Primary renal tumors are relatively uncommon in dogs, accounting for only 0.3% to 1.5% of all reported canine neoplasms [2, 9]. Renal tumors in the dog generally are classified into 4 types according to their cellular origin: epithelial (renal tubular or transitional cell), mesenchymal, mixed (epithelial and mesenchymal), and nephroblastic [9]. However, there have been few reports of primary benign or malignant renal mesenchymal tumors in young experimental dogs detected accidentally in clinical experiences.

In-depth research on the background data of experimental animals can help contribute to an appropriate diagnosis in toxicological studies. The present report describes the histopathological, immunohistochemical and ultrastructural characteristics of a congenital mesoblastic nephroma found incidentally in a young male beagle dog used in a 2-week toxicity study.

A right kidney from a 15-month-old male beagle dog (Marshall BioResources, NY, U.S.A.) at necropsy was used in this study. The dog was allocated to the control group of a 14-day toxicity study with 14-day recovery period and administered 10 ml/kg of 0.5 w/v% methylcellulose (methylcellulose400, Wako Pure Chemical Co., Ltd., Osaka, Japan) solution by gavage daily for 14 days. The dog was maintained on commercial food pellets and allowed free access to tap water. Experiments were conducted in accordance with the Guiding Principles for the Care and Use of Laboratory Animals in Kyowa Hakko Kirin, Co., Ltd (Shizuoka, Japan). On the day following the end of the recovery period, the animal was euthanized by exsanguination under deep anesthesia. At necropsy, a well-delineated, gray-white mass was found in the right kidney. The mass was approximately 8 mm in diameter and extended from the capsule to a position slightly compressing the medulla (Fig. 1a).

Histopathologically, the tumor was non-encapsulated and composed of interfacing bundles of homogenous spindle cells with small basophilic nuclei and scant eosinophilic cytoplasm (Figs. 1b, 1c). Tumor cells had invaded into adjacent renal tissues. Most parts of the tumor showed a myxoid pattern, in which the matrix was positive for alcian blue staining (Fig. 1d). In other parts of the tumor, the cells were arranged in a fascicular and wavy pattern, and the matrix was full of collagen fibrils as indicated by Masson’s trichrome (Fig. 1e). In the tumor, no mitotic figures, necrosis or hemorrhage was observed.

Immunohistochemical examinations were conducted using mouse anti-human vimentin antibody (Nichirei, Tokyo, Japan), mouse anti-human cytokeratin AE1/AE3 (Nichirei, Tokyo, Japan), rabbit anti-human factor VIII antibody (Dako, Denmark, A/S), mouse anti-human desmin antibody (1:100; Dako, Denmark, A/S), mouse anti-αSMA antibody (PROGEN, Wieblingen), rabbit anti-human S-100 antibody (Nichirei, Tokyo, Japan), rabbit anti-human myelin basic protein antibody (Nichirei, Tokyo, Japan), rabbit anti-human fibronectin antibody (1:500; Dako, Denmark, A/S) and rabbit anti-murine COX-2 antibody (1:200; Cayman Chemical, Ann Arbor, MI) as primary antibodies. Immunohistologically, most of the tumor cells were positive for vimentin (Fig. 2a) and fibronectin (Fig. 2b). However, cytokeratin, desmin, α-smooth muscle actin (α-SMA), Von Willebrand factor, cyclooxygenase-2 and myelin basic protein. As a result, we diagnosed this case to be a renal mesenchymal tumor. Based on the microscopic findings, interstitial characteristics and immunohistochemical features, the present case was classified as a congenital mesoblastic tumor.

Key words: canine, congenital mesoblastic nephroma, renal mesenchymal tumor.
Willebrand factor (Factor VIII), cyclooxygenase-2 (COX-2) and myelin basic protein (MBP) staining were not observed in the tumor. A small amount of non-specific staining was present after treatment with the anti S-100 antibody in a portion of the marginal region.

Ultrastructurally, the tumor cells had an oval-shaped nucleus, a few mitochondria, and a small amount of rough endoplasmic reticulum (Figs. 2c, 2d). There were many collagen fibrils in the extracellular matrix.

In dogs, the most frequently reported tumors include adenomas, fibromas, leiomyomas, and lipomas, and the peak incidence is in middle-aged to older dogs [6, 7]. The present case was considered to be a rare since the dog was young and the cell origin was mesenchymal.

In humans, congenital mesoblastic nephroma (CMN) is often present at birth and the mean age of presentation is 3 months. The condition is designated as “congenital”, because the tumor cells are considered to have originated from the metanephrogenic blastoma during fetal development and may differentiate into various types of mesenchymal cells in different cases. CMN in humans is composed mainly of primitive mesenchymal cells which form dense aggregates or bundles [3]. The myxomatous area is positive for alcin blue staining and the intercellular collagen area is typically positive for both silver impregnation and Masson’s trichrome staining. This tumor is histologically categorized as two variants: the classical (conventional) and cellular (atypical) type. The classical type is composed of interlacing bundles of spindle cells lacking significant mitotic activity, while the cellular type tends to have a higher cellularity with many mitotic figures [3]. Mixed forms with a combination of the 2 patterns have also been reported. Based on the microscopic similarities, we thought that the present tumor in this canine case should therefore be diagnosed to be a congenital mesoblastic nephroma.

Only 2 previous cases of CMN in beagle dogs have been reported [13, 14]. In these reports, the spindle tumor cells had spindle-shaped or oval basophilic nuclei and scant cytoplasm with a few mitotic figures. In addition, in these tumors, one part of the tumor had a loose myxomatous pattern with an alcin blue-positive matrix, while the other part was dense, cellular, and fibromatous to the myxomatous areas. The microscopic characteristics of these canine CMN were similar to those of human CMN, as was true for our present case. The other 2 renal mesenchymal tumors in beagle dogs were reported to have areas composed of leiomyomatous and primitive mesenchyme-like cells which resembled canine CMN [1, 12]. Our case was different from the previous cases with regard to its immunohistochemical characteristics: it was negative for S-100, αSMA and desmin staining [14].

The present tumor in this paper must be distinguished from such tumors as fibromas and renomedullary interstitial cell tumors. Renal fibroma in dogs have been reported to be negative for alcin blue staining [10]. Renomedullary interstitial cell tumors were first introduced by Leyman et al. [8], and these tumors are composed of interstitial cells with characteristic light and electron microscopic features different from fibroblasts, i.e., positive extracellular alcin blue staining, lipid-rich cytoplasmic vesicles, high prostaglandin content and positive expression of COX-2 [5, 11]. In dogs, renal interstitial tumors occur in the cortex and medulla of older dogs (from 10 to 18 years), are often bilateral and multiple [4, 6]. In our case, the characteristics of the reported canine renal tumor were consistent with a renomedullary interstitial cell tumor with respect to the alcin blue positive matrix, but not with the other features, including the age of the dog (15 months), the unilateral and single nature of the tumor, and the negative results for COX-2 staining by immunohistochemistry. We concluded that the present tumor in this case was therefore not a renomedullary interstitial cell tumor.

In conclusion, we diagnosed this case to be a renal mesenchymal tumor based on the histological features, the findings of abundant collagen fibrils and myxomatous materials in the matrix, positivity for vimentin and fibronecin by immunohistochemistry, and negative staining for the other markers. We have classified this case as CMN, but more cases will be needed in order to confirm the presence of CMN in dogs, because CMN in humans are rich in terms of their diversity of histological and immunohistochemical findings.

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