Globule Leukocytes in Transitional Cell Hyperplasia and Carcinomas of Aged Mice

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Abstract: Globule leukocytes (GLs) infiltrating in transitional cell hyperplasia and carcinomas of aged BDF, mice were pathologically examined. The intracytoplasmic granules of globule leukocytes showed a variety of reactivity to histochemical staining for polysaccharides and were ultrastructurally composed of homogeneous electron dense material, occasionally containing crystaloids or vesicles. The GL infiltrating in tumor tissue is extremely rare.

Key words: globule leukocyte, mouse, transitional cell carcinoma

The globule leukocyte (GL), which contains large and eosinophilic granules in the cytoplasm, has been found within the mucosal epithelium of the alimentary, respiratory, urinary or reproductive tract in many animal species [1]. Although the GL prominently increased in spontaneous and experimental infections of parasites [4, 6], the pathological significance of GL accumulation has not been elucidated. The purpose of this study is to report extremely rare cases which GLs markedly infiltrate in transitional cell hyperplasia and carcinomas of aged BDF, mice.

A male (Case 1) and a female (Case 2) BDF, mice (SLC Japan Inc., Shizuoka) at 24 months old were euthanatized by exsanguination under ether anesthesia.

Grossly, a cyst-like tissue was seen adjacent to the right kidney and was partly connected with the renal pelvis in Case 1. The left renal pelvis and the ureter were dilated in Case 2. These tissues were fixed in 10% buffered neutral formalin solution. Paraffin sections were prepared by routine methods for hematoxylin and eosin staining or histochemical reactions shown in Table 1. Electron-microscopic sections were also prepared from formalin-fixed tissues.

Histopathologically, papillary and invasive transitional cell carcinomas were found in the ureter of Cases 1 and 2. GLs with large and eosinophilic granules in the cytoplasm infiltrated within the neoplastic tissue (Fig. 1). In the right kidney from Case 2 which had no urothelial tumor, pelvic transitional cells showed papillary hyperplasia and mild infiltration of GLs were seen in the interpithelium and the subepithelium.

To determine the histochemical characteristics of the GL granules, several histochemical staining methods were used. The granules showed negative or weakly

(Received 5 January 1995 / Accepted 13 May 1995)
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Table 1. Histochemical characteristics of intracytoplasmic granules in globule leukocytes of BDF, mice

<table>
<thead>
<tr>
<th>Stain</th>
<th>Histochemical reactivity of intracytoplasmic granules</th>
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<tbody>
<tr>
<td>Periodic acid-Schiff</td>
<td>Negative ~ Weakly positive (Reddish purple)</td>
</tr>
<tr>
<td>Toluidine blue (pH 2.5)</td>
<td>Non-metachromasia (Non-stain) ~ Metachromasia (Purple)</td>
</tr>
<tr>
<td>Toluidine blue (pH 7.0)</td>
<td>Non-metachromasia (Blue) ~ Metachromasia (Purple)</td>
</tr>
<tr>
<td>Alcian blue (pH 1.0)</td>
<td>Negative ~ Weakly positive (Pale blue)</td>
</tr>
<tr>
<td>Alcian blue (pH 2.5)</td>
<td>Negative ~ Positive (Red)</td>
</tr>
<tr>
<td>Safranin</td>
<td>Red ~ Reddish purple</td>
</tr>
<tr>
<td>Giemsa</td>
<td>Deep blue</td>
</tr>
<tr>
<td>Phosphotungstic acid-hematoxylin</td>
<td>Deep purple</td>
</tr>
<tr>
<td>Aldehyde-Fuchsin</td>
<td>Deep purple</td>
</tr>
<tr>
<td>Naphthol AS-D chloroacetate</td>
<td>Positive (Orange)</td>
</tr>
</tbody>
</table>

Positive (reddish purple) to periodic acid-Schiff reaction, deep blue to phosphotungstic acid-hematoxylin staining and deep purple to aldehyde-fuchsin staining. In toluidine blue (pH 2.5 and 7.0), alcian blue (pH 1.0 and 2.5), safranin and Giemsa stainings, they exhibited a variety of stainability to each histochemical reaction as shown in Table 1 and Fig. 2. Although the GL granules showed a positive reaction to naphthol AS-D chloroacetate staining, they stained less intensely (orange) than those of mast cells (red).

In electron-microscopic examination, the GL granules were of various sizes and shapes. Most of them were 400–2,600 nm in diameter and were composed of homogeneous electron-dense material (Fig. 3). Occasionally, they contained intragranular crystaloids and consisted of vesicles which were 40–60 nm in diameter. The electron-microscopic findings of the GL granules were consistent with the findings previously reported [1].

Metachromasia of the GL granule was reported to fade out in formaldehyde solution [7]. Intracytoplasmic granules of the GLs in both mice showed obviously varied intensity and metachromasia to histochemical staining for polysaccharide in this study. Histochemical difference between the GL granules in this study and those in the previous reports may indicate the heterogeneity of the GLs such as that of the mast cells [5].

It is supposed that the GL originates from the mucosal mast cell [6] or the large granular lymphocyte [2]. The mast cell contributes to the intense angiogenic activity found near tumors [3]. The large granular lymphocyte expresses perforin, which plays an important role in killing target cells, in their granules [8]. However, it has not yet been reported that the GL indicate the angiogenic or cytotoxic activities. Further investigation is necessary to determine the relationship between the transitional cell hyperplasia/tumor and the GL.

Fig. 1. Globule leukocytes infiltrating in transitional cell carcinoma. HE. ×200.
Fig. 2. Globule leukocytes (a) and a mast cell (b) stained with toluidine blue (pH 7.0). The granules of the mast cell generally show metachromasia. Some granules of the globule leukocytes also show metachromasia. Toluidine blue. ×2,000.

Fig. 3. Electron micrograph of globule leukocyte. Various sizes of electron dense granules are seen in cytoplasm. ×5,600.

References