

Epithelial cytological atypia associated with intrauterine contraceptive devices

Maha Shakir Hassan* Ph.D



Summary :

Background Prolonged usage of an intrauterine contraceptive device (IUD) is often associated with exfoliation of atypical cells⁽¹⁻⁵⁾. These cells are commonly observed in gynecologic preparations and can cause considerable difficulty in their interpretation; misdiagnosed to represent adenocarcinoma, epidermoid carcinoma, or other dysplastic lesions.

Patients And Methods The study was conducted at AL-Kadhimiya Teaching Hospital from September 2003 till June 2005. Fifty PAP smears with atypical cells from women wearing IUD were examined cytologically.

Results The age range was 18-42 with average age of 29 years. Ten had at least one previous smear from a period of three months to 5 years, the most common cause of IUCD removal were menstrual disorders.

The cases were categorized cytologically into two groups: the first consisted of nine cases considered to represent atypia of reparative nature resulting from inflammation or infection, the remaining 41 cases of the second group fell into three subgroups: squamous, columnar, and indeterminate type of atypia.

Columnar atypia is characterized by abnormal cells which can resemble cells from carcinoma *in situ*. Unlike the latter the atypical cells from IUD are usually multinucleated contain nucleoli, and are not associated with cells from severe cervical atypia. They are probably endometrial in origin.

Conclusion There is no likelihood of an enhanced incidence of cervical dysplasia or carcinoma, however an awareness of IUCD associated cytomorphological alterations to avoid wrong diagnoses of carcinoma.

In every smear with columnar and/or indeterminate atypia in reproductive age group women, the patient should be asked if she wear an IUD to avoid wrong diagnosis of carcinoma.

Key words intrauterine contraceptive device, epithelial atypia

**Fac Med Baghdad
2007; Vol. 49, No.3
Received June 2006
Accepted June 2007**

Introduction:

The use of IUD may transform a normal cervical epithelium located adjacent to the body of IUD into a dysplastic one; this change could be reversible after removal of the device and electrocautry or cold conization⁽¹⁾. In addition to alteration in squamous epithelium of the endocervix among IUD users, changes in the columnar epithelium of the endocervix and/or endometrium have been reported⁽¹⁻⁶⁾. Morphologic cellular features simulating *in situ* squamous and adenocarcinoma have probably been observed more commonly than reported in the literature, but there is no conclusive evidence for the association of the squamous cell dysplastic changes and IUD usage⁽²⁾. Squamous cell changes are essentially reactive and reparative in nature^(7,8).

Ascending infection occurs in the presence of IUD. Most common type of infection is actinomycetes and trichomonas vaginalis⁽⁹⁻¹³⁾.

The present study describes detailed cytomorphologic features of IUD-associated cellular changes with appropriate tissue studies.

*Lecturer, Department of Pathology, College of Medicine -AL-Nahrain University.

Material And Methods:

The study was conducted at AL-Kadhimiya teaching hospital from Sep.2003 till June 2005. Fifty gynecologic preparations (pancervicovaginal fast smears) from women wearing an IUD. Information about duration of its usage, any gynaecologic problem, the day in the cycle.

Samples were collected from the ectocervical squamo- columnar junction, endocervical canal and vaginal pool using Ayre's spatula, smeared on slides and stained by Papanicolaou stain.

The epithelial atypia classified to reparative, and epithelial atypia related to the usage of IUD. The second group classified into: columnar, squamous, and indeterminate type of atypia⁽⁶⁾.

Results:

The results obtained in this paper belong to 50 women wearing IUD. These women ranged in age from 18-42 year with an average of 29 years. Of those women, ten had at least one previous normal smear before insertion of IUD for period ranging from 3 months to 5 years; the average range of IUD usage being 24 months. Of the 50 smears 48 were obtained at the luteal phase of the menstrual cycle. The most common recorded complaints and the most frequent cause of IUD removal were menstrual disorders: mainly of heavy periods. Other

complaints including of low abdominal pain and mucoid vaginal discharge.

After reviewing the material, the specimens were grouped into two groups. The first consisted of nine cases of epithelial atypia which were interpreted as healing or reparative changes resulting from inflammation or infection figure (1). The second group of 41 cases was interpreted to represent epithelial atypia which might possibly have been caused, aggravated or otherwise related to the usage of IUD table (1).

Of the nine cases considered to represent atypia of a reparative nature most have heavy population of polymorphnuclear leukocytes, histiocytes, and some lymphocytes. *Trichomonas vaginalis* was identified in two cases, *Actinomyces* in two figure (2), and in five cases no organism was identified. Five and four patients had squamous and columnar epithelial atypia respectively. Metaplasia was common with cytomorphologic features similar to those observed among women without IUDs but have acute and chronic cervicitis table(2). At subsequent clinic visit for four patients with appropriate therapy, with IUD removal, follow up smears on all of these patients reverted to normal after one month, and the follow up for the remaining five was difficult.

The remaining 41 cases of the second group fell into three subgroups, eleven cases of squamous atypia including metaplasia figure (3), 17 cases of columnar atypia figure (4), encompassing atypical endocervical and endometrial cells and 13 cases of indeterminate cell atypia table(3) figure (5).

Table (1): Classification of epithelial atypia in fifty Pap smears.

Type of atypia	Number of cases	% of cases
Reparative atypia	9	18
Epithelial atypia aggravated or related to the usage of IUCD	41	82
Total	50	100

Table (2): Cytological finding of nine smears with atypia of reparative nature.

Cytological findings	Number of cases	% of cases
Columnar epithelial atypia	5	55.55
Squamous epithelial atypia	4	44.44
<i>Trichomonas vaginalis</i> infection	2	22.22
<i>Actinomyces</i> infection	2	22.22

Table (3): Cytological finding of the 41 smears which might possibly related to IUCD.

Epithelial atypia	Number of cases	% of cases
Squamous atypia including metaplasia	11	26.82
Columnar atypia	17	41.46
Indeterminate cell atypia	13	31.7
Total	41	100

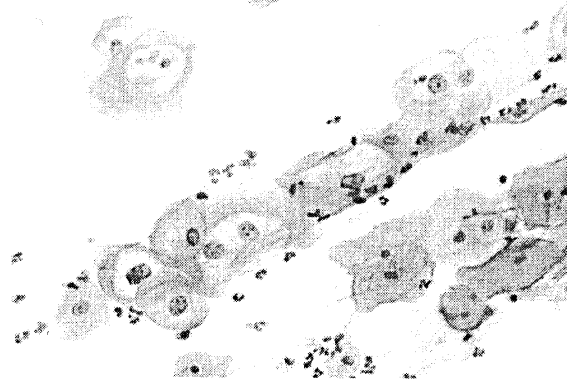


Figure (1): Epithelial atypia of reparative nature, note the enlarged somewhat irregularly shaped nuclei. Increased nucleocytoplasmic ratio. Finely granular, slightly to moderately hyperchromatic nuclear chromatin and presence of inflammatory cell infiltration.



Figure (2): Actinomyces typical aggregates of pseudofilamentous material.

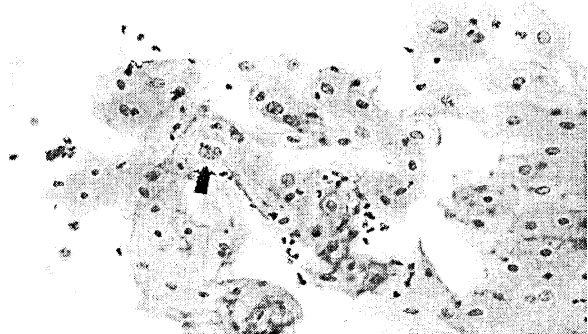


Figure (3): Squamous metaplasia, singly lying, and mature round to oval cells with relatively large nuclei. Cytoplasm showing dense outer zone and lighter inner zone (pointer).

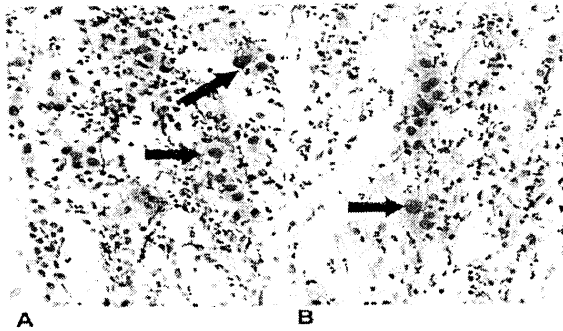


Figure (4): Glandular atypia, note the hyperchromatic large nuclei with cytoplasmic vacuolation (both A and B).

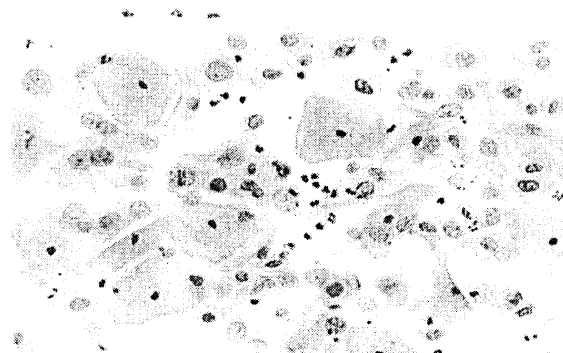


Figure (5): Indeterminate cell atypia, cells vary in size and shape, irregular shape nuclei, coarsely granular chromatin, and increase nucleocytoplasmic ratio.

Discussion:

The observation of squamous atypia among IUD users is somewhat higher than that found in the general population. This may be due to the selected nature of the cases in this investigation or in some way, may be IUD-related either from the outpouring of inflammatory cells from the uterus or from the carrier thread acting as a mechanical irritant and a potential source of persistence infection⁽⁸⁾.

The columnar atypia associated with IUD usage are characterized by their secretory vacuoles, some huge and hyper distended appearing to represent increased mucous production, usually associated with inflammation figure (4). At time especially in women over 40, they are found with adenocarcinoma of the endometrium or less often of the ovary or endocervix. Cytoplasm of some of these cells can be hard and crisp, suggesting keratinization⁽⁶⁾.

The indeterminate category of atypia figure (5) is the worrisome diagnostically especially to an uninitiated observer with high nuclear-cytoplasmic ratio, irregular nuclear membrane and hyperchromasia. they must be carefully discriminated from cells shed from in situ carcinoma. Nucleoli, a frequent occurrence in these atypical cells shed from IUD usage, are very rarely found in carcinoma in situ⁽⁸⁾. Most often these nucleoli are single, prominent and round but they can be multiple and inconspicuous. Bi- and

trinucleated forms are common occurrence.

The most helpful discrimination between smears with these atypical cells and those from carcinoma in situ is a pattern of uniformity of cell type. Smears from patients with in situ carcinoma invariably contain cells from different degrees of squamous atypia. In smears from IUD users there are usually only the types of atypical cells described. Occasionally there may be fragment of the more classically atypical columnar cells or cells from minor squamous atypia.

The origin of these atypical cells associated with IUD usage is not completely understood. They could be histiocytes⁽²⁾, endometrial stromal cells⁽⁶⁾, or even metaplastic cells. IUD have been reported to erode through the surface epithelium to the stromal area and may simulate histiocytic response⁽¹¹⁾. This could be a cause of shedding of either active histiocytes, or endometrial cells reacting to the presence of an irritant. In some IUD users, and more commonly among patients with clinical pelvic inflammatory disease, the endometrium reveals chronic endometriosis with columnar and squamous metaplasia⁽¹⁴⁻¹⁸⁾ figure (2).

The result of the present work support the observation noted by other major studies^(8,19,20, 21) that there is no likelihood of an enhanced incidence of cervical dysplasia or carcinoma, however an awareness of the other IUCD associated cytomorphic alterations to avoid wrong diagnosis of carcinoma.

References:

- 1 Ashton, P.R. and Johnson, W.W.: *Cytopathologic alterations associated with intrauterine contraceptive devices. Acta cytol. 19:583, 1975.*
- 2 Bibbo, M. and Wied, G.L.: *LOOK-alikes in gynecologic Cytology: Tutorial of Cytology. Chicago: 1984.*
- 3 Fornari, M.D.: *cellular changes in the glandular epithelium of patients using IUCD. Acta cytol. 18:341-343, 1984.*
- 4 Gupta, P.K., Malkani, P.K. and Bhasin, K.: *Cellular response in the uterine cavity after IUD insertion and structural changes of the IUD. Contraception 4:375-384, 1971.*
- 5 Ishilam, A., Kagabu, T., and Shima: *Cytologic studies after insertion of IUDs. Acta cytol. 14:35-41, 1990.*
- 6 Ng, A.B.P. and Regan, J.W.: *Cytology of uterine adenocarcinoma. Chicago: Tutorials of cytology, 1974, p. 19.*
- 7 Bibbo M, Harris MJ, Wied GL: *Microbiology and inflammation of the female genital tract. Chicago. Tutorial of cytology, 1987, pp61-75.*
- 8 Gupta PK, Burroughs F: *Epithelial atypia associated with IUD. Acta cytol 22:286-291, 1988.*
- 9 Burkman RT, Schlesselman S, McCaffrey L: *The relationship of genital tract actinomycetes and the development of pelvic inflammatory disease. Am J Obstet Gynecol 143:585-589, 1982.*
- 10 De la Monte SM, Gupta PK: *Systemic Actinomyces infection. A potential complication of IUD. JAMA 284:1876-1877, 1992.*
- 11 Gupta PK: *Intrauterine contraceptive devices: Vaginal cytology, pathologic changes and their clinical implication: Review and lead article. Acta cytol 26:571-613, 1982.*
- 12 Gupta PK: *Actinomycetes in cervico-vaginal smear: An association with IUD usage. Acta cytol 20:295-297, 1988.*
- 13 Luff RD, Gupta PK: *Actinomycetes-like organism in wearer of IUD. American J Obstet Gynecol 129:476-477, 1990.*

- 14 Gupta PK, and Malkani, PK: Cellular response in the uterine cavity after IUDinsertion . *Contraception* 4:375-384, 1993.
- 15 Hollander, DII, and Frost: Actinomyces in cervico-vaginal smear. *Acta Cytol* 20:295-299, 1988.
- 16 Jennings J.:Report of safety and efficacy of the IUDs. *Acta Cytol.* 14:35-41, 1974.
- 17 Piver, M.S., and Bolognese, r.j.:Effect of IUD upon cervical and endometrial exfoliative cytology. *Obstet. GYNECOL.* 528-531, 1976.
- 18 Sagiroglu, N: The cytology of IUD . *Acta cytol.* 14:58-46, 1970.
- 19 Sagiroglu, N. and Sagirglu, E.: Changing concept of IUD. *Prog. Gynecol.* 6:381-399, 1985.
- 20 N. Al-Ahwan, Z. Al-Saadi, k. Al- Rawi:Long-Term Cytologic Follow-Up Studies of Copper IUCD Users. *J. Faculty of Medicine* 37:113-118, 1995.
- 21 Luthra, U.K. Mitra, A.B. Prabhakar, et al:Cytologic monitoring of women using copper containing IUCD. *Acta Cytol* 26: 619-622; 1982.

