MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Women's Health Science Journal
ISSN: 2639-2526

Excurve and Emit Lobular Endocervical Glandular Hyperplasia

Anubha B*

Consultant Histopathology, AB Diagnostics, India

***Corresponding author:** Anubha Bajaj, Consultant Histopathology, A. B.diagnostics, A-1,Ring Road Rajouri Garden, New Delhi, 110027, India, Tel: 00911141446785; Email: anubha.bajaj@gmail.com

Mini Review

Volume 7 Issue 2

Received Date: September 28, 2023

Published Date: October 30, 2023

DOI: 10.23880/whsj-16000189

Abstract

Lobular endocervical glandular hyperplasia of uterine cervix is a benign, exceptional lesion with a characteristic proliferation of miniature, spherical glands accompanied by gastric type differentiation. The discrete lobules incriminate upper endocervical canal of predominantly premenopausal women. Lobular endocervical glandular hyperplasia and gastric subtypes of cervical glandular lesions appear non concurrent to persistent infection with high risk variants of human papilloma virus (HPV). Cytological examination depicts mono-layered sheets of tall, columnar, mucinous cells demonstrating smooth nuclear outline with absent cellular or nuclear atypia or mitotic figures. Papanicolaou stained smears exemplify extracellular or intracellular, golden yellow mucin, indicative of gastric subtype of cellular differentiation. The well-defined lobular or acinar lesion is comprised of a centric crypt with circumscribing glandular articulations and miniature, spherical cysts which configure a floret-like pattern. Centric and peripheral glands are layered with columnar epithelial cells pervaded with pale, eosinophilic cytoplasm, bland, miniature, basal nuclei with mild nuclear atypia. Atypical cytological and architectural features may progress into the malignant 'atypical lobular endocervical glandular hyperplasia', currently contemplated as a category of gastric type adenocarcinoma in situ (GAIS). The lesion is immune reactive to pyloric gland mucin (HIK1083), MUC6, PAX2 or chromogranin A. Lobular endocervical glandular hyperplasia of uterine cervix requires segregation from neoplasms such as human papilloma virus (HPV) independent endocervical adenocarcinoma, gastric type, pyloric type metaplasia, gastric type adenocarcinoma in situ, type A tunnel clusters, micro glandular hyperplasia and mesonephric remnants or mesonephric hyperplasia of uterine cervix. Lesions detected upon surgical tissue sampling, cervical loop electrosurgical excision procedure (LEEP) or conisation may be optimally managed with total abdominal hysterectomy.

Keywords: Glandular Proliferation; Gastric Differentiation; Atypical Variant

Abbreviations: CEA: Carcinoembryonic Antigen; HPV: Human Papilloma Virus; ER: Oestrogen Receptors; PR: Progesterone receptors; LEGH: Lobular Endocervical Glandular Hyperplasia; MDA: Minimal Deviation Adenocarcinoma; GAIS: Gastric Type Adenocarcinoma In Situ; LEEP: Loop Electrosurgical Excision Procedure; MDA: Minimal Deviation, gastric type Adenocarcinoma; SMMN/FGT: Synchronous Mucinous Metaplasia and Neoplasia of Female Genital Tract; PAS: Periodic Acid Schiff's; CEA: Carcino Embryonic Antigen.

Introduction

Lobular endocervical glandular hyperplasia of uterine cervix is a benign, exceptionally encountered lesion characteristically displaying proliferation of discrete

lobules of miniature, spherical glands accompanied by gastric type differentiation. Initially scripted by Nucci MR [1] lobular endocervical glandular hyperplasia is incidentally discovered and frequently associated with concomitant malignant metamorphosis wherein lesion may be challenging to alleviate [1]. Generally, lesion incriminates upper endocervical canal and is predominantly discerned within premenopausal women. High risk variants of human papilloma virus (HPV) are non-concurrent with the lesion which appears immune nonreactive to human papilloma virus(HPV). Lobular endocervical glandular hyperplasia represents with a spectrum of gastric type epithelium layering uterine cervix. Lesion appears immune reactive to HIK1083+, MUC6+ or PAX2+ and immune nonreactive to carcinoembryonic antigen (CEA), oestrogen receptors (ER) or progesterone receptors (PR). Atypical cytological and architectural features may incur progression into malignant counterpart, designated as 'atypical lobular endocervical glandular hyperplasia', which is currently contemplated as a category of gastric type adenocarcinoma in situ (GAIS). Segregation is necessitated from well differentiated, minimal deviation, gastric type adenocarcinoma (MDA), additionally denominated as adenoma malignum or a malignant neoplasm designated as human papilloma virus (HPV) independent endocervical adenocarcinoma, gastric subtype.

Mean age of disease emergence is 45 years to 49 years whereas the lesion is encountered within comprehensive age range of 37 years to 71 years. Disease incidence is apparently underestimated, possibly on account of inadequate tissue sampling of the grossly benign appearing uterine cervix [2,3]. Lobular endocervical glandular hyperplasia is situated upon superior segment of endocervical canal and appears confined to inner half of cervical wall, in contrast to the transformation zone.

Lobular endocervical glandular hyperplasia emerges as a spectrum of pyloric gland metaplasia exemplified within uterine cervix. The lesion is posited to constitute as a metaplastic process on clinical and molecular grounds. Nevertheless, lesion is frequently associated with gastric type adenocarcinoma (~20%). Additionally, chromosomal gain 3q and loss 1p loss may be exemplified, akin to gastric type adenocarcinomas. Lobular endocervical glandular lesion appears concurrent with Peutz-Jeghers syndrome arising in concurrence with germ line mutation STK11 / LKB1. Besides, lesion may be accompanied by the contemporary synchronous mucinous metaplasia and neoplasia of female genital tract (SMMN/ FGT) [2,3]. Lobular endocervical glandular hyperplasia and various gastric subtypes of cervical glandular lesions appear non concurrent to persistent infection with high risk variants of human papilloma virus (HPV). An estimated 58% of lobular endocervical glandular hyperplasia delineate precise genetic mutations within GNAS, STK11 or KRAS genes. Possibly, accrual of STK11 genomic mutations permits neoplastic progression from lobular endocervical glandular hyperplasia (LEGH) to minimal deviation adenocarcinoma (MDA) of the uterine cervix [2,3]. Whole exome genetic sequencing adopted within pure lesions of lobular endocervical glandular hyperplasia delineates absence of established carcinogenic chromosomal mutations, thereby indicating possible contribution into epithelial metaplasia. Driver genomic mutations may appear within lesions of delayed emergence as atypical or minimal deviation adenocarcinoma (MDA) associated lobular endocervical glandular hyperplasia. Atypical lobular endocervical glandular hyperplasia enunciates molecular alterations concurrent with minimal deviation adenocarcinoma such as chromosomal 3q gain and chromosomal 1p loss [2,3].

Lobular endocervical glandular hyperplasia frequently appears as an incidental lesion discovered upon evaluation of specimens of total abdominal hysterectomy or cervical loop electrosurgical excision procedure (LEEP) [2,3]. An estimated 50% lesions represent with symptoms indicative of minimal deviation adenocarcinoma (MDA). Incriminated subjects manifest with watery or mucoid vaginal discharge. Besides, a tumefaction may be confined to uterine cervix [2,3]. Cytological examination depicts mono-layered sheets of tall, columnar, mucinous cells demonstrating smooth nuclear outline. Cellular or nuclear atypia or mitotic figures are exceptional to absent. Features such as glandular complexity or loss of polarity are absent. Papanicolaou stained smears exemplify extracellular dissemination or intracellular accumulation of golden yellow mucin, indicative of gastric subtype of cellular differentiation. Intra-nuclear cytoplasmic inclusions are commonly encountered, in contrast to cells configuring minimal deviation adenocarcinoma (MDA). Smears stained with Periodic acid Schiff's (PAS) stain exhibit intra cytoplasmic impaction of neutral mucin. Apical localization of neutral mucin appears indicative of atypical lobular endocervical glandular hyperplasia or invasive adenocarcinoma [4,5]. Grossly, lesion is characteristically confined within inner half of uterine cervix and situated upon superior aspect abutting the internal os. Cut surface depicts cystic spaces of variable magnitude encompassed within a thickened, fibrotic cervical wall. Upon microscopy, well defined lesion with lobular or acinar architecture appears comprised of a centric crypt. Occasionally, cystic dilation may ensue. Circumscribing glandular articulations and cysts appear miniature, spherical and configure a floret-like pattern. Majority of lesions are confined within wall of inner one third of uterine cervix. Additionally, enlarged, cystic lesions appear embedded within the cervical wall. Centric and peripheral glands appear layered with columnar epithelial cells pervaded with pale, eosinophilic cytoplasm and bland, miniature, basal nuclei. Nuclear atypia appears

mild. Centric glandular articulations may preponderantly depict foci of intestinal metaplasia. Foci of stromal desmoplasia, irregularly articulated glandular structures or squamous differentiation appear absent. Mitotic figures are absent [4,5]. Atypical lobular endocervical glandular hyperplasia, currently designated as a variant of gastric subtype of adenocarcinoma in situ (GAIS), appears to simulate the architecture of lobular endocervical glandular hyperplasia in concordance with ≥ 4 morphological features designated as

- nuclear enlargement
- irregular nuclear outline
- distinct nucleoli and coarse nuclear chromatin
- loss of cellular polarity
- occasional mitotic figures
- apoptotic bodies or occurrence of luminal nuclear debris
- Intraluminal papillary projections [4,5].

Cytological features	HSIL with Glandular Involvement	Glandular lesion
Architecture	Syncytial clusters	Loss of honeycomb pattern
	Peripheral nuclear flattening	Loss of nuclear polarity
	Central whirling	Nuclear crowding with overlapping
Nuclear features		
Chromatin pattern	Coarse	Fine
Nuclear grooves	Frequently present	Absent
Nucleoli	Absent	Frequently present
Cytoplasmic features		
Cytoplasmic processes	Present	Absent
Vacuolation	Absent	Present

HSIL: high grade squamous intraepithelial lesion

Table 1: Differentiation between HSIL with glandular involvement and glandular lesion [4].

Lobular endocervical glandular hyperplasia exhibits pale red or magenta cytoplasmic hue of neutral mucin upon staining with Periodic acid Schiff's (PAS)- Alcian blue stain, in contrast to acidic endocervical type mucin which stains dark blue or purple. Staining profile of neutral mucin is significantly specific and sensitive while segregating gastric type from nongastric type of endocervical adenocarcinoma. Besides, the lesion is immune reactive to pyloric gland mucin (HIK1083), MUC6, PAX2 or chromogranin A.

Atypical lobular endocervical glandular hyperplasia demonstrates elevated Ki67 proliferative index which varies from 1% to 10%. Few instances display abnormal expression of p53 [5,6]. Lobular endocervical glandular hyperplasia appears immune nonreactive to carcinoembryonic antigen(CEA), oestrogen receptor(ER), progesterone receptor(PR), p16 or human papilloma virus (HPV) as discerned with in situ hybridization(ISH) [5,6]. Lobular endocervical glandular hyperplasia of uterine cervix requires segregation from neoplasms such as human papilloma virus (HPV) independent endocervical adenocarcinoma, gastric type, pyloric type metaplasia , gastric type adenocarcinoma in situ, type A tunnel clusters, micro glandular hyperplasia and mesonephric remnants or mesonephric hyperplasia of uterine cervix [5,6]. Lobular endocervical glandular hyperplasia may be indicated upon assessment of conglomerate of features discerned with magnetic resonance imaging (MRI) and Papanicolaou smear of cervix. Nevertheless, precise histological evaluation remains mandatory for definitive disease discernment and exclusion of occult, malignant disorders. Imaging studies depict multiple, enlarged cysts encompassing a miniature, centric, solid component confined within upper cervix, designated as the 'cosmos' pattern, as the countenance is reminiscent of flower 'Cosmos bipinnatus' [6,7]. Gastric type adenocarcinoma and minimal deviation adenocarcinoma predominantly represent as solid lesions. Few lesions may display concordant morphological features. T1 weighted magnetic resonance imaging (MRI) may enunciate a hypo-intense lesion with 'cosmos' pattern, in contrast to circumscribing cervical stroma. Aforesaid features are preponderantly (95%) specific for gastric type, mucin secreting lesions [6,7]. Additional therapy or follow up appears unnecessary for managing 'pure', benign lesions of lobular endocervical glandular hyperplasia devoid of atypical morphology, which are discerned upon examination of surgical specimens of total abdominal hysterectomy [6,7]. Lesions detected upon surgical tissue sampling, cervical loop electrosurgical excision procedure (LEEP) or conisation may be managed with total abdominal hysterectomy is preferred in order to exclude absence of coexistent minimal deviation

adenocarcinoma or gastric type adenocarcinoma in situ (gAIS). Aforesaid surgical manoeuver may be deferred in instances where preservation of fertility is necessitated. ~appearance of cogent clinical symptoms as vaginal discharge or cervical tumefaction warrants extensive monitoring with adoption of diagnosticimaging and surgical tissue sampling. ~cogent disease discernment upon surgical tissue sampling necessitates active adoption of cervical loop electrosurgical excision procedure or conisation of uterine cervix. ~multi-cystic, gastric mucin secreting lesions of uterine cervix detected upon magnetic resonance imaging (MRI) or Papanicolaou smear of cervix require additional evaluation [6,7].

Majority of lesions appear benign and devoid of reoccurrence or distant metastases. Subsequently, minimal deviation adenocarcinoma coexistent with lobular endocervical glandular hyperplasia may manifest with premalignant countenance [6,7]. Molecular assay aptly classifies premalignant potential of lobular endocervical glandular hyperplasia. Whole exome genetic sequencing appears to lack evident transformation of lobular endocervical glandular hyperplasia into minimal deviation adenocarcinoma (MDA). Atypical lobular endocervical glandular hyperplasia with aberrant cytological or architectural features is exceptionally observed and may metamorphose into a malignant neoplasm. Comprehensive surgical extermination is an optimal and recommended mode of therapy. Around 41% of gastric type adenocarcinomas of uterine cervix appear concurrent with lobular endocervical glandular hyperplasia [6,7] Figures 1 & 2.

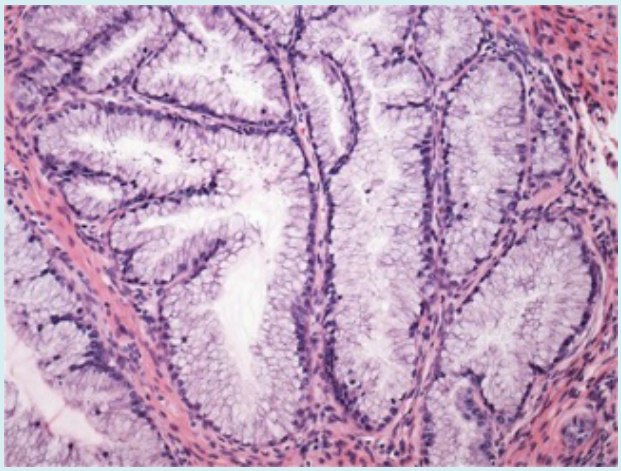

Figure 1: Lobular endocervical glandular hyperplasia demonstrating lobular architecture comprised of glandular articulations layered by tall, columnar, mucin secreting epithelium imbued with eosinophilic cytoplasm, basal nuclei and minimal atypia. Mitotic activity is minimal [8].

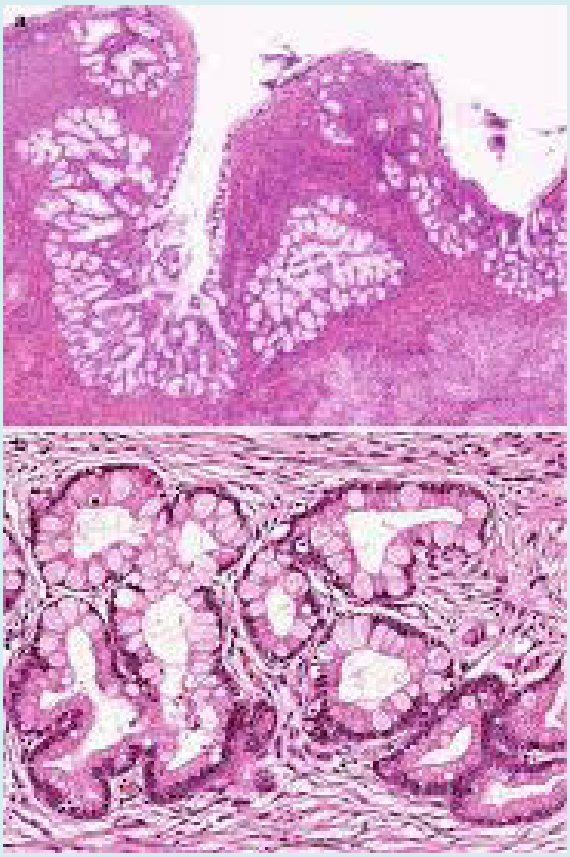

Figure 2: Lobular endocervical glandular hyperplasia delineating acinar architecture constituted of glandular configurations lined by tall, columnar, mucin secreting epithelium permeated with eosinophilic cytoplasm, basal nuclei and minimal atypia. Mitotic activity is minimal [9].

References

1. Nucci MR, Clement PB, Young RH (1999) Lobular endocervical glandular hyperplasia not otherwise specified a clinic pathologic analysis of thirteen cases of a distinctive pseudoneoplastic lesion and comparison with fourteen cases of adenoma malignum. AmJ Surg Pathol 23: 886-891.

2. Molero A, Parra A, Blanco I, Ascensión A (2023) Lobular Endocervical Glandular Hyperplasia a mimicker and potential pitfall for HPV independent well differentiated Gastric type Endocervical Adenocarcinoma Case report and literature review focusing on histology. immunophenotype and molecular findings. SAGE Open Med Case Rep.

3. Kimura F, Ohshima K, Shirai K, Kanai R, Sonohara M, et al. (2023) Discriminant Analysis using Gabor Filter Sets for Lobular Endocervical Glandular Hyperplasia

Numerical Interpretation of Nuclear Atypia by Gabor Filter Features. Acta Cytol 67(5): 539-549.

4. Shin E, Yu J, Hong SW (2023) Trouble makers in cytologic interpretation of the uterine cervix. J Pathol Transl Med 57(3): 139-146.

5. Miyamoto T, Kobara H, Shiozawa T (2022) Biology and management of lobular endocervical glandular hyperplasia. J Obstet Gynaecol Res 48(12): 3056-3067.

6. Yoshino A, Kobayashi E, Tsuboyama T, Fukui H, Tomiyama N, et al. (2023) Novel Strategy for the Management of Cervical Multicystic Diseases. Ann Surg Oncol 30(5): 2964-2973.

7. Shiro R, Kotani Y, Ohta M, Sato H, Kashima Y, et al. (2023) Diagnostic Utility of Hysteroscopic Biopsy in Cases of Suspected Lobular Endocervical Glandular Hyperplasia and Comparison with Cervical Conization. Healthcare (Basel) 11(11): 1619.

8. Image 1 Courtesy: Nature.com.

9. Image 2 Courtesy: Basic medical key.