epithelium, the layer of rods and cones, and the outer nuclear layer. In the present cases, the central retinal blood vessels were absent, and other retinal blood vessels were slender and rarely seen in histologic sections. These findings suggest that failure in differentiation or loss of the retinal ganglion cells and nerve fibers may be due to failure in the retinal vascularization with subsequent degeneration. It thus seems that as a result of failure in development of the ganglion cells, almost all nerve fibers may have failed to develop and reach the optic disk.

Retinal atrophy has frequently been observed in rats in association with aging and changes in lighting. In these cases, the outer layer of the retina particularly photoreceptor cells, became atrophic, whereas the ganglion cell and nerve fiber layers were absent or hypoplastic in cases of congenital aplasia or hypoplasia of the optic nerve. Our cases coincided with these observations, although the primary cause of these ocular defects remains unknown.

In our rats, the right half of the optic chiasma and the right optic tract appeared highly hypoplastic and rudimentary. These parts were interpreted as being composed exclusively of nerve fibers deriving from the right optic nerve, because of complete absence of the left optic nerve. This is based on the fact that the optic chiasma and tract of rats are composed of nerve fibers coming from the ipsilateral and contralateral optic nerves. This interpretation seems to be supported by the observation that neither degenerative nor inflammatory changes could be detected in any of the hypoplastic areas we examined.

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Cytologic, Histologic, and Ultrastructural Characteristics of a Canine Myxoid Liposarcoma

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Lipomas, the most common mesenchymal tumor of dogs, are located in subcutaneous tissues and grow slowly by expansion. A separate group of adipose neoplasms, infiltrative lipomas, are composed of well-differentiated adipocytes that aggressively invade surrounding tissues but do not tend to metastasize. In contrast to their benign counterparts, liposarcomas are uncommon in dogs, arising de novo and not from pre-existing lipomas or infiltrative lipomas. The favored sites for a liposarcoma in human beings are the deeper soft tissues, including gluteal region, the thigh, lower extremity, and retroperitoneum. In the dog, there is a predilection for subcutis and deeper soft tissue involvement, yet the thoracic and abdominal cavities are also frequent sites of liposarcoma.

Liposarcomas vary greatly in their histologic pattern, and, in human beings, different subtypes are associated with different biological behavior. The myxoid liposarcoma is the most common subtype and has low metastatic potential. Other subtypes include pleomorphic, round-cell, and sclerosing liposarcoma. Round-cell and pleomorphic subtypes have a more malignant behavior and greater metastatic potential than other types of liposarcomas. The diagnosis of myxoid liposarcoma is based primarily on histologic criteria of mucinous areas within the tumor. Unlike the myxoma or myxosarcoma, in the myxoid liposarcoma mature and immature adipocytes are admixed with stellate- to spindle-shaped cells. An anastomosing vascular pattern is also characteristic. This paper records cytologic, histologic, and ultrastructural char-

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characteristics of a well-differentiated myxoid liposarcoma in the thorax of a dog.

An 8-year-old, male Golden Retriever was admitted to the Ohio State University Veterinary Teaching Hospital with a 2-month history of chronic cough, exercise intolerance, and facial edema. In thoracic radiographs, the cardiac silhouette was dorsally and caudally displaced by a large, soft tissue density mass in the cranial mediastinum, and the caudal lung lobes were markedly compressed.

A fine needle aspirate of the mediastinal mass was submitted for cytologic evaluation. In Wright-Giemsa stained smears of the tumor aspirate there was a prominent population of moderately pleomorphic adipocytes with a low nuclear to cytoplasmic (N:C) ratio and abundant pale staining cytoplasm (Fig. 1). In many of these cells, the nucleus was displaced to the periphery and compressed by a single lipid droplet. Other cells contained a large lipid droplet and one to multiple more centrally located round nuclei. Nuclear molding was occasionally observed. A prominent population of smaller cells with a high N:C ratio, lightly basophilic cytoplasm, and one or multiple small lipid droplets were present. These cells were interpreted as immature adipocytes. The chromatin pattern varied from hyperchromatic to finely granular with one to two prominent small nucleoli. Cells that were similar morphologically to these immature adipocytes, but lacked evidence of lipid storage, were interpreted as primitive mesenchymal cells. The changes were suggestive of a well-differentiated liposarcoma.

A median sternotomy for removal of the mass was performed. Lung metastases were not evident, but the tumor was firmly attached to the mediastinum and to the floor of the thorax. The dog did well post-operatively and was discharged. At 4 months the dog was clinically normal.

The tumor was 15 x 18 x 8 cm with intermingled soft areas of a yellow, mucoid and glistening tissue and firm fibrous areas on cut section. Histologically, the tumor was subdivided into irregular lobules by a fibrovascular stroma and consisted of variable sized well-differentiated adipocytes. The tumor was not encapsulated and had invaded the adjacent soft tissues of the sternum and mediastinum. Many of the adipocytes had a single large lipid droplet that displaced and flattened the nucleus. Stellate- to spindle-shaped cells containing few lipid droplets or lacking evidence of lipid storage were scattered throughout the tumor and, in multifocal areas, were the prominent cell type. These cells had a high nuclear to cytoplasmic ratio, a finely granular chromatin pattern with peripheral margination, and one to two prominent nucleoli. Occasional immature adipocytes with multiple nuclei were observed. The mitotic rate of the tumor was low. The tumor had a prominent anastomosing vascular network and contained multifocal areas of abundant basophilic ground substance. This myxoid ground substance stained with Alcian blue (Fig. 2). Although stellate- to spindle-shaped cells were prominent in these myxoid areas, scattered, well-differentiated adipocytes attested to the true nature of this neoplasm (Fig. 3).

With electron microscopy, mature adipocytes were characterized by their large size, eccentrically placed nucleus, large lipid droplet, few profiles of endoplasmic reticulum and free ribosomes, and numerous micropinocytotic vesicles. The lipid droplets were of medium electron density and were not membrane bound. In anaplastic adipocytes the nuclei were rounded and contained one to multiple smaller intracytoplasmic lipid droplets. Mitochondria and micropinocytotic vesicles were prominent in immature adipocytes, and an external lamina was occasionally observed. Flattened Golgi

Fig. 1. A well-differentiated liposarcoma. Moderately pleomorphic adipocyte containing a single, large lipid droplet and multiple nuclei with prominent nucleoli (large arrow). Immature adipocyte with multiple small lipid droplets (small arrow). Fine needle aspirate. Wright-Giemsa stain.

Fig. 2. A tumor containing mature adipocytes and lipoblasts, adjacent to an area of abundant ground substance rich in mucopolysaccharides that stained positive for Alcian blue. Variable differentiated adipocytes are embedded in the myxoid matrix. HE.

Fig. 3. Myxoid area with primitive mesenchymal cells that are the prominent cell type; however, an occasional mature adipocyte attests to the true nature of the neoplasm (arrow). Masson's trichrome.
Fig. 4. A well-differentiated liposarcoma with bands of microfilaments partly surrounding the nucleus and a lipid droplet. Electron micrograph.

Fig. 5. Lipoblasts contain multiple lipid droplets of varying size. Penetrating and interdigitating processes lie between adjacent lipoblasts (arrow). Electron micrograph.

zones, scattered free ribosomes and rough endoplasmic reticulum, as well as prominent microfilaments were present. Microfilaments were most prominent adjacent to the nucleus and lipid droplets and were arranged in parallel bundles (Fig. 4). Extracellular ground substance consisting of aggregates of finely granular material was abundant. Inter cellular contacts between adipocytes characterized by penetrating and interdigitating cellular processes (Fig. 5) were occasionally observed. Previous studies described similar peculiar intracellular contacts between immature adipocytes. This finding was in accordance with the work of researchers who demonstrated electrical coupling between developing white adipocytes.

In this study, we found a continuum of developing adipocytes that ranged from primitive mesenchymal cells to mature adipocytes. In general, cells with few or no lipid droplets contained an abundance of cytoplasmic components. These components were lost as lipid accumulated in the cell. This finding was consistent with previous ultrastructural studies of human liposarcomas in which researchers found evidence that adipocytes differentiated from a primitive, fibroblast-like adipocyte precursor cell in human beings and dogs. It is the extent to which neoplastic adipocytes differentiate may vary. It has been observed that neoplastic transformation of tumor cells may be associated with relative prominence or absence of certain cytoplasmic components. A structure normally seen in developing adipocytes may become unusually prominent, such as the microfilaments in this case. A previous report describing ultra-structural details of canine liposarcoma did not include microfilaments. Microfilaments have been inconsistently found in cases of human myxoid liposarcoma.

Our histopathologic diagnosis was a well-differentiated myxoid liposarcoma based primarily on histologic criteria of myxoid areas containing neoplastic adipocytes, frequent differentiation to mature adipocytes, and invasion of surrounding soft tissues. We felt this classification most accurately reflected both the cellular characteristics and the biological behavior of the tumor.

References


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