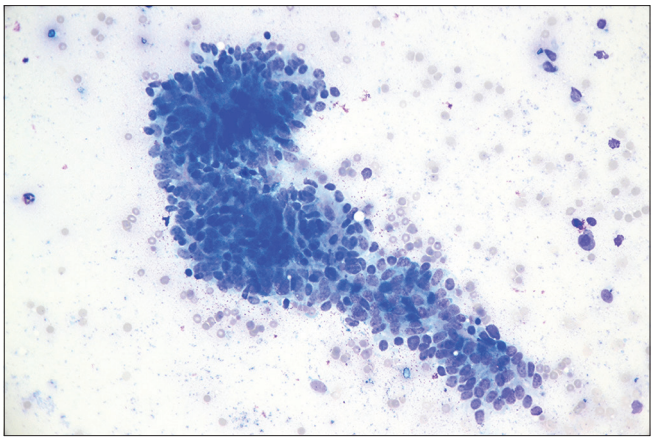

Figure 3: Endometrial carcinoma revealing malignant cells in papillary clusters (Giemsa, ×40)

of macro nucleoli, loss of cohesiveness, and abnormal mitotic figures [Figure 3]. Sensitivity and specificity of EAC in the detection of endometrial malignancy was 90% and 96.25% respectively with a positive predictive value of 75%, negative predictive value of 98.72%, and accuracy of 95% [Table 3].

Discussion

Endometrial carcinomas are the most common pelvic gynecologic malignancy in developed countries, with its incidence rising in developing countries.[12] Patients with a higher risk for harboring endometrial cancer might benefit from an effective and low-cost screening test for endometrial cancer. Earlier tumor detection in such patients offers the opportunity to improve patient survival.[13]

Endometrial aspiration is not a very popular and well-accepted procedure in India due to various reasons. One of the factors is the unavailability and the high cost of the aspiration instrument. To overcome this obstacle, we used 5F infant feeding tube attached to 20cc disposable syringe which is an easily available low-cost device. The other factors being that the diagnostic criteria of endometrial cytology have not yet been fully established. Although endometrial histology is the confirmatory test in our study, yet we recommend the use of EAC as a routine preliminary procedure in women with PMB as it is an easier, safer, and reliable OPD procedure. Moreover, when the cellular material is inadequate, this procedure can be repeated without much inconvenience to the patient, as was done in our study.

Cytological examination of the endometrium is particularly useful in postmenopausal women having endometrial atrophy that may result in a high inadequacy rate of endometrial biopsies. In this context, endometrial cytological samples have been shown to be diagnostic in a significantly higher percentage of cases with respect to biopsy sample.[14]

Many instruments for endometrial cytological sampling have been designed, and promising results from tests have been published. The accuracy of cytological technique versus curettage and histological investigation has been tested by many investigators using different instruments. Most reports show satisfactory results in the detection of malignant lesions,[9,15-20] including Infant feeding tube attached to 20 ml disposable syringe which we used in our study. In this study, the adequate material was obtained in 90% of cases. Using No. 4 infant feeding tube Jadhav *et al*.[21] also reported adequate material in 90% cases which is comparable to the present study.

In terms of malignancy, sensitivity was 90%, specificity was 96.25%, with a positive predictive value of 75%, negative predictive value of 98.72%, and accuracy of 95%. Similar values of sensitivity (100), specificity (96.5%), positive predictive value (75%), negative predictive value (100%), and accuracy (96.84%) for the diagnosis of malignant lesions of endometrium were also observed in a study conducted by Kaur *et al*.[22] There were three false positive and one false negative case in the current study. Among the three false positive cases, one was diagnosed as complex hyperplasia on HPE, and the other two cases were showed atypia associated with endometritis. Inflammation obscured cellular detail. The inflammatory debris was confused with tumor diathesis. Inflammatory smears may assume all the characteristics of endometrial cancer cells including enlarged nuclei with variation in size, even in shape, hyperchromasia as well as prominent and multiple nucleoli. Atrophic smears could be a pitfall due to their dark staining nuclei. It is important to note that in no case was a malignancy missed on cytology. Hence, EAC is clearly of special value as the preliminary investigation of women with PMB or those who are at a risk of endometrial carcinoma.

In all the smears, positive for malignancy and confirmed by histopathology, abnormal cell clump rate was more than 70% in the present study which is in agreement with a study done by Yanoh *et al*.[11] Cytoarchitectural patterns observed in the present study were also observed in the

EAC smears of endometrial carcinoma in a study conducted by Norimatsu *et al*.[23]

In a study conducted by Kawana *et al*.[24] EAC was found to be useful for endometrial cancer cases with normal curettage findings as part of early detection. In another study by Segadal *et al*.,[25] cytology and curettage gave a diagnosis in 96% of patients while curettage alone gave a diagnosis in 82%, and cytology alone in 90%. They concluded that cytological method is simple and may be of special value in postmenopausal patients. Sister *et al*.[26] in a similar study in symptomatic peri- and post-menopausal patients concluded that a negative result on cytological aspiration smears does not rule out a malignant process, especially in persistently symptomatic patients and further investigations are mandatory.

Thus in Japan, when atypical endometrial hyperplasia or carcinoma is suspected on cytology, biopsies are usually performed. On the other hand, when normal or atrophic endometrium is reported, no additional biopsies are required, unless carcinoma or a precursor lesion cannot be excluded on clinical grounds. Therefore, for the cytological diagnosis of the endometrium, complete agreement between the cytology and the histopathology is not essential. What matters is whether a biopsy is necessary to establish the final diagnosis.[11]

Universal endometrial sampling on a periodic basis is probably impractical and may be unnecessary. However, surely the patient at high risk for endometrial cancer requires close periodic screening. Cytological technique can be used as the primary means of morphological investigation in patients with PMB. A negative result from the cytological investigation, together with a negative result from the clinical investigation and a negative cervical smear, is considered sufficient investigation for PMB. If the cytological findings indicate that further investigation is necessary curettage with histological analysis can be performed. With the intelligent and aggressive application of outpatient screening, uterine cancer can be diagnosed when patients are virtually completely curable, thus resulting in further reduction in mortality from this disease.

Conclusion

We thus conclude from the study that endometrial aspiration is an effective, useful, and a minimally invasive procedure. Infant feeding tube attached to a disposable syringe is a cheap and easily available device that yields good cellular material. With an experienced cytologist, it can be used routinely for the primary investigation of postmenopausal women with AUB, provided all the points of discrepancies are taken care of. Endometrial aspiration is of special value in the investigation of women in whom there are much greater risks associated with general anesthesia and in whom no curettings are obtained. This technique would eliminate an endometrial curettage in those patients in whom there is no clinical suspicion of endometrial carcinoma, and the cytology is negative. Unnecessary hospital expenditure as a result of indoor admissions and anesthesia required for D and C can be avoided. We hope that this study will inculcate further interest amongst the gynecologists and cytologists and a good coordination among them are required to make aspiration cytology a routine screening procedure.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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