Case Report

Spontaneous Thymoma in a 10-Week-Old Sprague-Dawley Rat

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Abstract: Spontaneous thymoma was found in the left lobe of the thymus of a male 10-week-old Sprague-Dawley (SD) rat. Microscopically, the thymic mass showed a sheet of dark area with multiple pale foci. The dark area mainly consisted of densely compacted small lymphoid cells with sporadic large epithelioid cells and mitotic figures. The epithelioid cells and mitotic figures were more frequent than those of the normal thymic cortex in this animal. The multiple pale foci were similar to the normal thymic medulla and occasionally had Hassall’s corpuscles; thus, they were regarded as medullary differentiation areas. Furthermore, some perivascular spaces recognized as characteristics of thymoma were present in the center of the mass. Immunohistochemically, the epithelioid cells in the dark area were positive for cytokeratin. Ultrastructurally, desmosomes and tonofilaments were observed in the epithelioid cells. Thus, this tumor was diagnosed as a thymoma. This is a rare case of thymoma occurring spontaneously in young adult SD rat. (DOI: 10.1293/tox.25.37; J Toxicol Pathol 2012; 25: 37–40)

Key words: thymoma, thymus, rat, medullary differentiation, perivascular space

Thymomas are commonly observed in aged rats1–3 and are considered to exhibit strain differences in experimental rats. In most cases, thymomas of rodents are age-related and have been scarcely reported in young rats4. Moreover, the rate of occurrence in male Sprague-Dawley rats is described as being in the range of 0.03–0.4% and is recognized as quite rare compared with other strains5,6. Here, we report a case of thymoma that occurred in a 10-week-old SD rat. To our knowledge, this is rare and the youngest case of thymoma in SD rat.

The animal was a 10-week-old male Sprague-Dawley [Crl:CD (SD), Charles River Laboratories Japan, Inc., Hino, Japan] rat used in the vehicle control group of a toxicity study. The animal showed no remarkable changes in clinical signs, body weight, hematology and blood chemistry. In the terminal necropsy at the end of the administration period, a milky white mass approximately 15 × 15 × 7 mm in diameter was found on the left lobe of the thymus. There was no adhesion between the mass and surrounding tissues (Fig. 1). No remarkable findings were observed in other organs and tissues.

The thymus with mass and other organs were fixed in 10% neutral-buffered formalin, embedded in paraffin, sectioned and stained with hematoxylin and eosin (HE) staining. Immunohistochemical staining was performed on sections from the thymus using antibodies against cytokeratin (34βE12; Dako, Denmark, dilution 1:50), CD3 (1F4; Serotec, UK, dilution 1:20), CD79α (HM57; Dako, Denmark, dilution 1:50) and Ki-67 (MIB-5; Dako, Denmark, dilution 1:100). Antigen retrieval was performed using an autoclave with citrate buffer (pH 6.0), and the HRP-conjugated polymer method (Histofine® Simple Stain MAX-PO(M) Nichirei, Tokyo, Japan) was applied to detect positive signals. For transmission electron microscopic examinations, 10% phosphate-buffered formalin fixed mass was postfixed in 1% osmium, routinely processed into epoxy resin-embedding. Ultrathin sections stained with uranyl acetate and lead citrate were examined using a JEM-1200EX electron microscope (JEOL, Tokyo, Japan).

Microscopically, the mass surrounded by a fibrous capsule occupied the left lobe of the thymus and was clearly separated from the right lobe. Thymic lobular structures disappeared inside the mass and were replaced by dark and pale area resembling the normal thymic tissue (Fig. 2). The dark area was composed of a mixture of densely compacted small lymphoid cells and sporadic large epithelioid cells, the proportions of which varied within the dark area (Fig. 3b,c). The nuclei of epithelioid cells were round to polygonal with prominent nucleoli and vesicular chromatin. Mitotic figures were more frequently observed in dark area of the tumor.
Spontaneous Thymoma in a 10-Week-Old Sprague-Dawley Rat

than in the cortex of the normal thymus. The pale foci of the tumor, which was thought to be a medullary differentiation, included Hassall’s corpuscles (Fig. 3d). Some perivascular spaces recognized as characteristics of thymoma were present in the center of the tumor (Fig. 3e). Microscopic examination of other organs and tissues showed no significant changes. The results of immunohistochemistry of the tumor and normal parts of the thymus are summarized in Table 1.
Cytokeratin-positive cells were prominent in the dark area of the tumor compared with the normal thymic cortex (Fig. 4a). The cytoplasm of positive cells showed a meshwork-like structure (Fig. 4b). CD3-positive T-cells were more frequently observed in the pale foci than the dark area of the tumor, and a few CD79α-positive B-cells were observed in the pale foci only. Ki-67-positive cells were mainly located in the dark area and were sparse in the pale foci. These labeling patterns of the tumor except for the positive index of cytokeratin were similar to the corresponding area in the normal thymic tissue (Table 1). Ultrastructurally, desmosomes and bundles of tonofilaments were observed in the epithelioid cells, but the dense-core secretory granules were not confirmed (Fig. 5). Based on histopathological, immunohistochemical and electron microscopic findings, this tumor was diagnosed as a benign thymoma. Thymic lymphoma was ruled out as a differential diagnosis because of the presence of cytokeratin-positive epithelioid cells and lack of atypical lymphocytes.

The cellular components of thymomas are considered to vary from an epithelial cell type to lymphoid cell type3,7. Thymoma in rodents was previously categorized into three histological types by its predominant cellular population, that are epithelial cell type, lymphoid cell type and mixed cell type8. The present case was mainly composed of lymphoid cells with slightly increased numbers of epithelioid cells compared with the normal cellularity in the thymic cortex. Therefore, it was considered to be a lymphoid cell type. In addition, the present case was characterized by the

Table 1. Results of Immunohistochemistry

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<th>Tumor</th>
<th>Normal part of the thymus</th>
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<tr>
<td></td>
<td>Dark area</td>
<td>Pale foci</td>
</tr>
<tr>
<td>Cytokeratin</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>CD3</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>CD79α</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>Ki-67</td>
<td>+++</td>
<td>+</td>
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−, +, ++ and +++: Negative, very few cells positive, some cells positive and most cells strongly positive, respectively.

Fig. 4. Immunohistochemistry for cytokeratin. a: Cytokeratin-positive cells are prominent in the tumor compared with the normal thymic cortex. Bar=1000 μm. b: Higher magnification of Fig. 4a. The cytoplasm of positive cells show a meshwork-like structure. Bar=10 μm.

Fig. 5. Electron micrograph of the epithelioid cells. Desmosomes are found between the epithelioid cells, and bundles of tonofilaments are also observed in the cytoplasm. Bar=500 nm.
predominant lymphocytes, medulla differentiation and perivascular space resembling a B1/B2 type thymoma, which is its counterpart in humans.

Thymomas commonly grow slowly in an expansive fashion and are recognized accidentally in aged rats\textsuperscript{10}. Actually, thymomas have been reported to occur in W/Nhg rats\textsuperscript{7} from around 12 months of age and in Wistar (Cpb:WU) rats\textsuperscript{5} from after 104 weeks of age. Furthermore, the occurrence of thymoma in SD-derived rats (Tif:RAI) under 400 days old is quite rare\textsuperscript{11}. Moreover, the occurrence of thymoma in the Sprague-Dawley strain\textsuperscript{5,6} is recognized as being quite rare compared with certain inbred strains of rats such as the W/Nhg and BUF/Mna strains\textsuperscript{7,12}, which have a higher incidence. Therefore, the present case was quite rare and the youngest case of spontaneous thymoma occurring in SD rat.

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References