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EXPRESSION OF EBV LATENT MEMBRANE PROTEIN IN ESOPHAGEAL CARCINOMA AND PARA-CANCEROUS MUCOSA

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MATERIALS AND METHODS

Eighty cases of esophageal carcinoma (EC) and para-cancerous mucosa of resection specimens were selected from our surgical pathology laboratory in 1990–1992. The slides were 5 μm thick, HE and S-P immunohistochemistry were performed. The first antibody mouse anti-EBV membrane protein (LMP-1) and the S-P kit (mouse) were purchased from MaXim Co. Positive control: Vesicular- nuclear type of nasopharyngeal carcinoma with EBV LMP-1 positive; negative control: normal mouse serum and PBS instead of 1st antibody; DAB visualization, hematoxylin counterstain, light microscopy. The positive cases were re-stained with positive control to confirm the positivity.

RESULTS

EBV LMP-1 Immunohistochemistry

Five cases were EC tissue positive (5/80, 6.3%). The positive signals were located both in cytoplasm and nuclei, but cytoplasm was much more. The signals were brown-colored, with small granules, in focal or scattered distribution (Figure 1). The cancer stroma (collagen and lymphocytes) were clearly negative. 12 cases (15.0%) were para-cancerous mucosa positive. The positive signals were located in acantho-layer with focal or zonal distribution. The granules were massive and deep brown without orientation. 5 cases were both cancer and para-cancer positive, the other 75 cases and negative controls were all negative. In some cases, the muscular layer was slightly stained.

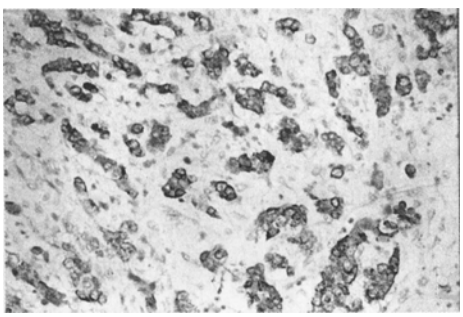

Fig. 1. Poorly differentiated squamous cell carcinoma. The cytoplasm of cancer cells is EBV LMP-1 positive diffusely. S-P method, hematoxylin counterstain × 200.

The Morphology of EBV LMP-1 (+) Cancer and Para-cancerous Tissue

Of the 5 cancer tissue positive cases, 2 were undifferentiated carcinoma with small-round or small-oval nuclei stained in deep brown; there were halos around the nuclei. These rather special appearances were not seen in the nearby negative cancer cells. Other 3 cases were poorly differentiated carcinoma

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(grade III squamous cell carcinoma) with cytoplasm positive; the cancer nests were small and cord-shaped, and some positive cytoplasm was rarefied and even with vacuolar degeneration; some nuclei were pressed eccentric (Figure 2). The stroma somewhat underwent mucoid degeneration; only one case had large amount of lymphocyte infiltration. The acantho-layer of para-cancerous mucosa was thickened (acanthosis); cells were enlarged and nuclei were rather big but no anaplasia; the cytoplasm was clear, similar to the so-called vacuolar cell. In the submucosa, there was marked lymphocyte infiltration.

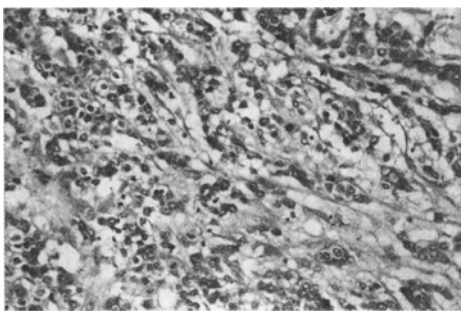

Fig. 2. Cancer tissue of EBV (+), the cytoplasm of cancer cells is rarefied and vacuolar, HE × 200.

DISCUSSION

Concerning the relationship between EBV and cancer, there has been some reports of nasopharyngeal carcinoma (NPC) in the literature, but for EC, up to now reports are few. (one report with 3.3% positive in 1994).[1] In this paper, using EBV LMP-1 monoclonal antibody immunohistochemistry, we found that in EC the positive rate of EBV LMP-1 was 6.3% (5/80); the rate was somewhat higher than ever. The relationship between EBV and NPC has been the hot spot in studying the viral cause of cancer. In NPC, the histology type related to EBV is poorly differentiated squamous cell carcinoma with marked lymphocyte infiltration. Recently, some authors found that carcinomas of stomach, salivary gland, lung, nasosinus and thymus, similar to "lymphoepithelioma of NPC" were also EBV positive.[2] In this paper 5 positive cases were all poorly differentiated squamous cell carcinoma or undifferentiated carcinoma; there was only one case with a large amount of lymphocytes. The cytoplasm of EBV (+) cases both in cancer and para-cancerous tissues, the epithelia were all vacuolar or rarefied in HE stain. This might be related to the reaction of these EBV infected cells. Virus-related carcinoma was not necessary to induce host immune reaction with marked lymphocyte infiltration. Shibata[3] recently reported that in stomach adenocarcinoma without lymphocyte infiltration 16% of cases were EBV positive.

About the relationship between EBV (+) cancers and EBV, there are two theories: 1. EBV infection is after transformation. In these cases, the para-cancerous mucosa is often EBV negative. 2. EBV infection is before transformation and participates the transforming steps. In this paper, the case number is not enough to make conclusion about cancer and EBV. More studies are necessary.

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