

Viruses Causing Neoplastic Diseases

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Editorial

The current issue of Journal of Cell science & Apoptosis focuses on one of my fields of interest - the role of the local viral status - especially the presence or absence of HPV and EBV in some rare histological types of cervical carcinoma such as LELC and warty.

According to IARC there are seven viruses causing neoplastic diseases and classified as Group I. Two of them are HPV and EBV. The long exposure to the viral agent and the severity of the infection are crucial for unlocking the oncogenes that give the start of the malignant process. Both EBV and HPV could lead to carcinoma in number of locations. The different localizations are more frequent in different parts of the world - for example for EBV: It is most widely known as the causative agent of infectious mononucleosis but in Central China it is related to carcinoma of the nasopharynx and in Central Africa - with Burkitt's lymphoma. Epidemiology clearly shows that the age of the patients with malignancy, caused by EBV decreases in the so called Third world countries.

In contrast, HPV is described as the classic causative agent for carcinoma of the uterine cervix. Despite the fact that the majority of the surgical specimens present with HPV infection when examined and the wide spread of the revolutionary vaccine, there are still a lot of new cases every year. This could be explained with the fact, that 10% of cervical cancer is not a result of HPV infection. This is where the role of EBV becomes interesting for the gynecologists.

Lymphoepithelioma is described for the first time as a neoplasm of the nasopharynx. The histological features of this tumor are a syncytial growth pattern of undifferentiated malignant cells with prominent lymphoplasmacytic stromal infiltration. Later the similar tumors have been described in salivary gland, lung, stomach and thymus and have been called lymphoepithelioma-like carcinoma (LELC). In the uterine cervix it was reported for the first time by Hamazaki et al. in 1968. Although it is a very rare tumor it is necessary to be differentiated from the squamous cell carcinoma because of its better prognosis. It is considered that LELC is associated with EBV infection in Asian women and with HPV or no infection in Caucasian patients. Our aim is to confirm whether or not LELC is more commonly associated with HPV infection rather than with EBV infection in Caucasian patients or whether there is no correlation to the previous viral exposure.

Lymphoepithelioma-like cervical cancer is a very rare tumor. First it was thought to be a subtype of poorly differentiated squamous cell carcinoma, histologically characterized by nests of undifferentiated epithelial cells with a syncytial growth pattern infiltrated by a severe lymphocytic infiltrate.

This type of cervical cancer has low frequency - 5.5% in Asians and even less - 0.7% in Caucasians. In the female genital tract it has been reported in the vulva, vagina, uterine cervix and endometrium. It affects mostly younger women than the common cancer of uterine cervix - often less than 40 years old and the tumor size can vary from no visible lesion to a large exophytic mass. The pathogenesis of LELC is unknown but it is suggested that this carcinoma is associated with Epstein Barr Virus (EBV) in the Asian population - Tseng et al. reported

that 73.3% (11/15) of Asian women with this type of cervical cancer were positive for the antibody of EBV. In Caucasians it is suggested that LELC is associated with Human Papilloma Virus (HPV) or have no virus genesis - Noel et al. did not detect EBV and found HPV in some of their patients. Bais et al. also detected HPV in part of their patients. The same results report and Chao et al. - in no western women they detected EBV and in 48% of Asian women with LELC they found EBV. They suggest that racial and geographic factors might have role of the pathogenesis of LELC.

The LELC has better prognosis than common cervical cancer such as squamous cell carcinoma and adenocarcinoma. Hasumi et al. reported that the 5-year survival of such patients is also better than the other squamous cell carcinomas.

The etiology of those tumors is not researched enough, mostly due to the fact that they are so rare. Our team presents 16 cases of Lymphoepithelioma like carcinoma, which is one of the largest studies in this field so far. We also present 13 patients with Warty carcinoma and 6 patients with Mucoepidermoid carcinoma. The further research on the three cohorts clearly shows that LELC has better prognosis than the rest two groups. This means that the identification of EBV/HPV presence in the malignant cells can alter the standard operative and post-operative behavior. In theory, this could lead to reducing the expenses in healthcare, concerning this disease and being more beneficial for the young patients themselves (mean age for the malignancies in mind is 49 y.o.).

The research is a result of combining the following:

Revisiting surgical specimens, revisiting paraffin blocks with tissue samples, performing IHC, performing in situ hybridization, studying the epidemiology, pro-retrospective study of the patients' status - alive/dead and have/doesn't have recurrence.

My team's results demonstrate that almost half of the patients did not have detection of HPV or EBV infection. Underlying HPV infection was proven in three cases and EBV infection - in two. The two cases of EBV infection are in Caucasian women thus contrast with the data of other authors, which describes this infection mostly in Asian women. With this single exception our findings confirm the results published in the literature.

My team's results show that not every patient with LELC has presence of HPV or EBV. The role of these two viruses in the pathogenesis of the tumor is not fully understood. This could indicate

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that immunohistochemistry cannot be a sole indicator for the viral presence in LELC of the uterine cervix. The immunohistochemically

results should be compared with in situ hybridization and Polymerase Chain Reaction (PCR).