Canine mesenchymal hamartoma of the eyelid

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Abstract

Objective Characterization of a benign disease syndrome involving the eyelids of dogs, describing the signalment, clinical appearance, anatomic location, and pathologic features.

Animal studied The records and submitted tissue of 10 dogs with mesenchymal hamartomatous lesions of the periocular connective tissues were retrieved from the Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW) database.

Procedure The submitted tissue in each case was stained with hematoxilyn & eosin and Masson’s Trichrome stain and examined histopathologically. Clinical information was collected from the submission requests. The clinical history, treatment, and follow-up are described in more detail for one of the 10 dogs.

Results Seven different breeds, including four Golden Retrievers, were represented. The ages of affected dogs ranged from 6 to 11 years. Eight of 10 lesions were located at the temporal canthus, ranging in diameter from 0.6 to 3 cm. Clinically, the masses were subcutaneous, firm, lobular soft-tissue growths, which were in some cases adherent to the underlying orbital rim, and in others, freely palpable between the skin and conjunctiva of the eyelid. Histologically, all had distinct margins but were not encapsulated and contained normal appearing collagen-rich connective tissue with some adipose tissue. Five also contained fully differentiated skeletal muscle tissue arranged in poorly formed aggregates or as individual muscle fibers.

Conclusion Mesenchymal hamartoma of the eyelid has not been previously described. The mass has a predisposition to occur at the temporal canthus and should be included in the list of differential diagnoses of benign eyelid masses in dogs.

Key Words: benign, canine, canthal, dog, eyelid, hamartoma

INTRODUCTION

The most common tumors of the eyelids in dogs are tumors generally found in the skin, including sebaceous gland adenomas, Meibomian gland adenomas, squamous papillomas, melanocytomas, mast cell tumors, trichoblastomas (basal cell tumor), trichoepitheliomas, lymphosarcoma, histiocytic tumors, hemangiomas and hemangiosarcomas. In a study of 202 canine eyelid tumors, 75.3% was benign lesions. Meibomian gland adenomas represented approximately 40% of all eyelid tumors.1–3

Hamartomas are benign mass lesions made up of fully differentiated but disorganized tissues normally present in the affected areas. They tend to affect one type of tissue predominantly. These disorganized, proliferative lesions are mass-forming nodules, but they do not meet all of the necessary requirements to be classified as neoplasms.4,5 Unlike neoplasms, their growth is limited and they retain their size with no further expansion.4

Canine hamartomas have been described in dogs in several different tissues and organs, including kidney, lung, skin, periodontal ligament, vasculature, musculature, peripheral nerve, spinal cord, and hypothalamus.7–18 Although canine hamartomas are reported in several different anatomic locations, the reports are mostly single case reports or sporadically descriptions of 3–5 patients. To the best of the authors’ knowledge, there are no (published) reports of any ocular adnexal hamartoma in dogs.

In the human-based literature, hamartomas have been described in several anatomic locations, including the eyelids as well as intraocular structures. The term phakomatosis (disseminated hereditary hamartomas) includes diseases such as angiomatosis retinae, meningocutaneous angiomatosis, and neurofibromatosis type 1. Angiomatosis
retinae (von Hippel’s disease) presents with retinal capillary hemangioma and retinal hamartoma. Meningocutaneous angiomatosis (Sturge–Weber Syndrome) presents with choroidal cavernous hemangioma. Neurofibromatosis type 1 presents with iris nevi (Lisch nodules) and retinal glial hamartoma as well as angiofibromas of the eyelids, iris, lens, and choroidal colobomas (Bourneville’s disease). Neurocutaneous syndromes such as encephalocraniocutaneous lipomatosis (Haberland syndrome) demonstrates among other defects, lipomatous hamartomas of the eyelid.

Single eyelid and conjunctival hamartomas without other ocular lesions have been reported rarely in humans. Examples include rhabdomyomatous mesenchymal hamartomas of the eyelid, fibrous and phakomatous hamartomas as well as conjunctival smooth muscle hamartoma of the fornix and pigmented hamartoma with apocrine, follicular, and sebaceous differentiation.

Herein, we report a series of 10 dogs with mesenchymal hamartoma of the eyelid and thus provide the first report of this rare and unusual tumor-like mass affecting canine ocular tissues.

MATERIALS AND METHODS

All canine cases with a diagnosis of mesenchymal periocular hamartoma were selected from the database of the Comparative Ocular Pathology Laboratory of Wisconsin, which includes 18,431 canine ocular pathology submissions. The following criteria were recorded and evaluated for each specimen: signalment, clinical history and diagnosis, tumor appearance, distribution, and cellular morphology.

Clinical information was collected from the accompanying submission forms. In one of the 10 cases, a detailed clinical description and follow-up is illustrated.

RESULTS

A total of nine completely excised tumor masses and one incisional biopsy specimen were evaluated between 2001 and 2009. The signalment and clinical features are summarized in Table 1.

Clinical findings

The age of the dogs ranged from 6 to 11 years with a mean age of 8.1 years. There were five neutered males, one intact male, two spayed females, one intact female, and one dog of unspecified gender. Golden Retrievers were the most common breed (n = 4); other breeds with one each included: Giant Schnauzer, German Shepherd, Rottweiler, English Cocker Spaniel, Weimaraner, and Doberman Pinscher. The lids of both eyes were equally affected. In 8/10 dogs, the tumor was located in the temporal canthus. In one dog the tumor was excised from the central superior eyelid, while another, the mass was in contact with the lid margin but the location was not specified. The duration of clinical signs in 7/10 cases ranged from 1 to 24 months (mean = 6 months). The duration of clinical signs was not given in three dogs.

Clinically, the eyelid masses were described as subcutaneous or subconjunctival tumors in all samples. In 7/10 cases an intact epidermis covering the mass was reported. Regarding the clinical description, a lipoma was suspected in three dogs. Fine needle aspiration was performed in 2/10 cases and was inconclusive due to inadequate cell sampling. A previous biopsy in one case was interpreted as a benign mass lesion with fibroma being suspected. During the surgical procedure, in 4/8 patients, a tight adhesion to the temporal/lateral palpebral ligament was described. No additional ocular findings were reported, apart from a concurrent nuclear sclerosis in one case and previous limbal melanoma excision in another.

Table 1. Signalment and clinical appearance of dogs diagnosed with mesenchymal eyelid hamartoma

<table>
<thead>
<tr>
<th>Case #</th>
<th>Specimen/Location</th>
<th>Breed</th>
<th>Age</th>
<th>Gender</th>
<th>Clinical appearance</th>
<th>Duration of clinical signs (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Eyelid mass</td>
<td>Giant Schnauzer</td>
<td>7</td>
<td>MC</td>
<td>Subconjunctival mass</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>Eyelid mass</td>
<td>English Cocker Spaniel</td>
<td>7</td>
<td>FS</td>
<td>Subconjunctival mass, intact epidermis</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Eyelid mass</td>
<td>Rottweiler</td>
<td>6</td>
<td>M</td>
<td>Subcutaneous mass, intact epidermis</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Eyelid mass</td>
<td>Golden Retriever</td>
<td>7</td>
<td>MC</td>
<td>Subconjunctival mass, intact epidermis</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>Eyelid mass</td>
<td>Golden Retriever</td>
<td>10</td>
<td>MC</td>
<td>Subcutaneous mass</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Eyelid mass</td>
<td>German Shepherd</td>
<td>10</td>
<td>FS</td>
<td>Subcutaneous mass, intact epidermis</td>
<td>24</td>
</tr>
<tr>
<td>7</td>
<td>Biopsy, temporal</td>
<td>Doberman Pincher</td>
<td>11</td>
<td>MC</td>
<td>Subcutaneous mass, intact epidermis</td>
<td>nfs</td>
</tr>
<tr>
<td>8</td>
<td>Eyelid mass, ventro-temporal canthus</td>
<td>Golden Retriever</td>
<td>6</td>
<td>MC</td>
<td>Subconjunctival mass, intact epidermis</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>Eyelid mass</td>
<td>Golden Retriever</td>
<td>9</td>
<td>F</td>
<td>Palpebral mass, intact epidermis</td>
<td>nfs</td>
</tr>
<tr>
<td>10</td>
<td>Eyelid mass</td>
<td>Weimaraner</td>
<td>8</td>
<td>nfs</td>
<td>nfs</td>
<td>nfs</td>
</tr>
</tbody>
</table>

MC, male castrated; M, male; F, female; FS, female spayed; nfs, not further specified.
A detailed clinical description and follow-up information was available in one dog (case 6).

The patient was referred to a veterinary ophthalmologist after two prior incomplete excisions. The mass had grown slowly over 2 years, to involve approximately one-half of the lower eyelid margin, the lateral canthus, and one-quarter of the upper eyelid margin. The mass was firm, lobular, and seemed adherent to the underlying orbital rim at the lateral canthus (Fig. 1). A fine needle aspirate was performed, which revealed few squamous epithelial cells, plump mesenchymal cells, and occasional blood leukocytes. The diagnosis was inconclusive. Excision of the mass with histopathology and eyelid reconstruction was planned. The abnormal tissue separated easily from the surrounding normal tissues, except at the lateral canthus, where it seemed to extend under the lateral orbital rim. The defect left by the mass removal was closed via an upper eyelid Z-plasty, and a lower eyelid H-plasty, which were joined to form a new lateral canthus. Fifteen months later, no re-growth has been reported and the dog remained comfortable and visual.

**Histopathologic findings**

In all 10 samples, the firm masses were poorly delineated and surrounded by connective tissue of the dermis.

Histologically, all 10 tumors had poorly distinct margins. Compressed stroma was observed surrounding the expansile mass (Fig. 2). In several cases, the tumor was covered by intact epidermis and conjunctival epithelium. The masses consisted of disorganized dense bundles of collagen, scant fully differentiated fibroblasts interspersed with multiple foci of fully differentiated adipocytes. In 5/10 samples, individual fibers or small bundles of skeletal muscle were present (Figs 3, 4). The collagenous connective tissue, adipose islands, and skeletal muscle bundles were fully differentiated, with normal appearing cell nuclei without signs of atypia (Fig. 4). In two cases, the mass included fully differen-

tiated peripheral nerve tissue and several dilated vessels scattered throughout. In one case, there were a small numbers of perivascular lymphocytes, however, in the remaining cases, there was no sign of inflammation. In all 10 cases, there were no characteristics suggestive of malignancy.

**DISCUSSION**

Hamartoma was used by Albrecht in 1904 to describe tumor-like lesions with a quantitative increase in mature cells and tissue normally present at the particular site of origin. Although the cellular elements of a hamartoma are identical to those found in the anatomic location, they are disorganized. Recently, hamartoma was classified as an
intermediate form of tissue proliferation between malformation and neoplasm. However, classification of such lesions remains confusing, because the terminology used varies.

In some definitions, the mass is designated as congenital. Although there are several examples of congenital hamartomas none of the definitions include congenital as an absolute criterion. The cases presented here were not known to be congenital and the criteria are not usually a part of the definition of hamartoma. In the human literature, hamartomas are reported mainly in newborns and are usually present from birth, except in two reports of hamartomas in adults. Interestingly, all dogs in this study, as well as those described in the veterinary literature, were middle-aged and older dogs, ranging between 2 and 15 years of age.

We hypothesize that lesions presented in this report could have been subclinical, small lesions present from birth but this was not ever suggested by the clinical histories. One dog (case 6) had a recurrence after the first excision suggesting that the tissues of the mass have a potential to grow (Fig. 1). There is a report of a 57-year-old woman with a similar clinical history of unexplained regrowth. The connection to and extension into the epithelial tissue could be the tissue of origin or if these lesions could originate from the tarsal plate. The presence of lipocytes suggests a more orbital origin; however, this was not seen clinically. The connection to and extension into the epidermis is not described as, in our tissue samples, the epidermis was not sampled in an attempt to preserve the temporal eyelid canthi during the surgical procedure.

Clinical, a tight adhesion to the temporal canthal region was observed in these cases. In dogs, the retractor anguli oculi muscle and the robust temporal fascia replace the temporal palpebral ligament. One might speculate whether this tissue could be the tissue of origin or if these lesions could originate from the tarsal plate. The presence of lipocytes suggests a more orbital origin; however, this was not seen clinically. The connection to and extension into the epidermis is not described as, in our tissue samples, the epidermis was not sampled in an attempt to preserve the temporal eyelid canthi during the surgical procedure.

Rhabdomyomatous mesenchymal hamartomas (RMH) in humans have histological features very similar to the five canine cases, which had skeletal muscle as part of the lesion. It has been suggested that RMH of the eyelids develops in anatomic areas containing second branchial arch-derived, superficially located, striated muscle, such as the orbicularis oculi muscle. Read et al. noted several associated ocular abnormalities such as colobomas, limbal dermoid, orbital cysts and sclerocorneas, as well as Goldenhaar and Delleman syndromes. Because of the association of neurocutaneous syndromes and phakomatosis with dermal hamartomas in humans, we recommend a complete ophthalmic and systemic evaluation, with a focus on neurological work-up, in patients diagnosed with this rare entity.

Clinically, the hamartomas, described herein, present as slow growing, soft, poorly circumscribed masses with mostly intact epidermis and palpebral conjunctiva. Fine needle aspiration and cytology provide inconclusive results, whereas biopsy should be diagnostic. Complete local excision should have features of cellular atypia and a dense pattern of repetitive collagen and interwoven fascicles. Fibrosarcomas are spindle cell tumors with an interwoven, herringbone pattern, cellular pleomorphism, and cell atypia. Myxomas are tumors of fibroblast origin and are rich in mucopolysaccharides, but, again, the cells are not typical of the area in which they originate. Neurofibromas, or benign peripheral nerve sheath tumors occur rarely in the eyelids of dogs. These tumors are composed of wavy spindle cells in loosely arranged whorls in a mucinous matrix; the typical Antoni A or Antoni B patterns are important to recognize. Lipomas are usually only composed of adipocytes, which can be fully differentiated. Lipomas might qualify as hamartomatous lesions, but they often show uncontrolled and invasive growth, not typical of a hamartoma. Liu and Mikaelian describe tumors arising from the arrector pili muscle in the skin. They described arrector pili muscle hamartomas, which were well-differentiated masses with a moderate amount of smooth muscle bundles.

Dermal collagenous hamartomas (collagenous nevus) are described in elderly dogs; they are located mainly in the dermis and are composed of collagen bundles. The hamartomas described in this study are composed of two or three different components.

Interestingly, in 8/10 dogs, the lesions were seen in the temporal canthal region.

In this study, the diagnosis is based on the characteristic histological features, such as disorganized but fully differentiated fibrous tissue, adipose tissue and often, skeletal muscle tissue. Histopathologically, other entities must be considered in the list of differential diagnoses. Fibromas are benign neoplasma of fibrocytes with an abundant collagenous stroma, but in contrast to hamartomas, these tumors show

**Figure 4.** Collagen bundles between fully differentiated skeletal muscle fibers (•) and adipocytes; ×400, HE (case 8).
be successful in most cases, because no malignant degeneration or spontaneous regression has been documented so far in the human literature or the veterinary literature.21

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REFERENCES