Comparison of co-presence of Epstein–Barr virus and high-risk human papillomaviruses in colorectal cancers from the Middle East region

Karim Nagi[1], Ishita Gupta[1], Hamda Al-Thawadi[1], Ayesha Jabeen[1], Mohammed Imad Malki[1], Semir Vranic[1], & Ala-Eddin Al Moustafa[1,2]

[1]College of Medicine & [2]Biomnedical Research Centre, Qatar University, Doha, Qatar

Faculty and PostDoc, Medical, Biomedical and Health Sciences

Abstract

Background: Several studies have shown the presence of onco-viral DNA in colorectal tumor tissues. Viral infection by onco-viruses such as Human papillomaviruses and Epstein–Barr virus are well-known to be involved in the onset and/or progression of numerous human carcinomas.
Methods: We explored the co-presence of high-risk HPVs and EBV in a cohort of colorectal cancer samples from Lebanon (94) and Syria (102) by PCR, immunohistochemistry and tissue microarray.
Results: The results of the study point out that 54% of colorectal cancer cases in Syria are positive for high-risk HPVs, while 30% of the cases in Lebanon are positive for these viruses; the most frequent high-risk HPV types in these populations are 16, 18, 31, 33 and 35. Analysis of LMP1 showed similar results in both populations; 36% of Syrian and 31% of Lebanese samples. Additionally, we report that EBV and high-risk HPVs are co-present in these samples. In Syrian samples, EBV and HPVs are co-present in 16% of the population, however, in the Lebanese samples, 20% of the cases are positive for both EBV and HPVs; their co-presence is associated with high/intermediate grade invasive carcinomas.
Conclusion: These data suggest that EBV and high-risk HPVs are co-present in human colorectal cancers where they can cooperate in the progression of these cancers. Further studies are needed to elucidate the role of those oncoviruses in the development of human colorectal carcinomas.

Background

Colorectal cancer, the third most common form of cancer accounts for approximately 10% of all cancer cases. Various pathogens including viruses and bacteria have suggested as risk factors for colorectal cancers. Viral infection accounts for 20% of human cancers including gastric malignancies and are linked with carcinoma progression. The role of Human papillomaviruses (HPVs) in colorectal cancer is still nascent. However, the role of Epstein–Barr virus (EBV) in colorectal carcinogenesis is not completely understood and is contradictory.

Based on the fact that there are only few studies in the Middle east covering only three countries, Iran, Turkey and Israel; This study aimed to explore the co-prevalence of HPV (E6) and EBV (LMP1) in colorectal samples from the Lebanese and Syrian populations.

Methodology

Colorectal samples were explored using tissue microarray for EBV (LMP1 protein, clone1–4, DAKO Agilent) and HPV expression (E6 onco-protein, clone C1P5, Calbiochem, Canada) using IHC analysis. The tumors were considered positive for LMP1 and E6 onco-proteins if cancer cells exhibited positivity ≥1%.
Five micrograms of purified genomic DNA (Qiagen) from each sample was analyzed for EBV and HPV by PCR using specific primers for LMP1 as well as E6/E7 of HPV, while, primers for GAPDH gene were used as an internal control.

Results

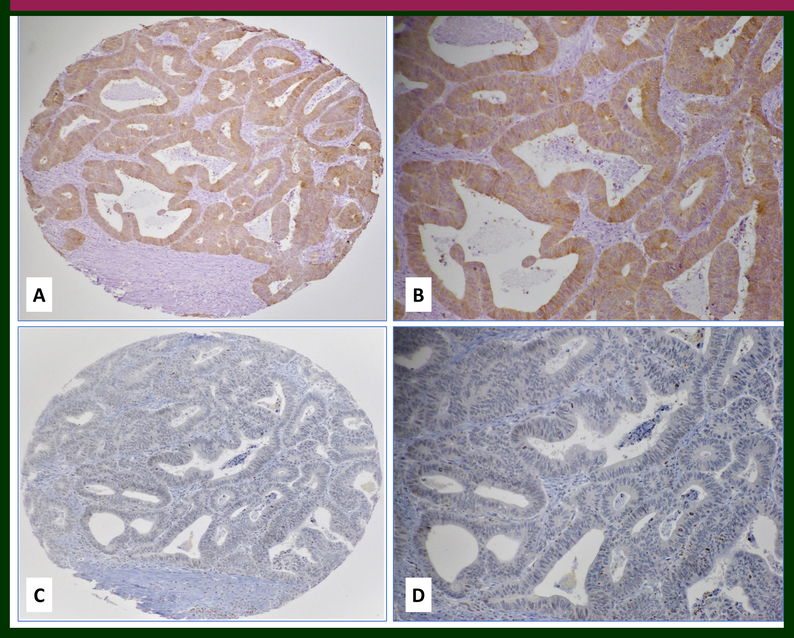

Figure 1A-D. Representative IHC images revealing oncoproteins E6 of high-risk HPVs (A-B, magnifications 10x and 20x) and LMP1 of EBV (C-D, magnifications 10x and 20x), respectively, in the same colorectal cancer sample, which was moderately differentiated (G2) intestinal adenocarcinoma.

Table 1. Prevalence of Human papillomaviruses (HPV) and Epstein–Barr virus (EBV) in the Lebanese Colorectal Cancer Patients

Samples	HPV (E6) Number (%)	EBV (LMP1) Number (%)	HPV (E6) + EBV (LMP1) Number (%)
Normal (n=13)	0 (0)	0 (0)	0 (0)
Cancer (n=94)	34 (36.1)	29 (30.8)	19 (20)

Table 2. Prevalence of Human papillomavirus (HPV) and Epstein–Barr virus (EBV) in Syrian Colorectal Cancer Patients

Samples	HPV (E6) Number (%)	EBV (LMP1) Number (%)	HPV (E6) + EBV (LMP1) Number (%)
n=102	55 (54)	37 (36)	17 (16.6)

Conclusions

Our study indicates that EBV and high-risk HPVs are commonly present in human colorectal cancers in two middle eastern countries (Lebanon and Syria). A substantial proportion of cancers (16-20%) showed co-expression of two viruses indicating their potential cooperation in cancer initiation and/or progression.