NOTE  Pathology

Polypoid Eosinophilic Cystitis with Pseudosarcomatous Proliferative Tissue in a Dog

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ABSTRACT. A dog presented with hematuria, and two small polypoid masses were detected in the urinary bladder. Histopathologically, the masses were located in the mucosal or submucosal layer. That tissue consisted of a random proliferation of spindle-shaped, round and pleomorphic cells with single or multiple large atypical nuclei and abundant cytoplasm, and eosinophil infiltration. These large cells were confirmed by immunohistochemical staining as fibroblasts, myofibroblasts and macrophages. Mitotic figure was rarely seen. These masses were diagnosed as eosinophilic polypoid cystitis with pseudosarcomatous proliferative tissue, since they consisted of a wide variety of cells and showed low growth activity.

KEY WORDS: canine, eosinophilic cystitis, pseudosarcomatous proliferation.

Eosinophilic polypoid cystitis is a relatively common canine disease characterized by the development of a polypoid mass with fibrous connective tissue and a marked infiltration of eosinophils [2, 3]. It was thought to be a variant of polypoid cystitis [2, 3]. The nature of the lesions is nonneoplastic, but a differential diagnosis from true neoplasm might be needed in cases with abundant mesenchymal components. This is a case report of canine polypoid eosinophilic cystitis with pseudosarcomatous proliferative tissue.

A 5-year-old spayed female ShihTzu-dog presented with hematuria, and two small polypoid masses were detected in the urinary bladder. When the masses were resected from the bladder, the hematuria completely disappeared and showed no recurrence 11 months after surgery. The two polypoid masses, 25 × 15 × 10 and 12 × 12 × 10 mm in size, protruded into the lumen. Both masses were solid and firm with an irregular surface, and brown to white in color. The mucosal surface covering the masses was ulcerated. The cut surface of two masses was also solid and white in color.

Specimens were fixed in 10% neutral formalin (pH 7.4), dehydrated in a graded series of ethanol, and embedded in paraffin, after which 4-µm-thick sections were stained with hematoxylin and eosin. Immunohistochemical staining was performed by labeled polymer method using N-Histofine MAX PO (M or R) (Nichirei, Tokyo, Japan). The primary antibodies used for each section were anti-human c-kit (diluted at 1:800, rabbit polyclonal antibody, DAKO Japan, Japan), anti-human Ki-67 (diluted at 1:50, mouse monoclonal antibody MIB-1, DAKO, Denmark), anti-canine CD18 (diluted at 1:100, mouse monoclonal antibody CA16.3C10, obtained from Dr. P.F. Moore), anti-vimentin (diluted at 1:200, mouse monoclonal antibody V9, DAKO), anti-human lysozyme (diluted at 1:200, rabbit polyclonal antibody, DAKO), anti-human myeloid histioctye antigen/Mac387 (diluted at 1:100, mouse monoclonal antibody MAC387, DAKO), anti-cow S100 (diluted at 1:25, rabbit polyclonal antibody, Nichirei), anti-human desmin (diluted at 1:100, mouse monoclonal antibody D33, DAKO), and anti-human smooth muscle actin (SMA) (diluted at 1:400, mouse monoclonal antibody 1A4, DAKO). To evaluate cell proliferation activity using Ki-67 staining (Ki-67 index), we counted the number of strongly positive cells among more than 500 cells.

Histopathologically, the masses were located in the mucosal or submucosal layer without invasion to the muscular layer. They were composed of fibrous tissue covered with partially ulcerated hyperplastic epithelium (Fig. 1). Inflammatory cells, predominantly eosinophils and a small number of lymphocytes and plasma cells, had infiltrated the fibrous tissue (Figs. 1 and 3). That tissue in one polyp consisted of large spindle-shaped round and pleomorphic cells with abundant cytoplasm and large single or multiple atypical nuclei (Figs. 2 and 3). The stroma varied in appearance from myxoid to collagenous depending on their location. These large cells with atypical nuclei were confirmed as vimentin-positive fibroblasts, SMA/desmin-positive myofibroblasts (Fig. 4) and Mac387-positive macrophages by their immunohistochemical nature (Fig. 5). In addition, some cells with atypical nuclei were c-kit positive. Mitotic figures were rarely seen, and the Ki-67 index was 1% (Fig. 6). These cells were negative for S100, CD18 and lysozyme. Fibrous tissue of the other polyp mainly consisted of fusiform cells with relatively scanty cytoplasm having single ovoid to elongated nuclei like those of fibroblasts. The fusiform cells that were arranged randomly among a moderate amount of intercellular collagen were confirmed as vimentin-positive fibroblasts and desmin-positive myofibroblasts. Mitotic figures were rarely observed, and the Ki-67 index was 1%.

The histopathologic features of our case are similar to those in eosinophilic polypoid cystitis expect for pseudosarcomatous proliferative tissue. The appearance of cells with...
Fig. 1. Urinary bladder, dog. Mass is composed of fibrous tissue covered with hyperplastic epithelium. Hematoxylin and eosin (HE) stain. Bar=50 µm.

Fig. 2. Urinary bladder, dog. Fibrous tissue of one polyp consists of large spindle-shaped, round and pleomorphic cells with collagenous stroma. HE stain. Bar=50 µm.

Fig. 3. Urinary bladder, dog. Large spindle-shaped, round and pleomorphic cells have abundant cytoplasm and a single or multiple atypical nuclei. HE stain. Bar=50 µm.

Fig. 4. Urinary bladder, dog. Immunoreactivity for smooth muscle actin is detected. Spindle to pleomorphic cells are positive. Universal Immuno-enzyme Polymer method, Mayer’s hematoxylin counterstain. Bar=50 µm.

Fig. 5. Urinary bladder, dog. Immunoreactivity to Mac387 is detected. Round to pleomorphic cells are positive. Universal Immuno-enzyme Polymer method, Mayer’s hematoxylin counterstain. Bar=50 µm.

Fig. 6. Urinary bladder, dog. Immunoreactivity to Ki-67 is detected. Ki-67 index is 1% (Universal Immuno-enzyme Polymer method, Mayer’s hematoxylin counterstain. Bar=50 µm.
large atypical nuclei indicates the need for a differential diagnosis other than true neoplasm such as fibromas and sarcomas.

Fibromas are mainly located in the lamina propria, and are composed of an irregular network of loosely arranged fusiform cells, with ovoid to elongated pale nuclei without cell atypia [1]. Some tumor masses have been associated with severe inflammatory cell infiltration with lymphocytes, plasma cells and eosinophils, and were thought difficult to distinguish from chronic inflammatory changes. Under these circumstances, some fibromas might easily be misdiagnosed as non-neoplastic lesions. Whether polypoid cystitis with fibroplasia is a pure inflammatory change or a fibroma with overlapping inflammation remains controversial.

Immunohistochemically, fusiform cells are reported to be negative for desmin and SMA [3], in contrast to the positive results in our case. The appearance of the cells in the present case is markedly different from that of previous cases of fibroma, because the stromal cells constituting the polyp had large atypical and pleomorphic nuclei together with immunohistochemical characters clearly different from fibroblasts or fibrocytes.

Despite a morphological characteristic suggesting a neoplastic nature, immunohistochemical stain clearly revealed that these pleomorphic cells with large atypical nuclei were composed of fibroblasts, myofibroblasts and macrophages with a low growth rate by the low Ki-67 index. The differential diagnosis between neoplastic and non-neoplastic nature of these cells was very difficult, because of two distinct evidences, low growth rate suggested by the low Ki-67 index, and cell atypia. However, the lesions in our cases showed no distinct invasive potential, and the origin of their atypical pleomorphic cells was heterogeneous. In addition, inflammatory cells were diffusely infiltrated throughout the polyp. These morphological and immunohistochemical characteristics were suggested that the lesions were non-neoplastic nature, but it was impossible to deny that the present case was neoplastic nature.

Immunohistochemically, there are no SMA- or desmin-positive smooth muscle cells in fibromas or polypoid eosinophilic cystitis [3, 4]. In our case, SMA and/ or desmin positive cells were scattered randomly arrangement among the collagen fibers. These cells did not form the long bundles or fascicles thought to be characteristic of smooth muscle cells. Based on their morphologic and immunohistochemical characteristics, these cells are more likely to be identified as myofibroblasts, which are widely distributed in all visceral organs and increase in number due to inflammation, wound healing and tissue fibrosis. In the urinary bladder, myofibroblasts are located in the lamina propria [5]. There are no reports of myofibroblasts in fibromas and canine polypoid cystitis. This is, to our knowledge, the first report on the involvement of myofibroblasts in canine polypoid eosinophilic cystitis.

REFERENCES