The relationship between HPV16 and expression of CD44v6, nm23H1 in esophageal squamous cell carcinoma

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Summary. The esophageal squamous cell carcinoma (ESCC) has high incidence in Shaanxi Province of China. More and more researches indicated that human papillomavirus type 16 (HPV16) might play an important role in carcinogenesis of ESCC but the relationship between HPV16 and CD44v6, nm23H1 has not been elucidated. HPV16 was detected by amplifying HPV16 E6 gene through polymerase chain reaction (PCR) method and the expression of CD44v6, nm23H1 in 40 ESCCs and fifteen normal esophageal mucosa (NEM) from Shaanxi Province was examined by Streptavidin-Peroxidase (SP) method using monoclonal antibody specific to CD44v6 and nm23H1. The positive rates of HPV16 E6 gene, CD44v6 and nm23H1 were 60% (24/40), 65% (26/40) and 45% (18/40) respectively in ESCCs and 26.67% (4/15), 33.33% (5/15) and 86.67% (13/15) respectively in NEMs. There existed statistical difference for HPV16, CD44v6 and nm23H1 between NEMs and ESCCs respectively (p < 0.05). The relationship between HPV16 and the expression of CD44v6 in ESCCs was statistical significance (P = 0.021), but no significant correlation was found between HPV16 and the expression of nm23H1 (P = 0.436) in ESCCs. The infection rate of HPV16 had no statistical difference in all pathological features we observed, but the expression rates of CD44v6 and nm23H1 had statistical correlation with invasion (p = 0.001, 0.013) and lymph nodes metastasis (p = 0.014, 0.002) respectively. In different histology grade of ESCCs, the relationship between HPV16 and CD44v6 was statistical significance in grade I (p = 0.044) but was not in grade II (p = 0.165) and grade III (p = 0.658), however as to the expression of nm23H1 there exited no statistical significance in all histology grades of
The expression rates of CD44v6 and nm23H1 were statistically different between grade I and II (p = 0.004, 0.016) respectively and between grade I and grade III (p = 0.014, 0.020), but not statistically different between grade II and III (p = 0.792, 0.943) respectively. Our data firstly suggested that there existed the statistical relationship between the infection of HPV16 and the expression of CD44v6 in ESCCs and that HPV16 may be involved in invasion and metastasis of ESCC.

**Introduction**

The esophageal squamous cell carcinoma (ESCC) is one of the upper-digestive tract neoplasms and has high incidence, high mortality and poor prognosis in China. There exited high incidence for ESCC mainly aggregated in North China such as Shaanxi Province, as well as Henan and Shanxi Provinces. The confirmed causes and the mechanism of ESCC have not been elucidated yet. The variation of geographical distribution suggests a dominant role of environmental factors in the etiology of ESCC such as nitrate salt, nitrite salt and second-degree amine in drinking water, which can cause transformation of epithelium cells. In addition, other risk factors such as nutrition imbalance (lack or absence of vitamins and minerals such as vitamin A, B2 and C) and improper life style (cigarette smoking and consumption of pickled food) give rise to the damage, proliferation and inflammation of esophageal mucosa cells. These may result in weakness of esophageal mucosa cells against microbiology. Moreover the factor of genetic susceptibility to microbiological infection may not be neglected [4, 33].

Human papillomavirus (HPV), especially high risk HPV16 is regarded as one kind of important tumor-related virus, which was firmly recognized in cervical cancer. HPV16 E6 and E7 can interfere normal cell cycles by degrading tumor suppressor protein P53 and Rb respectively in cervical carcinoma; moreover the virus causes instability of host genome through integration of viral DNA into host genome randomly and increases centrosome number in cervical carcinoma [32, 35]. The role of HPV16 in ESCC becomes a research hotspot on ESCC with more and more reports about the relationship between HPV16 and ESCC [8, 17, 19, 26, 37–39]. But in past two years most reports suggested that HPV16 was associated with carcinogenesis of ESCC especially in some areas of china although there were some reports that no relationship was found between HPV and ESCC in other countries and regions such as Germany and so on [1, 11, 14, 30, 31]. According to the precious study results through different methods, types of HPV in ESCC were mainly some high risk HPV such as HPV16, HPV18, but HPV16 was the most common HPV type which was implicated in ESCC [4, 33, 39]. The more important is that there were some reports that about HPV18 E6 and E7 gene can immortalize fetal esophageal epithelial cell in ESCC in terms of DNA level, mRNA level and cellular level, which supported that high risk HPV might have an important role in ESCC [25, 26, 39]. Considering the poor prognosis and high mortality of ESCC in China, it is very necessary to investigate the role of HPV16 in invasion