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The virus etiology of warty carcinoma of the uterine cervix

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Abstract: Warty carcinoma is a rare form of squamous cell carcinoma of the uterine cervix and has better prognosis than the high-differentiated squamous cell carcinoma. It is suggested that human papilloma virus (HPV) is causing this type of cancer. Our results show that not all patients have presents of HPV and probably not only this virus is responsible for this type of cervical cancer.

keyword: cervical cancer, warty carcinoma, human papilpma virus

Introduction:

Warty carcinoma is a rare variant of the malignant diseases that affect the uterine cervix (1, 2). The most common location of this tumor is in the anal and genital area- vulva, vagina and uterine cervix, anus and penis. (3) As a clinical behavior, it stands between the varicose and the low grade squamous cell carcinoma. Warty carcinoma consists of invasive tumor cells, amid which there are condyloma cells.

Aim: Our aim is to find out if HPV is the only viral etiology in the pathogenesis of warty carcinoma.

Materials and methods: There are 775 women with carcinoma of the uterine cervix, who were operated in the Clinic of Oncologic Gynecology, UMHAT "Doctor Georgi Stranski"-Pleven for a period of eight years (2007-2015). Warty carcinoma is the histologic variant in fifteen of the cases. We used immunohistochemically analysis with the antibodies Mo a Hu Papillomavirus (HPV), Clone K1H8 and FLEX Monoclonal Mo a Epstein-Barr Virus, LMP, Clone CS.1-4, RTU to see if there are traces of HPV. The tested typing included staining for two viruses- HPV and EBV.

Results: The retrospective analysis of the fifteen cases show that all patients are alive until the moment of this publication, (4-93 months survival mean 48.5 months), which resonates with the better prognosis, described in the latest research on the topic.

The conventional immunohistochemically stain proves viral presence (HPV/EBV) in five cases, but generally the staining intensity and distribution were very weak and limited. Immunohistochemistry proves the presence of HPV in only two cases (13.3%). This viral expression is lesser than the results of Nam Hoon Cho et al. (4) who prove HPV in 55.6% by conventional immunohistochemistry. The HPV signals were absolutely detected within the nuclei of the uppermost layer and occasionally within those of koilocytes in the intermediate layer, but not within the basal level. Surprisingly, the presence of EBV was detected in another three samples (20%). The stains were positive in the cell's cytoplasm. The remaining 10 samples did not show the presence of either HPV or EBV. The viral positivity was only partial- 20-30% (mean 25%). Importantly, the viral positivity of the latest sample from less than a year before the immunohistochemistry was 60% positive.

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Discussion: Malignant warty lesion of the uterine cervix is a rare histologic type. It has been recently sub classified as a variant of squamous cell carcinoma (SCC). A typical feature of warty carcinoma is the presence of koilocytes, in the superficial and intermedia area of the epithelium and the microscopic examination reveals a biphasic pattern composed of a condylomatous and papillary configuration at the surface and SCC at the bottom. It seems that the malignant foci are directly transformed from condyloma. Commonly there is polypoid growth into the cervical lumen and infiltrative dyskeratosis. (4). Koilocytes are traditionally related to HPV infection, although according to our data the viral presence may be of EBV, instead of HPV, regardless of the microscopic findings.

This histologic type has better prognosis, when compared to well differentiated cervical sqamous cell carcinoma. However this histologic type has metastatic potential when it affects other organs - for example the penile warty give metastasis in 17-18% and there are metastasis in the vulvar area too (5). This, however, does not affect the five-year survival rate.

Our results demonstrated variable intensity of HPV/EBV typing with a common finding of strong signals in the most recent sample. Not all koilocytes contained HPV. This can be explained by differences in membrane permeability, nuclear protein, the age of the sample or other causes for accessibility to the viral nuclear acid. Another possibility may be the loss of amplification during the washing step necessary for the abolishment of nonspecific signals. False positive signals cloud interpretations.

Conclusion: Our results show that not every patient has presence of HPV. This can indicate that immunohistochemistry cannot be a sole indicator for the viral presence in warty carcinoma of the uterine cervix. There are many factors that can interfere with the results. They should be compared with in situ hybridization and PCR.

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