Molecular pathophysiology behind gynecologic cancers-vulvar, cervical and cancer in corpus uteri.

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Introduction

Gynecologic cancer refers to cancer that starts in a woman's reproductive organs. Cancer is named by the part of the body where cancer first occurs. Gynecologic cancers can begin anywhere in a woman's pelvis, the area beneath her stomach and between her hip bones. Pathology reports provide histopathologic diagnosis as well as detailed information on prognosis and treatment options. As a result, pathologists must be knowledgeable about the staging, classification, and treatment of gynecologic cancers to ensure that their results are therapeutically relevant [1]. Similarly, in order to properly appreciate the pathology report, the gynecologic oncologist must be familiar with the terminology used in gynecologic pathology.

Pathology behind vulvar cancer

It starts in the vulva, the female genital organs' outer layer. There are various types of vulvar cancer. Squamous intraepithelial lesions (VIN) that are single or several can be macular, papular, or plaque-like. Mild dysplasia is represented by low-grade SIL (VIN 1), while moderate and severe dysplasia is represented by high-grade SIL (VIN 2–3). High-grade SIL (VIN 3) is the most common kind of SIL (squamous intraepithelial lesion), which includes squamous cell carcinoma in situ [CIS]. This disease is treated with a broad excision.

Although most tumours are exophytic, ulcerative tumours do exist. The tumour is made up of keratin pearls in the centre of invasive nests of malignant squamous epithelium [2]. The tumours often expand slowly to the surrounding skin, vagina, and rectum. The superficial inguinal lymph nodes are frequently the first to be affected, followed by the deeper inguinal, femoral, and pelvic lymph nodes.

Pathology behind cervical cancer

The cervix, or lower, narrow end of the uterus, is where cervical cancer begins. The uterus is also known as the womb. Persistent HPV infection is the cause of CIN (cervical intraepithelial neoplasia) and cervical cancer. SIL (CIN1) is a permissive infection (i.e. HPV is episomal, freely replicates, and thereby causes cell death). A huge number of virus particles must clump together in the cytoplasm before a koilocyte can be observed. In the majority of cases with high-grade SIL, viral DNA integrates into the cell genome (CIN2-3).

The E6 and E7 genes create HPV 16 proteins that bind to and inactivate the tumour suppressor proteins p53 and Rb, rendering them ineffective. When HPV integrates into host DNA, copies of the whole virus do not accumulate in many cases of high-grade dysplasia and all invasive cancers, and koilocytes are absent. In high-grade CIN cells, HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68 are usually observed [3]. With some geographical variation, HPV types 16 and 18 are found in 70% of invasive malignancies worldwide; the other high-risk variants account for the remaining 25%.

SIL CIN is nearly always a metaplastic squamous epithelium transformation zone disease. As evidenced by morphological anomalies in cellularity, differentiation, polarity, nuclear features, and mitotic activity, CIN disturbs the normal maturation process of cervical squamous epithelium. High-grade SIL is synonymous with severe dysplasia and CIS (CIN3).

Pathology behind cancer in corpus uteri

Endometrial carcinoma is the sixth most common cancer diagnosed in women globally, with an age-standardized incidence rate of 8.2 per 100000. In developed countries, it is the most common gynecologic cancer and the fourth most common cancer in women. Three-quarters of postmenopausal women develop endometrial cancer.

Pathophysiology

Normal endometrial cells become endometrioid carcinoma, according to the dualistic model of endometrial carcinogenesis, due to replication errors, so-called microsatellite instability, and the accumulation of mutations in oncogenes and tumour suppressor genes. Nonendometrioid carcinomas undergo malignant transformation due to changes in p53 and loss of heterozygozity on multiple chromosomes [4].

In type I endometrioid carcinomas, microsatellite instability (25-30%), PTEN mutations (30-60%), PIK3CA mutations (26-39%), ARID1A (20%), K-RAS mutations (10-30%), and CTNNB1 (-catenin) mutations with nuclear protein accumulation (25-38%) have all been discovered. On the other hand, most type II nonendometrioid carcinomas have p53 mutations, Her-2/neu amplification, and heterozygosity loss on several chromosomes. Nonendometrioid carcinomas can arise from endometrioid carcinomas with microsatellite instability due to tumour growth and subsequent p53 mutations.

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***Received:** 11-May-2022, Manuscript No. AABMCR-22-63622; **Editor assigned:** 13-May-2022, PreQC No. AABMCR-22-63622(PQ); **Reviewed:** 21-May-2022, QC No AABMCR-22-63622; **Revised:** 24-May-2022, Manuscript No. AABMCR-22-63622(R); **Published:** 27-May-2022, DOI:10.35841/aabmcr-6.3.112*

***Citation:** Fox S. Molecular pathophysiology behind gynecologic cancers-vulvar, cervical and cancer in corpus uteri. Biol Med Case Rep. 2022;6(3):112*

The Cancer Genome Atlas (TCGA) has completed the most comprehensive genomic study of endometrial carcinomas yet undertaken. To the dualistic classification of endometrial carcinoma (types I and II), the TCGA has added four new molecular subgroups: (1) an ultra-mutated POLE subgroup; (2) a hyper mutated microsatellite unstable subgroup; (3) a copy-number low/microsatellite stable subgroup; and (4) a copy-number high/serous-like subgroup. Despite overlapping molecular genetics data making it difficult to discern meaningful prognostic categories, POLE mutations indicate better prognosis, particularly in high-grade malignancies [5]. Patients with serous-like endometrioid tumours, on the other hand, might benefit from serous carcinoma treatment.

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