Primary chondrosarcomas arise from existing normal cartilage and perichondrium at sites such as the pelvis, nasal cavity, sternum, and ribs, and less often in long bones. Extraskeletal chondrosarcoma was first described as an entity in 1953 by Stout and Verner [23]. Characteristically, in most reported cases, extraskeletal chondrosarcoma exhibits less aggressive behaviour than its skeletal counterpart [5, 21, 24].

A series of extraskeletal myxoid chondrosarcoma in man was described in 1972 by Enzinger and Shiraki [5]. Almost all the tumors in this series affected adults (mean age 49 years), and the only child was a 13-year-old girl. In animals, reports of extraskeletal chondrosarcoma are rare, and most cases have been described as a single mass in adult or old dogs [1, 9, 13, 19, 22]. In this case report, we describe an extraskeletal myxoid chondrosarcoma with systemic metastasis in a five-month-old dog.

A five-month-old male Irish setter dog was referred to our veterinary hospital with a history of anorexia, dyspnea, diarrhea, and exophthalmos of the left eye. The dog had been fully vaccinated, and there was no previous medical or surgical history. Under sedation, radiographs of the thoracic cavity were taken and confirmed the presence of a large, poorly defined mass lying within the right caudal lobe of lung. Approximately three-fourths of the thoracic cavity was occupied by the pulmonary mass, and systemic metastasis was confirmed by abdominal radiographs. Because of the poor prognosis, the dog was euthanized. A necropsy examination was performed.
Microscopically, the femurs of the hind limbs had no macroscopic changes.

Microscopically, the largest mass in the lung was surrounded by thickened fibrous tissues, but fibrous capsules were not observed in the metastatic areas. The mass was divided into variably sized lobules by thin fibrovascular stroma. The lobules comprised myxoid stroma and loosely or densely arranged sheets of neoplastic mesenchymal cells (Fig. 3). The myxoid stroma stained blue with Alcian blue (Fig. 4). Most of the tumor cells had large round to oval nuclei with a reticular chromatin pattern, one or more large nucleoli, and a deeply eosinophilic cytoplasm (Fig. 5). Occasionally, these cells streamed around vascular spaces. The tumor cells exhibited moderate anisokaryosis, and many mitotic figures [4–6 per high-power field (400×)] were noted. Mitotic figures were observed more frequently near the vessels than in peripheral areas. PAS-positive granules were observed rarely in the cytoplasm of the tumor cells. Differentiation into immature cartilaginous tissue was only identified very rarely in the lung and cerebellum (Fig. 6), but osteoid formation was not visible in any of the lesions. Necrotic foci were significant in the tumor of the lung. These areas contained cell debris that was occasionally mineralized, hemosiderin-laden macrophages, and foreign body giant cells. Fibrin and neoplastic thrombi were observed occasionally in the lung. Tumor cells were not observed in the pre-existing bone, cartilage tissue, and bone marrow of the bilateral femurs.

Immunohistochemically, most of the tumor cells stained positively for vimentin (Fig. 7), and 10–30% of the cells were positive for S-100 protein (Fig. 8) and NSE antibodies. The tumor cells stained positively and focally for chromogranin A and calretinin but did not react with antibodies to SMA, desmin, synaptophysin and CK AE1/AE3 (Table 1).

Ultrastructurally, the tumor cells showed nuclear pleomorphism and often had deeply invaginated nuclei. The cytoplasm was comprised abundant rough endoplasmic reticulum, mitochondria, well-developed Golgi complex and free ribosomes, and short irregular microvillous processes was observed from the cytoplasm surfaces was observed (Fig. 9). Intracellular bundles of intermediated filaments with moderate densities were observed. Intracellular or extracellular desmosome-like structures without tonofilaments were also observed. Rarely, cilia and centrosome-like structures, irregular dense core secretory granules 80–150 nm in diameter, and lipid droplets were found.

In man, two distinct histological subtypes of soft tissue extraskeletal chondrosarcoma have been described: myxoid and mesenchymal [6]. Myxoid chondrosarcoma is characterized by a multinodular pattern and well-circumscribed masses comprising round or elongated cells of uniform shape and size separated by variable amounts of mucoid material [25]. Unlike chondrosarcoma of bone, differentiated cartilage cells with distinct lacunae and ossification are rare. By contrast, mesenchymal chondrosarcoma exhibits a bimorphic pattern comprising sheets of undifferentiated mesenchymal cells and well-defined islets or nodules of well-differentiated benign-appearing cartilaginous tissue, and areas resembling vascular tumors such as a hemangiopericytoma [2, 4]. Extraskeletal myxoid chondrosarcoma shows slow growth and delayed metastasis compared to mesenchymal counterpart. Metastasis rate is 31 to 46% and 10-year survival rate is 65 to 78% after the initial diagnosis of the tumor [7, 11, 12]. The differential diagnosis of extraskeletal mesenchymal chondrosarcoma and myxoid chondrosarcoma is sometimes difficult, because these tumors share similar myogenic and neurogenic differentiation [14, 18].

In the tumor described here, the most characteristic features were mixed components of mesenchymal cells and myxoid stroma, and had no relationship to pre-existing cartilage and bones. Generally, tumor cells of the extraskeletal myxoid chondrosarcoma have intracytoplasmic PAS positive granules [6, 18], and diffusely positive for vimentin and S-100 protein [17, 18], but negative for epithelial cell markers [18]. In addition, a small number of tumor cells stain for neural or neuroendocrine markers, such as NSE, chromogranin A, and synaptophysin [10, 18]. Electronmicroscopically, the components of organelle of tumor cells are
Fig. 3. The lobules comprise myxoid stroma and loosely or densely arranged in sheets of neoplastic mesenchymal cells. Occasionally, these cells stream around vascular spaces (*). HE. Bar=50 µm.

Fig. 4. The myxoid stroma stain blue with Alcian blue stain. Alcian blue. Bar=30 µm.

Fig. 5. Most of tumor cells have large round to oval nuclei with large nucleoli, and deeply eosinophilic cytoplasm. Mitosis (arrow) is also observed. HE. Bar=30 µm.

Fig. 6. Differentiation into cartilaginous tissue is observed in the cerebellum. HE. Bar=50 µm.

Fig. 7. Most of tumor cells stain positively for vimentin. Immunohistochemistry. Bar=20 µm.

Fig. 8. Tumor cells are occasionally positive for S-100 protein. Immunohistochemistry. Bar=30 µm.

Table 1. Immunohistochemical reaction patterns of tumor cells in the present case

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Vimentin</th>
<th>S-100</th>
<th>NSE</th>
<th>Chromogranin A</th>
<th>Calretinin</th>
<th>SMA</th>
<th>Desmin</th>
<th>Synaptophysin</th>
<th>CK AE1/AE3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor cells</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

-- Negative, +: under 10%, ++: 10–30%, +++: over 30%.
similar to those of chondrocytes, and irregular microvillous processes at the cell surface are one of the evidence of definitive diagnosis [8, 17]. Our histological, immunohistochemical and ultrastructural findings are similar to those reported previously for extraskeletal myxoid chondrosarcoma in man and other animals [8, 17, 18].

In dogs, extraskeletal chondrosarcoma occurs in the lung [19], omentum [19], heart including pericardium [1, 9, 13, 19, 22], spleen [15], abdomen [20], retroperitoneum [16], and liver [3]. Most previously reported cases involved variants of extraskeletal mesenchymal chondrosarcoma and occurred in adult or old dogs aged 18 months to 17 years (mean 7.8 years). Interestingly, 83% (10/12) of cases were observed in males, and 25% (3/12) were German shepherd and 17% (2/12) were Golden retriever dogs. Heart (5/12) and lung (2/12) were the most frequent sites of involvement (Table 2).

The dog in our study was five months old and showed systemic metastasis, but the tumor had no relationship with pre-existing cartilage and bones. On the basis of the gross and pathological findings, the tumor was diagnosed as an extraskeletal myxoid chondrosarcoma. The origin of this tumor was unknown, but the largest tumor with necrosis and hemorrhage was found in the right caudal lobe of the lung.

We conclude that the tumor arose from pre-existing primitive cartilage-forming mesenchymal cells in the lung.

REFERENCES


Table 2. Summary of extraskeletal chondrosarcoma reported in dogs

<table>
<thead>
<tr>
<th>Age, sex, breed</th>
<th>Site of tumor</th>
<th>Histological classification</th>
<th>Site of metastasis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 months, male, Irish setter</td>
<td>Lung</td>
<td>Myxoid</td>
<td>Liver, kidney, greater omentum, pancreas, lymph nodes, the base of left eyeball, cerebellum, adrenal gland, diaphragm, heart</td>
<td>Present case</td>
</tr>
<tr>
<td>11, 14, and 17 years, male, 2 of 3 were</td>
<td>Omentum</td>
<td>Mesenchymal</td>
<td>None</td>
<td>19</td>
</tr>
<tr>
<td>12 years, male (castrated), Labrador retriever</td>
<td>Heart</td>
<td>Mesenchymal</td>
<td>None</td>
<td>19</td>
</tr>
<tr>
<td>3 years, male (castrated), Golden retriever</td>
<td>Spleen</td>
<td>Mesenchymal</td>
<td>Necropsy was not performed</td>
<td>15</td>
</tr>
<tr>
<td>18 months, male, German shepherd</td>
<td>Right atrium</td>
<td>Unclassified</td>
<td>Necropsy was not performed</td>
<td>20</td>
</tr>
<tr>
<td>3 years, male, Mixed breed</td>
<td>Abdominal</td>
<td>Mesenchymal</td>
<td>None</td>
<td>22</td>
</tr>
<tr>
<td>6 years, male, Golden retriever</td>
<td>Liver</td>
<td>Unclassified</td>
<td>Lung, diaphragm, omentum, perineum, spleen, adrenal glands, kidneys, abdominal wall, serosa of gastrointestinal tract</td>
<td>3</td>
</tr>
<tr>
<td>20 months, female, Mastiff</td>
<td>Retroperitoneum</td>
<td>Mesenchymal</td>
<td>Pulmonary, pleural</td>
<td>16</td>
</tr>
<tr>
<td>7 years, male (castrated), Schnauzer</td>
<td>Pericardium</td>
<td>Mesenchymal</td>
<td>None</td>
<td>13</td>
</tr>
<tr>
<td>13 years, female, Mixed breed</td>
<td>Mitral leaflet</td>
<td>Unclassified</td>
<td>None</td>
<td>9</td>
</tr>
</tbody>
</table>

Fig. 9. Tumor cells show nuclear pleomorphism and have deeply invaginated nuclei, and short irregular microvillous processes (arrows) extending from the cytoplasm are seen. Electron microscopy. Bar=5 μm.
EXTRASKELETAL MYXOID CHONDROSARCOMA

421–435. [Medline] [CrossRef]


