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Letter to Editor

Pathology Section

Multinucleated Cells in PAP Smear- An Institutional Experience

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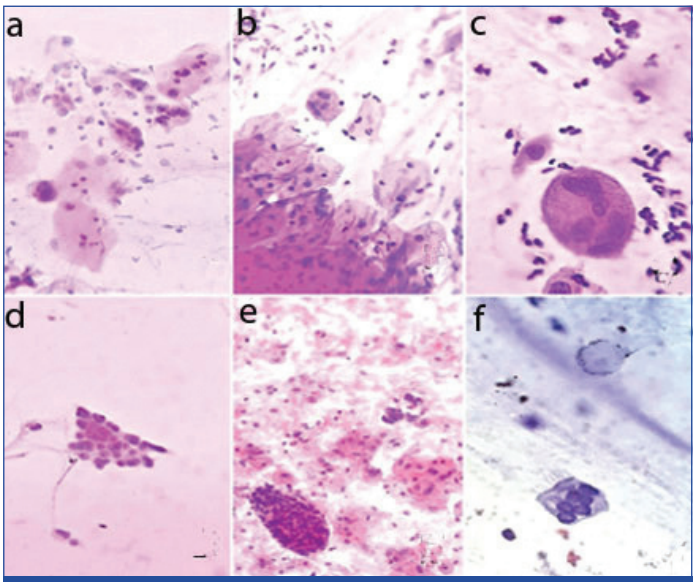
Dear Editor,

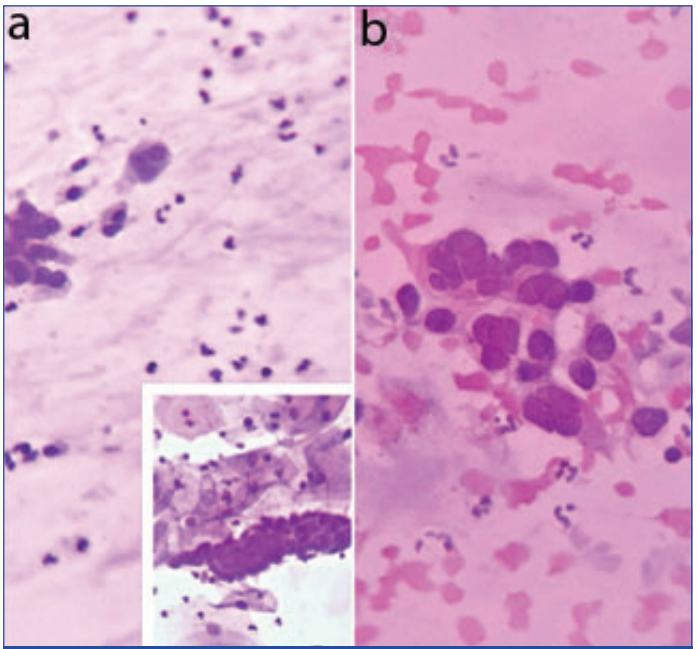
The cases which showed multinucleated cells in the papanicolaou smear, were collected after informed consent from the patients from the Department of Gynaecology during the past six months, and stained using papanicolaou staining method [1] were procured. These slides were identified and probable aetiology confirmed by two cytopathologists. The case details are shown in [Table/Fig-1]. During the course of the study, it was noted, out of the 13 cases which had multinucleated cells, majority of the cases had reactive cellular changes due to inflammation, followed by atrophy, while one case had history of use of intrauterine contraceptive device, two had herpes infection and one had atypical glandular cell of uncertain significance. In the cases showing inflammation, binucleate and multinucleate cells were seen. The nuclei had regular nuclear contour, without nucleoli or pleomorphism. Some of the cells showed perinuclear halo and cytoplasmic vacuoles. In the case with intrauterine contraceptive device, multinucleate cells without pleomorphism or hyperchromasia were seen. In the cases showing ciliary metaplasia [Table/Fig-2], the multinucleate cells were columnar in shape with basally located multiple nuclei (3-5 nuclei). The nuclei were regular in shape, without atypia [Table/Fig-3]. The cell had an end plate from which multiple cilia were seen. The cases with atrophy showed parabasal cells and occasional multinucleate cells with 2-3 nuclei without atypia. In the case with history of tamoxifen intake, changes associated with inflammation were seen along with clusters of small round blue cells with scant cytoplasm, round to oval nuclei with fine chromatin and inconspicuous nucleoli. Few clusters of benign endometrial cells were seen, but there were no malignant cells. In the case with herpes simplex infection, there were multinucleate cells, nuclear overlapping, moulding, intranuclear inclusions and ground glass appearance. The case with atypical glandular cells of uncertain significance showed cells

Sl. No.	Age (years)	Clinical detail	Impression
1	70	Menopause, tamoxifen	Changes associated with inflammation and tamoxifen
2	63	Menopause	Atrophy
3	45	White discharge	Atypical glandular cells of undetermined significance
4	52	Menopause	Changes associted with inflammation
5	42	Cervical erosion	Changes associated with inflammation, ciliary metaplasia
6	57	Menopause	Changes associated with inflammation, ciliary metaplasia
7	51	Bulky cervix	Changes associated with inflammation
8	55	Menopause	Changes associated with inflammation
9	45	Menopause	Changes associated with inflammation Herpes simplex infection
10	33	White dischage. Intrauterine contraceptive deice	Changes associated with inflammation
11	26	Unhealthy cervix	Changes associated with inflammation Herpes simplex infection
12	58	Menopause	Atrophy
13	49	Cervical erosion, adnexal cyst	Changes associated with inflammation Herpes simplex infection

[Table/Fig-1]: Summary of the cases having multinucleate cells in Pap smears.



[Table/Fig-2]: Photomicrograph shows multinucleated cells: a) Herpes simplex infection (PAP,40x); b) Smear showing inflammatory changes (PAP, 40x); c) Intrauterine contraceptive device use (PAP,40x); d) Atrophy (PAP,40x); e) A case of tamoxifen use (PAP,40x); f) Photomicrograph shows multinucleated cell with ciliary metaplasia.



[Table/Fig-3]: Photomicrograph shows multinucleated cells in: a) Atypical glandular cells of uncertain significance (PAP, 40x)(10x for inset); b) Squamous cell carcinoma (PAP, 40x).

with nucleomegaly, hyperchromasia and irregular nuclear contour. The differential diagnosis for the presence of multinucleated cells in cervical pap smears include atrophy, histiocytes collection, tissue repair, ciliary metaplasia, viral infections, granulomas, radiation, folic acid deficiency, syncytiotrophoblast cells and malignancy [2].

In cases with inflammation and atrophy multinucleation was seen with other reactive changes in intermediate cells as described in Bethesda system of reporting cervical cytology [3]. The case with history of tamoxifen intake showed 'small blue cells' and multinucleate cells, which were similar to those described by Stewart LO et al., [4]. The absence of atypical cells in the background and the round regular nucleus with dispersed chromatin in multinucleate cells ruled out malignancy in this case. The presence of multinucleation and reactive changes in pap smear of a case with intrauterine contraceptive device use were similar to those changes reported by Kishan Prasad HL [5]. The changes include intracytoplasmic vacuoles, Intrauterine Device (IUD) cells, metaplastic cells, multinucleation and psammoma body formation. Tubal metaplastic cells were considered as a potential pitfall in cytological diagnosis [6], which mandated proper identification of these cells to avert biopsy. The findings in herpes simplex infection were similar to those reported by Coleman DV showing multinucleation with ground glass nucleus and intranuclear inclusions [7].

These findings suggest that cases with multinucleation in Papanicolaou Smear smear should be carefully screened and correlated with clinical history to prevent erroneous reporting of malignancies and subsequently subjecting the patient to unnecessary interventions.

REFERENCES

[1] Bales CE. Laboratory Techniques. In: L.G. Koss, editor. Koss' Diagnostic Cytology and it's Histopathologic Basis, 5th ed. Philadelphia: Wolters Kluwer Health; 2006. Pp. 1592-93.
[2] Hoda RS. Basic Cytology Principles. In: SA Hoda, RA Hoda, editors. Fundamentals of PAP test Cytology. New Jersey: Humana Press; 2007. Pp. 12.
[3] Daniel FI, et al. Non-neoplastic Findings. In: Ritu. N, David. CW, editors. The Bethesda System for Reporting Cervical Cytology, 3rded. New York, Springer; 2015. Pp. 29-90.
[4] Stewart LO, Jill C, Sandra KH, Diva RS. Small cells in cervical-vaginal smears of patients treated with tamoxifen. Cancer Cytopathology. 2001;93(1):23-28.
[5] Kishan Prasad HL. Intrauterine contraceptive device and the cervicovaginal smear– Exploring the enigma. Med J DY Patil Vidyapeeth. 2019;12:150-51.
[6] Novotny DB, Maygarden SJ, Johnson DE, Frable WJ. Tubal Metaplasia. A frequent potential pitfall in the cytological diagnosis of endocervical glandular dysplasia on cervical smears. Acta Cytol. 1992;36(1):01-10.
[7] Coleman DV. Cytological diagnosis of virus infected cells in papanicolauo smears and its application in clinical practice. J Clin Pathol. 1979;32:1075-89.

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