Antitumor immunity in patients with gastric cancer

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B-cell development

Illustration by A. Y. Chen
- B1-lymphocytes are a unique CD5+ B-cell subpopulation;
- Subpopulation first described in 1983 [Lee Herzenberg];
- B1-cells are characterized by an "activated phenotype": expression CD80, CD86;
- The B1-lymphocyte pool is maintained by the activity of progenitor cells through their very slow proliferation.
Subpopulations of B1-cells

**B1a**
- phenotype: CD19+CD21 low CD23-CD5+IgM++

**B1b**
- phenotype: CD19+CD21 low CD23-CD5 - IgM++

Antigen → B1-cells → Antibody-expressing cells
B1-lymphocytes, mainly cells secreting antibodies, are detected in the spleen, where they account for up to 5% of the number of B-cells.

B1-cells constantly circulate between the spleen and abdominal cavity, but do not enter the follicles.

Splenectomy for the purpose of adequate lymphodissection in stomach cancer causes pronounced and long-term dysfunction of the various parts of the immune system.
Patients with gastric cancer

1 group
- gastrectomy,
- spleno-protective
- D2-lymphodissection

2-nd group
- gastrectomy, splenectomy,
- D2-lymphodissection

before - 50 samples of peripheral blood
after 3 months - 29 samples

antigens
- CD20, CD21, CD23, CD38, HLA-DR,
- CD71, CD10, CD95, CD25, CD5, CD56
- IgG-λ, IgG-κ

Stage
- I - 16 patients
- II - 12 patients
- III - 18 patients
- IV - 4 patients
Before surgical treatment

- prominent proportion CD23+ B-cells

significant number of B-cells with a low level of CD21+ expression

Decreased
- relative number of B-cells in 33%
- absolute number B-cells in 38%
Subpopulation CD19+CD5+B-cells average -17.7%

- 23% patients more than 20%
- 3 patients more than 40%
- Some of these cells CD38+ and CD25+
1 group

<table>
<thead>
<tr>
<th></th>
<th>before the operation</th>
<th>after the operation</th>
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</tr>
</thead>
<tbody>
<tr>
<td>B-lymphocytes CD19+ %</td>
<td>5,36±0,65</td>
<td>6,1±0,94 (p=0,015)</td>
<td>12</td>
</tr>
<tr>
<td>B1-leucocytes CD19+ %</td>
<td>2,41±0,57</td>
<td>2,27±0,57 (p=0,04)</td>
<td>7</td>
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<tr>
<td>CD19+ (absolute)</td>
<td>134.3±25,3</td>
<td>121,8±30,4 (p=0,05)</td>
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<tr>
<td>CD19+CD5+</td>
<td>11,8±4,56</td>
<td>14,6±2,8</td>
<td>12</td>
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<tr>
<td>CD19+CD23+</td>
<td>21,2±4,62</td>
<td>24,4±6,5</td>
<td>14</td>
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<tr>
<td>CD19+CD20+</td>
<td>96,9±0,8</td>
<td>95,2±1,2</td>
<td>14</td>
</tr>
<tr>
<td>CD19+CD71+</td>
<td>11,1±3,1</td>
<td>9,8±1,6</td>
<td>12</td>
</tr>
<tr>
<td>CD19+CD10+</td>
<td>0,8±0,32</td>
<td>0,5±0,18</td>
<td>11</td>
</tr>
<tr>
<td>CD19+CD38+</td>
<td>16,0±4,4</td>
<td>22,8±6,1</td>
<td>14</td>
</tr>
<tr>
<td>CD19+HLA-DR+</td>
<td>98,6±0,3</td>
<td>97,6±0,99</td>
<td>14</td>
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<tr>
<td>CD19+CD25+</td>
<td>1,4±0,84</td>
<td>3,84±2,22</td>
<td>12</td>
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<tr>
<td>CD19+CD95+</td>
<td>8,3±2,3</td>
<td>8,0±1,4</td>
<td>10</td>
</tr>
<tr>
<td>CD19+CD21+</td>
<td>73,1±3,2</td>
<td>77,3±4,3 (p=0,034)</td>
<td>12</td>
</tr>
<tr>
<td>CD19+CD56+</td>
<td>1,0±0,3</td>
<td>1,6±1,2</td>
<td>12</td>
</tr>
</tbody>
</table>
In the 2-nd group, the relative number of B-lymphocytes ($p=0.018$), CD5+B-cells($p=0.012$), CD19+CD38+ ($p=0.035$) cells was reliably correlated.
What is the role of B1 lymphocytes?
The antibodies produced by B1-lymphocytes are almost exclusively IgM.
The response of B1-cells is mainly thymic independent.

IgM plays an important role in the induction of apoptosis of tumor cells

[Brandlein S., Lorenz J., Ruoff N.- Human monoclonal IgM antibodies with apoptotic activity isolated from cancer patients. // Hum. Antibodies. 2002. № 11(4);
Varambally S., Bar-Dayan Y., Bayry J. - Natural human polyreactive IgM induce apoptosis of lymphoid cell lines and human peripheral blood mononuclear cells. // Intern. Immunology. 2004. Vol. 16, No.3;
Piao X., OzawaT., Hamana H. - TRAIL-receptor 1 IgM antibodies strongly induce apoptosis in human cancer cells in vitro and in vivo. // Oncoimmunology 2016. №5(5)].

Approximately half of serum IgM is secreted by B1-cells.
Immunity disorders in patients after splenectomy primarily affect the B-cell immune response, including thymus-independent antigens of the second type, which is provided by the population of B1-lymphocytes.

Thus, in patients of the experimental group, there may be a decrease in antibody production, a weakening of both general and antitumor immunity.
Thank you for your kind attention!