Case Report

Spontaneous Granular Cell Tumor of Cecum in a Laboratory Beagle

Junko Sato¹, Maiko Tsurukame¹, Hiroshi Edamoto¹, Osamu Kusuoka¹, and Kazutoshi Tamura¹

¹Bozo Research Center Inc., 1284 Kamado, Gotemba-shi, Shizuoka 412–0039, Japan

Abstract: A spontaneous granular cell tumor was found in the cecum of a 9-month-old female beagle. The tumor cells were distributed widely and multifocally throughout the cecal submucosa and basal portion of the lamina propria, but never formed macroscopic nodular lesions. Partial infiltration into the muscular layer was observed, but neither metastasis nor invasion to other tissues was detected. The tumor cells were oval to polygonal and were characterized by abundant eosinophilic and PAS positive granules in the cytoplasm. Immunohistochemically, the tumor cells were positive for vimentin, but negative for S-100 protein, NSE, desmin, lysozyme, and α₁-antichymotrypsin. Ultrastructurally, various numbers of lysosomal bodies containing lamellar and membranous structures were present in the cytoplasm. Neither basal lamina nor cell-to-cell communications were observed. This is the first report of canine granular cell tumor arising in the cecum and is of interest as it occurred in a young laboratory beagle.

Key words: granular cell tumor, dog, cecum, young age

Since Abrikossoff first described a human case of granular cell tumor (GCT) in 1926¹, referring to it as granular cell myoblastoma, similar cases have been reported in various animals with species specific predilection sites. In laboratory animals, it is well-known that GCT frequently occurs in the meninges and the female genital tract in aged rats²–³, although no case has been reported in laboratory beagles. Canine GCTs arise mostly in the oral cavity such as gingiva, lip, and tongue at about 10 years of age⁴–⁵, and there have also been cases reported in the skin⁶–⁷, meninges⁸–¹⁰, heart¹¹, lymph nodes¹², brain¹³,¹⁴, pituitary gland¹⁵, and pleural surface¹⁶. The present report describes a GCT found in the cecum of a laboratory beagle, and this is believed to be the first case of intestinal GCT in dogs.

The present case is a female beagle, 9 months of age, used in a toxicological study. After complete necropsy, all tissues were fixed in phosphate buffered 10% formalin solution and were subjected to routine histological examination using hematoxylin and eosin staining. Sections were trimmed from 6 different parts of the cecum, and stained with periodic acid-Schiff (PAS) with/without diastase digestion and Masson’s trichrome. They were also allowed to react immunohistochemically with S-100 protein (1:400, rabbit anti-cow polyclonal), neuron-specific enolase (1:100, clone BBS/NC/V1-H14, mouse anti-human monoclonal, NSE), lysozyme (1:200, rabbit anti-human polyclonal), α₁-antichymotrypsin (1:200, rabbit anti-human polyclonal), desmin (1:100, clone D33, mouse anti-human monoclonal) and vimentin (1:50, clone V9, mouse anti-swine monoclonal, DAKO Japan Co., Ltd., Kyoto, Japan) using LSAB kit (DAKO Japan Co., Ltd., Kyoto, Japan). Additionally, small pieces of the tumor tissues originally fixed in formalin were processed for electron microscopical examination.

The present case did not show any abnormalities in clinical signs, hematological or serum biochemical analyses or at macroscopic examination.

Microscopically, the tumor cells were distributed widely and multifocally throughout the cecum in all sections from 6 different parts of the cecum, but never formed a macroscopic nodular lesion (Figs. 1, 2). The tumor cells were located mainly in the submucosa and less frequently in the basal part of lamina propria with sheet-like proliferation and sparsely in the muscular layer (Fig. 3). They were widely distributed throughout the cecum tissue, but neither metastasis nor invasion to other tissues was observed. Mitotic figures were rarely detected. These tumor cells were oval to polygonal in shape, with no atypical morphology, and were characterized by numerous eosinophilic granules in the cytoplasm (Fig. 4) which revealed strong positivity for PAS staining with/without diastase digestion. Moreover, in Masson’s trichrome stain, it was clearly demonstrated that...
Fig. 1. Diagram of distribution of tumor cells.

Fig. 2. The tumor cells located in the submucosa, basal part of lamina propria, and muscular layer. PAS stain. × 30.

Fig. 3. The tumor in muscle layer. The tumor cells are scattered in the muscle layer. PAS stain. × 110.

Fig. 4. The tumor in submucosa. Tumor cells have granular cytoplasm. H.E. stain. × 340.

Fig. 5. The tumor cells stained positively for vimentin. Immunohistochemistry for vimentin. × 340.
the tumor contained relatively abundant intercellular collagen in some parts.

Immunohistochemically, the tumor cells stained positive for anti-vimentin (Fig. 5), but negative for anti-S100 protein, NSE, lysozyme, α 1-antichymotrypsin, and desmin antibodies.

Ultrastructurally, the tumor cells contained many electron dense lysosomal bodies of varying size, containing many lamella and membranous structures (Fig. 6). No basal lamella, or cell-to-cell junctions were observed.

The present case is of interest in terms of age and location of occurrence, while the morphological and histochemical characteristics from the present case are comparable to those of GCTs reported previously. Most canine GCTs occur at about 10 years of age or more, while a GCT in the gingiva of a 6-month-old puppy has been reported and a similar tumor as congenital epulis in human neonates. A congenital GCT has also been reported in the arm in man. However, it is unclear whether the present case can be regarded as congenital.

One characteristic of the present lesion is multifocal occurrence. Although this pattern of occurrence is seen, for example canine lymphoma in the intestine, it is rare for tumors, so the possibility that the lesion is not neoplastic must be considered. However, since granular cells are not present in normal tissue, it could hardly have been formed by cell infiltration or hyperplasia. It is known that GCTs occur in the female reproductive tracts without forming nodules or distinct borders and expand along with tissue planes and ligaments. Therefore, taken together the reports about the occurrence of multifocal GCTs in humans and rodents, the present lesion is thought to be a multifocal GCT arising in the cecum.

Canine GCTs arise mostly in the oral cavity and also less frequently in other tissues, but no intestinal GCTs have been reported. In man, GCTs in the digestive tract comprise 10% or less of total GCTs, which commonly occur in the esophagus and rarely in the cecum. With recent development of endoscopy, such human cases have been increasing, which may suggest that more latent cases are present not only in man but also in other species including dogs. In fact, the present case was found unexpectedly during histological examination and there were no clinical abnormalities.

Most GCTs are thought to be benign, with malignant GCTs comprising only 2% of the total. However, a tumor should be considered malignant when it shows nuclear atypia, cellular pleomorphism, transformation to spindle cells, increased nuclear:cytoplasmic ratio, associated necrosis and infiltration into the muscle layer. In the present case, the tumor cells infiltrated sparsely into the muscle layer. Although this finding may indicate malignancy, a benign diagnosis could not be excluded since no cellular atypia and no evidence of destructive infiltration or metastasis to other tissues were observed.

GCT is a descriptive term including different tumors and several cells of origin have been proposed since no normal cell counterpart for granular cells is known. Granular cells appear not only in GCTs but also in various lesions such as granular adamantinomas, granular cell angiosarcomas, granular basal cell tumors, and granular cell meningiomas. The majority of human and rodent GCTs are considered to originate from peripheral nerve-related cells including Schwann cells, because of their immunohistochemical and ultrastructural features: positive reaction to NES and/or S100 protein and presence of basement lamina. On the other hand, most canine GCTs show positive reactions for vimentin but not for S100 protein, and their derivation is still undetermined. The results of the immunohistochemical and electron microscopic studies performed on the present case were comparable to those of previous reports but did not provide any new insight regarding histogenesis.

The present tumor is probably the first canine GCT arising in the cecum and is of interest as it occurred in a young laboratory beagle.

References


