IN VIVO COMPARATIVE OBSERVATION ON THE INVASIVENESS OF VARIOUS ORGANS BY DIFFERENT LEUKEMIA CELLS

Chu Jianxin 祝建新 Ying Hongguang 应红光 Ding Li 丁立

Institute of Hematology, Chinese Academy of Medical Sciences, Tianjin

Using patho-morphological method and transplantation bio-assay, the in vivo invasiveness of leukemia cells is three transplantable mouse T cell leukemia models was comparatively studied. The results showed that the invasion to the liver was consistent, but that to other organs was obviously different. L615 and L7212 leukemia cells preferred to the bone marrow and spleen than to the peritoneum while L7811 leukemia cells were just the opposite. Transplantation bio-assay demonstrated that leukemia cells were present in the bone marrow of L615 mice as early as 6 hours after leukemia cell inoculation, but no leukemia cells was detected in bone marrow of L7811 mice 2 days after inoculation. In the terminal phase, L615 mice bone marrow became filled with leukemia cells, but L7811 mice bone marrow contained only a few leukemia cells. The difference of invasiveness of leukemia cells among organs is probably related to "homing" receptor. The same type of leukemia cells may possess multiple "homing" receptors.

Although the leukemic cells showed spread and infiltration extensively as a role, recently some results suggested leukemic cells always tend to infiltrate some organs or tissues selectively.1-3 We observed three transplatable mouse T cell leukemia models, the invasiveness of leukemia cells among various organs is different. The results are reported as follows:

MATERIALS AND METHODS

Animal

Inbred 615 mice were provided by compartment of laboratory animal in our institute.

Experimental Leukemia Model

Three transplantable mouse T cell leukemia models (L615, L7212 and L7811). It was established by our laboratory and generated in vivo, continuously.

Patho-morphology Observation

Various organs of leukemia were removed and fixed in Bouin's solution. Plastic section and H E. stain were performed.

Transplantation Bio-assay

In order to detect the leukemic cells in bone marrow, a cell suspension of femur marrow from the test mouse was injected into the normal mice 615. According to leukemic features and survival time, it can be demonstrated whether leukemic cells present in the bone marrow suspensions or not. This is the most sensitive method for quantitatively detecting leukemic cells in organs to date.

RESULTS

Leukemia Cells Infiltration in Liver and Spleen

The weights of liver and spleen in leukemia mouse represented the infiltration degree of leukemic cells. The average weights of liver of dead mice in three strains were higher than that of control. The spleen weights of L615 or L7212 leukemia mouse were about 5—6 times higher
than control. But the spleen weight of \textit{L781i} were only slightly increased no matter what inoculation route was used (Table 1). Microscope observation showed the liver were diffusely infiltrated with leukemic cells in all the leukemic strains. The distribution of leukemic cells in liver chiefly lodged inside the lobulus. After \textit{L781i} leukemic cells were infected ip, it were infiltrated along portal vein. In spleens of \textit{L615} or \textit{L781i} mouse the normal structure were almost completely substituted by leukemic cells. However, in the spleen of \textit{L781i} mice only red pulp was focally infiltrated by leukemic cells. The normal structure of spleen remained intact.

**Leukemia Cells Infiltration in Abdominal Cavity**

Peritoneum is a vascular tissue full of stroma cells. Intraperitoneal inoculation is the common route used in transplantable leukemia. During the long-term generation in \textit{L615} or \textit{L7812}, neither tumor mass nor ascites was found in repeated inoculations. While in \textit{L781i} mice, after inoculation on 2,4,6,7,8,9 and 10 days leukemic masses appeared parapancreatically (omentum and mesenteric membrane) on the 2nd day and pancreatic infiltration and ascites were found on the 4th day. These were more significant after 6th day. Thus, it seems logically that the degree of peritoneal infiltration was determined by the difference of the leukemic strains.

**Invasion of Leukemia Cells in Bone Marrow**

Under microscope, after the death of the animals the bone marrows of \textit{L615} and \textit{L7812} mice are almost replaced by leukemic cells, only a few megakaryocytes remain. But it is different in bone marrow of \textit{L781i} mice, apparent invasion of leukemic cells can not be found whatever inoculation route was adopted (including iv, ip and sc), except focal growth of leukemic cells at femoral epiphysis in sc inoculation. Even in this situation the leukemic cells never spread to other bone marrows of the body.

**Transplantation Bio-assay**

Comparison between \textit{L615} and \textit{L781i} leukemic models, the mice were killed at different interval after inoculation of \textit{L615} and \textit{L781i} leukemic cells, their bone marrow cells were used for transplantation bio-assay. The results showed that the leukemic cells appeared in bone marrow of \textit{L615} mice 6 hours after sc inoculation and increased in number after 24 hours. All inoculated mice were died leukemia (Table 2). But in \textit{L781i} mice no leukemic cells could be detected in bone marrow until 4 days after ip inoculation, there could be found a few leukemic cells and only 1/3—2/3 of inoculated mice died of leukemia. The survival time was longer than that of \textit{L615} mice (Table 3). Transplantation bio-assay of \textit{L615} and \textit{L781i} leukemia at the terminal stage showed that the number of leukemic cells in bone marrow between two leukemias was quite different (Table 4).

### Table 1. Comparison of liver or spleen weights in three leukemia strains (mg/g body weight)

<table>
<thead>
<tr>
<th>Strain of leukemia</th>
<th>Inoculation route</th>
<th>No. of animal</th>
<th>Liver</th>
<th>Spleen</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{L615}</td>
<td>sc</td>
<td>5</td>
<td>76.4</td>
<td>25.7</td>
</tr>
<tr>
<td>\textit{L7812}</td>
<td>sc</td>
<td>5</td>
<td>58.7</td>
<td>19.4</td>
</tr>
<tr>
<td>\textit{L781i}</td>
<td>sc</td>
<td>6</td>
<td>76.6</td>
<td>5.9</td>
</tr>
<tr>
<td></td>
<td>ip</td>
<td>6</td>
<td>75.4</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td>iv</td>
<td>6</td>
<td>97.8</td>
<td>5.7</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td>6</td>
<td>46.5</td>
<td>3.8</td>
</tr>
</tbody>
</table>

sc: subcutaneous   ip: intraperitoneally  iv: intravenously