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Nuclear Co-Localization of Expressional Products of BRCA-2 and Epstein Barr Virus- Latent Membrane Protein-1 Genes: An Immunohistochemical Study of Breast Cancers Tissues from a Group of Iraqi Female Patients.

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Abstract :Background: Globally, and including Iraq, breast cancer is the commonest malignancy among women. BRCA1 and BRCA2 are human genes producing tumor suppressor proteins to help repairing damaged DNA and ensuring the stability of the cellular genetic material. A possible viral etiology was recognized in relation to the development and progression of breast cancers, among them mouse mammary tumor virus (MMTV), the Epstein-Barr virus (EBV) and the human papilloma (HPV) have prevailed linkages to these cancers.

Objective: To analyze the rate of EBV-LMP1 infection in the breast tissues in association with defects and / or mutations in BRCA-2 gene, by assessing the endogenous levels of the total expressed BRCA-1- as well as LMP-1 protein products, and their relations to the differentiation of primary invasive breast cancer tissues.

Patients and methods: Fifty-four (54) formalin-fixed, paraffin- embedded breast tissues were obtained in this study; (34) biopsies from breast cancers (BC) and (20) from apparently normal breast autopsies as a control group. Detection of protein expressional products of LMP-1 gene of Epstein Barr Virus as well as BRCA-2gene was done by HRP/DAB immune-enzymatic antigen detection system using specific rabbit- anti-human primary antibodies for EBV-LMP -1as well as defected or mutated BRCA-2 protein products.

Results: Detection of LMP-1 - immunohistochemical (IHC) reactions in tissues with BC was observed in 11 out of 34 (32.4%), while in healthy breast tissues in the control group was detected in 10% (2 out of 20). Detection of BRCA-2- protein- immunohistochemical (IHC) reactions in tissues with BC was observed in 14 out of 34 (41.2%), while none of the examined healthy breast tissues in the control group revealed such IHC- reactions. The difference between the percentages of BRCA-2- as well as LMP1 proteins detection in BC tissues & control group was statistically significant (<0.05). Among breast cancer tissues that showed score II of IHC reactions for BRCA2, 60% have well differentiated grade; and 50% of those tissues that have score I- IHC reactions showed moderate differentiated grade and lastly, 66.7% of the BC tissues which showed score III have presented as poorly differentiated BC tissues. However, statistical significant differences between the frequencies of EBV-LMP1 and BRCA-2- immunohistochemical reactions were neither observed in relation to the age of these breast cancer patients nor to the grade of invasive breast cancer tissues (P value > 0.05).

Conclusions: Our results indicate that the EBV might contribute to the development of subset of breast tumors. The present results of the rates of defects or mutations in the BRCA-2- genes in relation to the grade of breast cancer tissues also could point for their occurrence and contribution as early events in breast carcinogenesis.

Keywords : Breast cancer; LMP 1;Defects / Mutations; BRCA-2,IHC.

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