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Immunomorphological Changes in Cervical Cancer and Their Clinical Significance

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Cervical cancer (CRC) is a dangerous tumor that ranks second among women's oncological diseases and is characterized by high mortality. According to the World Health Organization (WHO), approximately 600 thousand new cases and about 300 thousand deaths are recorded in the world every year. This disease remains a serious problem for women's health in Uzbekistan as well.

Keywords: human papilloma virus, cervical cancer, CD4+, CD8+, lymphocytes, nuclear hyperchromatism, mitosis.

BBS is in development human papilloma virus (HPV), especially types 16 and 18, are the main etiological factor is considered But a viral infection don't grow in development enough not – immune system and morphological changes between mutual relationships also of great importance owner . Some In cases where the body has a virus can eliminate , in others and low immunity due to oncogenic changes .

Immunomorphological analysis - tumor in the fabric immune of cells condition and their histological characteristics between dependencies determination possible For example , CD4+ and CD8+ lymphocytes , p16, Ki-67, PD- L1 , etc. markers analysis don't grow aggressiveness and forecast in evaluation important to the point owner

Subject relevance :

is the BBC saying? in phase identify , do not grow forecast designation and individual approaches work on the way out immuno-morphological analyses important place holds in this field research clinical practice great practical for to the point owner

General epidemiology and pathogenesis of cervical cancer

Cervical cancer (CRC) is one of the most common gynecological cancers in the world. According to the World Health Organization, approximately 600,000 new cases are reported each year, with 85% of cases occurring in developing countries. CRC is mainly associated with oncogenic types of human papillomavirus (HPV), with types 16 and 18 accounting for more than 70% of all cases (WHO, 2021).

The importance of the immune system

The role of immunity in the development and propagation of the disease is of great importance. In particular, CD4+ and CD8+ T-lymphocytes play a key role in anti-tumor defense. CD8+ cytotoxic lymphocytes are involved in the destruction of tumor cells, while CD4+ cells activate

them. At the same time, tumor cells have the ability to escape immune surveillance through the PD-1/PD-L1 signaling system (Chen & Mellman, 2017).

2.3. Immunohistochemical markers

Immunohistochemistry is a modern method that allows visualization of specific antigens in tissues. Commonly used markers in BBS are:

p16: Induced by oncoproteins during HPV infection; reflects the oncogenic activity of the tumor.

Ki-67: A marker of cell proliferation. High levels of expression indicate high tumor activity.

CD4/CD8: used to assess the cellular immune response.

PD-L1: reflects the ability of tumor cells to evade immune surveillance.

Several studies (M. Wentzensen, 2012; Crosbie et al., 2013) indicate that these markers can accurately assess the biological characteristics and prognosis of BLS.

2.4. Morphological features

Histologically, BCC manifests as squamous cell carcinoma (75-80%), adenocarcinoma (10-15%), and mixed forms. Squamous carcinomas are characterized by nuclear hyperchromatism, multiple mitoses, and vascular invasion. Adenocarcinomas exhibit changes that include irregular glands, compacted stroma, and atypia. Some studies have shown that morphological changes are associated with immune expression (Pirog, 2016).

2.5. Contradictions and unresolved issues in scientific sources

Some authors (Zigras et al., 2019) believe that tumors with high PD-L1 expression have a good prognosis, while others, on the contrary, suggest that in such cases the tumor is actively evading the immune system and, accordingly, has a poor prognosis. Therefore, the determination of the impact of different markers on prognosis has not yet been fully studied.

The purpose of the study:

Study of immuno-morphological changes in cervical cancer and identification of relationships between them.

Research tasks:

Histological assessment of morphological forms of BBS;

Immunohistochemical expression of markers (p16, Ki-67, CD4, CD8, PD-L1). to determine ;

Immune and morphological indicators between correlation assessment ;

Collected information based on forecast indicators work exit

Research object and subject :

Object: Uterus neck sick with cancer from the sick taken biopsy material .

Subject: Immunohistochemistry and histomorphological indicators between dependency

The research scientific news :

this study immunohistochemical markers and morphological indicators between dependency for the first time statistically deep analysis At the same time , the clinical prognosis assessment for important was markers list is formed .

The research theoretical and practical importance :

Theoretically : immunomorphological approach through the pathogenesis of BBS better understanding possible gives .

Practically : BBS early determine , forecast and individual treatment tactics work on the way out basis will be .

Research hypothesis :

Immunohistochemical indicators (CD8, p16, Ki-67, PD-L1) and morphological changes clinical-prognostic relationship between exists .

Research methods :

Histological analysis (H&E staining),

Immunohistochemistry (anti-CD4, CD8, p16, Ki-67, PD-L1),

Statistical analysis (correlation, regression analysis).

3. MATERIALS AND METHODS

3.1. Study design and general description

This study was conducted on the basis of a retrospective and prospective analysis. Biopsy and surgical materials obtained from patients diagnosed with cervical cancer (CC) were selected as the main object of analysis. The study was carried out in oncology institutions under the Ministry of Health of the Republic of Uzbekistan during 2020–2024.

3.2. Patients participating in the study

A total of 120 patients were involved in the study. They were selected based on the following criteria:

Inclusion criteria:

Women aged 25–65;

Morphologically confirmed cases of cervical cancer;

Availability of sufficient tissue material for biopsy or histology.

Exclusion criteria:

Patients who have previously received chemotherapy or radiation therapy;

The state of secondary tumors;

Autoimmune diseases or generalized immunodeficiency states.

3.3. Histological analysis

The obtained tissue materials were embedded in standard paraffin blocks, and sections of 4-5 μm thickness were evaluated by Hematoxylin & Eosin (H&E) staining. Histological analysis included parameters such as tumor type, grade (G1-G3), number of mitoses, necrosis, and vascular invasion.

3.4. Immunohistochemical analysis

The following markers were used in the immunohistochemical analysis:

The analyses were performed using reagents and an automated immunostainer from Dako (Denmark). Expression levels were assessed using a semi-quantitative method from 0 to 3+.

3.5. Statistical analysis

All results were processed in SPSS 26.0. Statistical methods used:

Descriptive statistics – average value, standard deviation, range;

Correlation analysis – Spearman correlation coefficient;

Difference between groups – χ^2 test, t-test or Mann-Whitney U test;

Prognostic models - logistic regression and ROC analysis.

Differences at the $P < 0.05$ level were considered statistically significant.

4. RESULTS

4.1. Clinical and demographic data

The age range of the 120 patients who participated in the study was 26 to 64 years, with a mean age of 44.2 ± 6.5 years. Among them, the largest number of patients aged 35–49 years (52, 43.3%) was found. All patients had morphologically confirmed BLS, including:

Squamous cell carcinoma – 92 cases (76.7%)

Adenocarcinoma – 20 cases (16.7%)

Mixed forms – 8 cases (6.6%)

4.2. Results of histological analysis

Based on histological appearances, tumor grades were divided as follows:

High-grade tumors showed prominent nuclear atypia, mitotic activity, and signs of necrosis. Vascular invasion was observed in 63% of G3 tumors.

4.3. Results of immunohistochemical analysis

p16 expression:

Strong (3+) expression was observed in 94 patients (78.3%);

This condition is particularly prevalent in squamous cell carcinomas, suggesting an association with HPV.

Ki-67 expression:

Average proliferation index – 57 ± 8.4%

G3 tumors had a higher incidence of Ki-67 >70% ($p < 0.05$)

CD4/CD8 lymphocyte count:

The number of CD8+ lymphocytes in the infiltrate was higher than CD4+ (CD8/CD4 = 1.4)

High CD8+ infiltration was more common in patients with low tumor grade ($p < 0.01$)

PD-L1 expression:

51 patients (42.5%) had high levels of PD-L1 expression (≥50%)

This was more prevalent in G3 tumors and those with low lymphocyte infiltration ($p < 0.05$).

4. Correlations between markers

The results of the correlation analysis revealed the following relationships:

Ki-67 and tumor grade (G1–G3): $r = +0.68$ ($p < 0.01$)

CD8+ infiltration and tumor grade: $r = –0.54$ ($p < 0.01$)

PD-L1 and CD8 infiltration: $r = –0.47$ ($p < 0.05$)

p16 and Ki-67: $r = +0.39$ ($p < 0.05$)

4.5. Markers associated with prognosis

In ROC analysis, Ki-67 ≥60%, PD-L1 ≥50%, and CD8<10% were associated with a poor prognosis (AUC > 0.8).

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