Expression pattern and clinical significance of PD-1 and PD-L1 in squamous cell carcinoma of the cervix

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Objective

To determine the clinical significance of PD-L1 expression in tumor, and PD-1 expression in tumor infiltrating immune cells (TIC) in squamous cell carcinoma of the cervix (SCC).

Background

Cervical cancer is the third most common gynecologic cancer diagnosis and cause of death among gynecologic cancers in the United States, following uterine and ovarian cancer. Several studies have established the PD-1/PD-L1 pathway as a way for the tumor cells to evade the immune system. Targeted antibodies are used as therapeutic agents in an attempt to reactivate the immune system, however studies in expression of PD-1/PD-L1 in cervical cancer are limited. We wanted to determine the expression of PD-1 and PD-L1 in squamous cell carcinoma of the cervix in our patient population and whether it correlated with clinical outcomes.

Materials and Methods

A total of 198 patients with SCC were identified and 60 had evaluable tumor specimens and clinical data. Immunohistochemistry on PD-L1 and PD-1 expression using tissue microarrays were performed. PD-L1 expression was classified as negative (<1%), low (1 to 50%), and high (>50%). PD-1 expression of TIC was analyzed as low or high based on the median number of TIC per mm². Correlation between PD-L1, PD-1 expression and clinical parameters was analyzed using χ² or Fisher's exact test. Cumulative 5-year survival was calculated by the Kaplan Meier method and analyzed by the log rank test.

Results

Of the 60 patients, 90% were black, 55% between ages of 30-55, and 40% older than 55. 33 patients had poorly, 20 moderately, and 7 well differentiated tumors. At 5-year follow up, 14 patients died of disease, 40 were alive, and 6 lost to follow up; 12 of the 60 patients recurred. 93.3% of tumors had positive staining for PD-L1 with 56.7% showing high expression. Patients with ages 30-55 showed a higher rate of PD-L1 staining and high expression (p = 0.047). These patients also had higher PD-1 expression on TIC (p = 0.013). Mean disease free survival (DFS) was 43.7, 36.5, and 6.3 months for high, low, and negative PD-L1 expression, respectively (p = 0.002). In patients with stage I-II disease, mean DFS was 52.2, 42.6, and 7.6 months for high, low, and negative PD-L1 expression, respectively (p =0.001). In patients with stage III-IV disease, mean DFS was 26.1, 10.7, and 3.6 months for high, low, and negative PD-L1 expression, respectively (p = 0.37). Overall survival (OS) analysis also showed similar correlations. Early stage tumors had significantly higher PD-1 expression on TIC (p = 0.009), but there was no correlation between survival and PD-1 expression on TIC.

Conclusions

Contrary to previous studies, our results showed a remarkably high rate of PD-L1 expression in SCC. High PD-L1 expression was associated with longer DFS and OS, especially in early stage tumors. PD-1 expression on TIC was higher in patients with early stage tumors, but no correlation between PD-1 expression and cervical cancer survivals.

References