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Case Report
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Non Cervical Glandular Neoplasia on Cervical Cytology: Histological Outcome of Three Cases

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Keywords

Non-cervical glandular Neoplasia; Cervical screening

Introduction

Cervical cytology reporting glandular neoplasia is rare, with an incidence of 0.4% in England [1], which has been increasing since the widespread use of Liquid Based Cytology (LBC). Non-Cervical Glandular Neoplasia (NCGN) confirmed by cytological screening may represent cells from adenocarcinoma originating from endometrial, ovarian, fallopian tubes or metastatic lesions from beyond the genital tract [2].

We present three cases of Caucasian women, with previous normal smear tests, whom their cervical screening, revealed NCGN.

Case Presentation

Case 1

A 57 year old, was referred to gynecology clinic, following cervical screening showing vacuolated clusters of endometrial cells with focal engulfed neutrophils (no recent menstruation); cervical cells were normal.

Hysteroscopy directed endometrial biopsy showed complex hyperplasia with no atypia. After discussion at the Multi Disciplinary Team (MDT) meeting, tumor markers CA 125 (34.5 U/ml) and CEA (1.319 ng/ml) were within normal limits. A Computerized Tomography (CT) scan of the abdomen and pelvis demonstrated bulky uterus with no other abnormalities. She underwent Total Abdominal Hysterectomy (TAH) and Bilateral Salpingo-Oophorectomy (BSO). Histological examination confirmed an ovarian serous borderline tumor, FIGO Stage 1A.

Case 2

A 44 year old, underwent colposcopic examination following an abnormal smear test reported as NCGN, which revealed outlined an area of aceto-whitening, with mosaicism (appearances of CIN1). Large Loop Excision of the Transformation Zone (LLETZ) procedure was performed, the histology of which was normal. Endometrial biopsy revealed proliferative endometrium. A preoperative CT scan of the abdomen and pelvis, showed endometrial thickness of 10 mm with no evidence of invasion. An uneventful TAH with BSO was subsequently performed thereafter. Cytology of the peritoneal washings found malignant epithelial cells against a background of mesothelial cells.

Histological examination of both ovaries revealed an invasive, high-grade serous adenocarcinoma with focal psammomatous calcification; both ovarian capsules were breached with involvement of the surface, staged as FIGO Stage 1C. Thus, she completed six cycles of Carboplatin and Paclitaxel and is under three monthly surveillance with CA125 levels monitoring.

Case 3

A 49 year old, was seen in gynecology clinic duean episode of PMB. An opportunistic cervical smear test was taken, followed by hysteroscopy which revealed a 1.2 cm endometrial polyp. Colposcopic examination showed a low-grade intraepithelial lesion; cervical biopsy was obtained.

Cervical cytology reported numerous clusters of markedly atypical glandular cells and coexisting high-grade dyskaryosis. Following MDT meeting, LLETZ procedure along with hysteroscopy, polypectomy and endometrial biopsy were performed.

Histology of the endometrium confirmed a grade 1 endometroid adenocarcinoma, while that of the polyp revealed poorly differentiated clear cell mixed adenocarcinoma.MRI showed polypoidal

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Table 1: Details of the patients with non-cervical glandular neoplasia.

Abdominal/speculum examination	Hysteroscopy/ Endometrial biopsy	CT scan abdomen and pelvis	Final diagnosis	Stage
Unremarkable	Complexhyperplasia with no atypia	Bulky uterus only	Serous ovarian borderline tumor	1A
Mild cervical erosion	Proliferative endometrium	Endometrial thickness 10 mm. Right adnexal focus of 3.5cm with mixed signal and atypical imaging features	High-grade serous adenocarcinoma	1C
Unremarkable	EB: grade 1 endometroid adenocar	Polypoidal mucosal thickening of the endometrium with bilateral obturator and right common iliac lymph nodes Polyp: poorly differentiated clear cell mixed adenocarcinoma cinoma	High-grade endometrial mixed clear cell and endometroid adenocarcinoma	1A

PMB: Post Menopausal Bleeding
EB: Endometrial Biopsy

mucosal thickening of the endometrium with bilateral obturator and a right common iliac lymph nodes, hence staged the tumor as T1aN0 M0.

Subsequently, the patient underwent laparoscopic total hysterectomy with BSO and pelvic lymphadenectomy. Postoperative pathology confirmed high-grade endometrial mixed clear cell and endometroid adenocarcinoma, Stage 1A with no lympho-vascular space invasion.

Discussion

While the primary aim of cervical screening program is to screen for cervical neoplasia, the incidental finding of NCGN presents a diagnostic and cytological challenge [3]. The incidence of significant pathology and invasive cancer among women with atypical glandular cells on LBC varies between 15.3% to 43.3%, in some studies that included endocervical, endometrial and ovarian adenocarcinomas [1,3,4]; Thus a cytological diagnosis of NCGN requires investigations not only of the cervix but of the uterine body and associated glandular organs.

The risk of malignancy has been reported to be higher in women older than 40 years like in our report [3,4]. Women older than 51 years are more likely to have significant serious under lying lesions [3,4]. Incidence of non-cervical lesions is significantly higher in postmenopausal women [5,3]. By contrast, in premenopausal women the prevalence of cervical and non-cervical lesions was similar [5].

Atypical Glandular Cells (AGC) show changes not explained by reactive or reparative attrition and not demonstrating the unequivocal features of invasive adenocarcinoma [4]. Some difficulties in the identification of NCGN are recognized [6]. Firstly, changes associated with intrauterine devices may include clusters of highly vacuolated cells but are usually few and show minimal atypia. This can make it difficult to differentiate from vacuolated forms of adenocarcinoma. Secondly, presence of psammoma bodies, in cervical sample are rare but potentially sinister finding [7,8].

Immediate gynaecological referral and thorough evaluation of the genital tract within two weeks are important, rather than a colposcopic examination alone [1]. Investigations to exclude endometrial and other pathology, should include hysteroscopy, endometrial biopsy and CT scan of the abdomen and pelvis. Following this, the findings should be discussed at the gynaecology oncology MDT meeting. In conclusion, cervical cytology reported as NCGN is associated with a high probability of clinically significant lesions, such as endometrial and ovarian cancer. All cases should be registered nationally and protocols should be in place for the management of this significant finding.

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