Prognostic significance of tumor infiltrating immune cells and PD-L1 expression in gastric carcinoma in Chinese patients

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INTRODUCTION

Background: Gastric cancer (GC) is the 4th most common malignancy, but sets third as a cause of cancer death worldwide.1

• The highest incidence rates of GC are in Eastern and Southeast Asia, mainly in China, where higher incidence rates are associated with dietary habits, lifestyle factors, and higher prevalence of Helicobacter pylori (HP).2

• GC is a heterogeneous disease, and tumor progression is dependent on factors that are not well understood.

• The Infiltration of tumor-infiltrating lymphocytes (TILs) and tumor-infiltrating immune cells (TICs) have been implicated in tumor progression and immune response against cancer.

• The presence of different types of intratumoral immune cell infiltrates may provide information on selecting predictive biomarkers for ongoing clinical studies of immunotherapies.

• The presence of TICs and the expression of PD-L1 in GC may predict tumor types that are responsive to PD-1/PD-L1 pathway blockade.

OBJECTIVES

• Compare clinicopathological findings with tumor PD-L1 expression levels in Chinese patients with GC.

• Analyze the relationship of PD-L1 expression with the expression of immune checkpoint molecules (PD-1 and PD-L1).

• Correlate PD-L1 expression with clinicopathological parameters in Chinese patients with GC.

• Evaluate the expression of several immunomodulatory genes within the tumor microenvironment of GC patients.

METHODS

Patients and methods: A total of 341 GC tissues (46% PD-L1+ cases) were analyzed. PD-L1 expression was assessed using the Ventana Dako 22C3 antibody stain and an automated fluorescent streptavidin amplification detection system.

• PD-L1 expression was scored using the 22C3 fluorescence signal and was evaluated on both tumor cells and stromal cells. Tumor cell staining was scored as in Table 2.

• Clinicopathological analysis was performed according to standard protocols.

RESULTS

Patient demographics and disease characteristics

The majority of patients had stage III disease (Table 1).

Tumor expression of PD-L1 was positively associated with TIL density (Fig. 1; p = 0.0018). PD-L1 expression was associated with high density of TILs, EBV+ GC, and upregulation of several immunomodulatory genes within the tumor microenvironment.

Table 1. Correlation of PD-L1 expression with clinicopathological characteristics.

Characteristics              Number of patients (%)
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Age (years)                60 (17.6) 275 (78.7) 6 (1.8)
Gender                     Female 227 (57.0) 95 (27.3) 14 (4.1)
                                           Male 184 (46.2) 278 (78.0) 39 (11.2)
Stage                      I 24 (6.5) 15 (4.3) 7 (2.0)
                                        II 189 (55.4) 200 (58.7) 15 (4.3)
                                        III 173 (50.6) 216 (63.2) 10 (2.9)
Histologic type             Diffuse 243 (71.4) 248 (67.3) 15 (4.4)
                                        P-D 98 (28.6) 92 (25.7) 16 (4.7)
Histological grade         Grade I 15 (4.4) 17 (4.7) 2 (0.6)
                                        Grade II 185 (54.4) 221 (62.1) 26 (7.6)
                                        Grade III 141 (41.3) 152 (42.6) 16 (4.7)
Tumor size (cm)            ≤5 205 (59.9) 200 (57.2) 15 (4.4)
                                        >5 136 (39.8) 146 (41.9) 10 (2.9)
Tumor border                Cutaneous 117 (34.3) 114 (32.4) 3 (0.9)
                                        Subcutaneous 224 (65.7) 265 (75.6) 28 (8.1)
Histological subtype       Gastric type B 275 (79.8) 278 (80.1) 3 (0.9)
                                        Malignant lymphoma 66 (19.2) 57 (16.1) 9 (2.6)
Histological differentiation  Well differentiated 266 (77.8) 278 (80.1) 10 (2.9)
                                      Moderate 35 (10.3) 33 (9.5) 2 (0.6)
                                      Poor differentiated 39 (11.4) 40 (11.3) 1 (0.3)
Histology of related tumors  Primary tumors 299 (87.9) 300 (85.7) 1 (0.3)
                                      Secondary tumors 42 (12.1) 42 (11.8) 1 (0.3)
Histological grade of related tumors  Grade I 25 (7.4) 26 (7.4) 1 (0.3)
                                      Grade II 189 (55.4) 200 (58.7) 15 (4.3)
                                      Grade III 175 (51.1) 174 (50.0) 1 (0.3)
Tumor cell infiltration     Tumor cell infiltration (nmax=47) 29 (57.4) 24 (49.0) 5 (10.2)
                                        Low 12 (24.4) 35 (70.6) 2 (4.1)
                                        Moderate 19 (37.7) 19 (38.7) 1 (2.1)
                                        High 16 (32.7) 16 (32.7) 0 (0.0)
Prognostic factors associated with OS

Table 2. Independent factors associated with OS

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Hazard ratio (95% CI)</th>
<th>p value</th>
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<tbody>
<tr>
<td>PD-L1 expression</td>
<td>1.11 (0.86-1.44)</td>
<td>0.568</td>
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DISCUSSIONS

In conclusion, PD-L1 expression was positively associated with TIL density, EBV infection, and upregulation of several immunomodulatory genes within the tumor microenvironment.

REFERENCES


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DISCLOSURES

No conflicts of interest were reported for any of the authors.