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Adenocarcinoma of the nictitans gland in a dog

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Abstract: The case of a five-year-old spayed female French Bulldog with a mass in the right third eyelid is described. Ultrasonography and computed tomography were used to identify this pathological lesion and to visualise its morphology and extent. The mass was removed and submitted for histopathological examination. A final diagnosis of adenocarcinoma of the nictitans gland was made. In the discussion we compare the presented case with the available literature. Only limited information is published about this pathology.

Keywords: canine neoplasia; computed tomography; gland of the third eyelid; orbital neoplasia; retrobulbar space

Exophthalmos is the most common clinical sign associated with orbital mass lesions. Differential diagnoses for exophthalmos include orbital foreign body, abscess, cellulitis, orbital neoplasia, zygomatic sialadenitis, zygomatic salivary mucocele and masticatory myositis (Betbeze 2015). Generally, canine ocular neoplasia is uncommon when compared to neoplasms arising from other organs (Dubielzig 1990). Orbital neoplasia can have various origins and evaluating the exact anatomic location of the mass within the orbit is crucial for proper characterisation, further surgical planning and prognosis (Labelle and Labelle 2013; Betbeze 2015). Different types of orbital tumours have been described (Kern 1985; Burk 1992; Hendrix and Gelatt 2000; Betbeze 2015), but the extent of the here-described tumour is unusual and unique in the veterinary literature.

Case description

A five-year-old spayed female French Bulldog was presented with a mass associated with the right eye and a history of sudden loss of vision. Hyphaema and exophthalmos were detected (Figure 1). The right eye globe appeared smaller in size compared to the left globe, which did not show any morphological abnormalities. Intraocular pressure of the affected eye was elevated (35 mm Hg) compared to the healthy globe (22 mm Hg). All other organ systems were clinically unaffected.

Ultrasonography (US) of the right eye was performed using a 14 MHz linear transducer (Vivid 7, GE Vingmed Ultrasound, Norway). A heteroechogenic mass was found ventromedial to the right eye globe and extension into the retrobulbar space was noticed. The mass lesion was well

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Figure 1. Photograph of the right eye showing exophthalmos, redness, protrusion of the third eyelid and swollen eyelids

defined with a hyperechoic peripheral rim. The size of the mass was 28 × 23 mm. The right globe was smaller in size than the left and deformed. No ultrasonographic abnormalities of the intraocular structures were noted. The differential diagnosis after ultrasonography was neoplastic mass or granuloma. Computed tomography (CT) was recommended for better assessment of anatomical structures of the entire orbit. The dog was anesthetised using medetomidine (0.15 ml *i.v.*; Domitor 1 mg/ml, Orion Pharma, Czech Republic), butorphanol (0.3 ml *i.v.*; Butomidor 10 mg/ml, Richter Pharma, Austria) and propofol (2 ml *i.v.*; Propofol-Lipuro 1%, B Braun, Germany). A CT examination (LightSpeed 16, GE Medical Systems, USA) was performed with the animal in sternal recumbency and the scanned area covered the entire head to the level of the sixth cervical vertebra. The CT scans were performed in the helical mode with 100 kV, automatic mA, rotation time 1 s, slice thickness 2.5 mm, spiral pitch 0.9 and medium frequency kernel. After the pre-contrast examination, 2.3 ml/kg of a 300 mg/ml non-ionic iodine contrast medium (Iomeron 300, Bracco Imaging, Germany) were injected intravenously at 3 ml/s using a power injector system (MCT Plus, Medrad, USA). Scanning parameters were identical for the pre-contrast and post-contrast examinations. The examination showed the presence of a large mass of soft tissue density with a small elliptical hypoattenuating central area. The mass was located ventromedially to the right eye globe with extension into the retrobulbar space. Focal thickening of the upper eyelid was also observed (Figure 2). Both

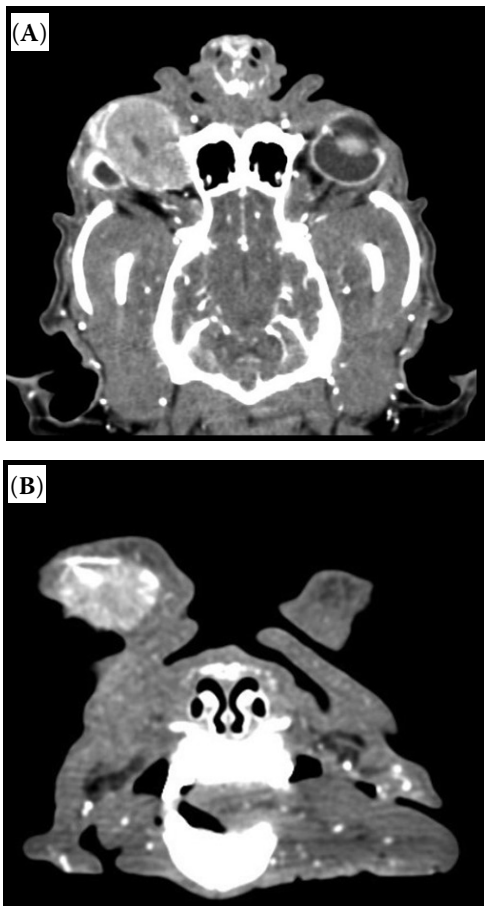

Figure 2. (**A**) Post-contrast CT image of the head reconstructed in a dorsal plane to show the whole mass in the right retrobulbar space and its extension through the medial commissure. The mass is well demarcated and strongly contrast-enhancing with a small central hypodense area without contrast enhancement. The compression of the right eyeball is clearly seen. (**B**) Post-contrast CT image of the head in transversal plane at a level rostral to the eyeballs. Note the thickened right upper eyelid with strongly contrast-enhancing mass in its distal portion, which was the extension of the retrobulbar mass to the upper eyelid. Please note the normal size of the opposite upper eyelid. In both images the right side of the animal is on the left side of the image

these lesions exhibited a strong degree of homogenous contrast-enhancement. The hypoattenuating central area in the retrobulbar mass was not contrast-enhancing. No signs of bone destruction were detected. The deformity of the eye globe was evident from both the pre-contrast and post-contrast scans. The mass focally invaded the posterior wall of the globe (Figure 3). The ipsilateral medial retropharyngeal lymph node was enlarged with ho-

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Figure 3. Post-contrast CT images of the head in transversal (**A**) and oblique dorsal (**B**) planes. The invasion of the mass to the posterior wall of the eyeball is seen from both views (black arrow)

mogeneous contrast enhancement. A neoplastic process with a possible origin in the base of the nictitans membrane was suspected based on the CT examination.

Surgery of the eye was performed the following day. For anaesthesia premedication medetomidine (0.2 ml *i.v.*; Domitor 1 mg/ml, Orion Pharma, Finland) and fentanyl (2 ml *i.v.*; Fentanyl Torrex 50 mg/ml, Torrex Chiesi, Czech Republic) were used, while for induction propofol (4 ml *i.v.*; Propofol-Lipuro 1%, B Braun, Germany) and for maintenance isoflurane (Isofluran, Torrex Chiesi, Czech Republic) in an oxygen/air mixture were used. For the postoperative analgesia, carprofen (0.6 ml *s.c.*; Rimadyl 50 mg/ml, Pfizer, Belgium) and buprenorphine (0.6 ml *i.v.*; Vetergesic vet. 0.3 mg/ml, Orion Pharma, UK) were administered. A lobulated neoplastic mass with infiltrative growth originating from the base of the third eyelid was detected during the surgery. The entire

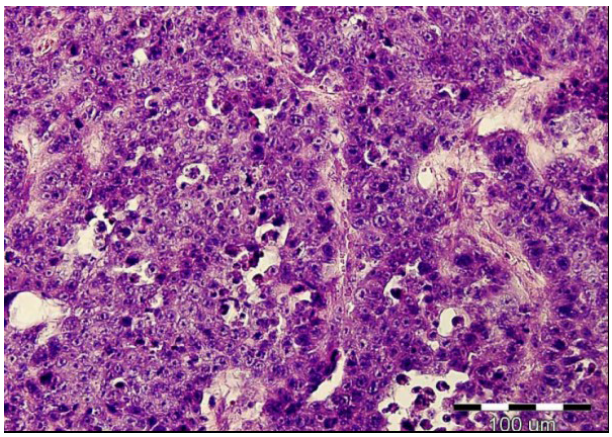

Figure 4. Nictitans gland adenocarcinoma. Cellular atypia represented by anisocytosis, anisokaryosis, prominent nucleoli and mitotic figures. HE, 400 ×

macroscopically visible mass was extirpated, and the third eyelid was amputated. Haemostasis was performed by electrocoagulation. No conjunctival sutures were required. A partial temporal tarsorrhaphy at the medial commissure was undertaken to prevent a globe prolapse. The patient recovered from the surgery uneventfully and was discharged the following day.

The resected mass was submitted to histopathological examination. Histopathology showed the presence of a neoplastic glandular epithelial cell population proliferating in the sparse fibrous mucosal stroma. The neoplastic cells proliferated focally in a tubulopapillary form. In the major part of the tumour parenchyma cells showed a solid type of growth. Cellular atypia was of moderate intensity and was present multifocally within the tumour tissue, characterised by anisocytosis, anisokaryosis with cells demonstrating prominent nucleoli and mitotic figures (Figure 4). Infiltrative growth of the neoplastic cells into fibrous stroma in some areas was detected. A secretion was noted in the apical parts of the cells and in the glandular lumen. The presence of a mild lymphocytic and neutrophilic inflammatory reaction was detected focally in the neoplastic tissue. The surrounding stroma was sparse and formed by well differentiated fibrous tissue. Based on the histopathological examination, the tumour was diagnosed as a nictitans gland adenocarcinoma, grade II.

The dog was euthanised six months after the surgery due to recurrence of the mass. The owners did not wish to continue with any diagnostic or other therapeutic procedures.

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DISCUSSION AND CONCLUSIONS

The most common neoplasias of the third eyelid are adenocarcinoma, papilloma and malignant melanoma (Ward 1999). Thbue third eyelid gland neoplasia is relatively uncommon in dogs. Between the years 2003 and 2013 only 15 cases of epithelial neoplasms of the third eyelid gland were detected among 39 213 canine cases. Eight of these 15 cases were adenocarcinomas (Miyazaki et al. 2015).

Third eyelid gland neoplasia is clinically characterised by protrusion of the third eyelid, exophthalmos, strabismus, resistance to retropulsion or enophthalmos (Headrick et al. 2004; Labelle and Labelle 2013).

In the available literature, adenocarcinomas are overrepresented, but a few reports of adenoma and pleomorphic adenoma can also be found (Wilcock and Peiffer 1988; Wang et al. 2001; Headrick et al. 2004). There is one case report of a third eyelid adenocarcinoma in a cat (Komaromy et al. 1997). As well as the third eyelid gland, the lacrimal gland and the zygomatic salivary gland can also be sources of intraorbital neoplasias. These neoplastic processes may have similar histological and behavioural features and their differentiation is, therefore, problematic (Wilcock 1993; Wang et al. 2001). These structures can be differentiated based on the anatomical location; however, the clinical appearance and symptoms are in most cases identical. In this situation, diagnostic imaging, especially transversal imaging modalities, are very helpful. A thorough description of periorbital glands and their differentiation can be found elsewhere (Wang et al. 2001).

The mass in this case shares some of the macroscopic features such as lobulation and firmness, with already described cases (Ward 1999; Headrick et al. 2004).

Diagnostic imaging modalities should be used as a helpful clinical and diagnostic tool to distinguish the origin of a mass lesion. Ultrasonography is an easily performed examination; however, the interpretation is operator-dependent. It can be used to diagnose intraocular as well the retrobulbar disorders. CT offers a detailed view of all body areas without the superimposition of nearby structures. It is a valuable imaging modality for orbital diseases. Due to presence of vitreous body and very good tissue contrast intraocular structures can be readily identified. The use of contrast media makes this differentiation even better. In this case, it was impossible to identify the structure that gave rise to the mass based on ultrasonographic examination and only a heteroechoic mass in the retrobulbar space was detected. The CT, however, revealed a connection of the mass with the upper eyelid through the medial commissure. Based on the CT appearance neoplastic rather than merely granulomatous processes were suspected. The focal invasion of the posterior wall of the eye globe was observed. To the authors' knowledge, this behaviour has not previously been described in this type of neoplasia and is considered unique. It has already been mentioned that adenocarcinomas have an expansive and variably infiltrative character (Wang et al. 2001; Labelle and Labelle 2013), but only infiltration to the loose connective tissue was noticed (Wang et al. 2001). Focal invasion to the globe wall, as in this case, can be used as a sign of aggressive nature and a potential complication of the neoplastic process. This feature must be considered for planning the surgery and to provide a better outcome for the patient. In the case described herein removal of the visible mass together with third eyelid amputation was performed. To remove the mass, which was located predominantly in the retrobulbar space, a complete orbital exenteration must be performed. It is stated that complete surgical excision should provide a good prognosis (Labelle and Labelle 2013).

The patient was managed after the surgery in a private veterinary practice and we were only informed about the recurrence of the mass in the same eye six months after the surgery. Based on the owners' decision euthanasia was performed. Because no additional examinations were performed, we can only speculate as to whether or not this was a recurrence of the previous neoplastic process; however, this would be a highly probable course of disease due to the fact that a complete resection of the mass was not possible.

The CT examination covered the cranial part of the neck and ipsilateral regional lymphadenopathy was detected. Because no tissue samples were collected for histopathology from this lymph node, we can only speculate as to whether the enlargement of the lymph node was a result of metastatic spreading from the primary neoplastic process. The causes of enlarged lymph nodes are in general inflammation, neoplastic infiltration and metastatic spread (Taeymans 2011; Zwingenberger and Taeymans 2015). There is only one report where possible metastasis, represented by enlargement of the man-

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dibular lymph node, after an incompletely excised adenocarcinoma occurred (Wilcock and Peiffer 1988). No necropsy was provided in that case.

In conclusion, here we provide a case description of a nictitans gland adenocarcinoma that is relatively uncommon in dogs. The invasion of the neoplastic mass into the eye globe wall seen in this case is unique and has been not described yet in the available veterinary literature. We suggest that these features should be investigated in patients with retrobulbar masses. CT is recommended in similar cases because of its superior visualisation of anatomical details and the possibility to appropriately plan the surgical procedure.

REFERENCES

Betbeze C (2015): Management of orbital diseases. Topics in Companion Animal Medicine 30, 107–117.

Burk RL (1992): Computed tomographic imaging of nasal disease in 100 dogs. Veterinary Radiology and Ultrasound 33, 177–180.

Dubielzig RR (1990): Ocular neoplasia in small animals. Veterinary Clinics of North America: Small Animal Practice 20, 837–848.

Headrick JF, Bentley E, Dubielzig RR (2004): Canine lobular orbital adenoma: A report of 15 cases with distinctive features. Veterinary Ophthalmology 7, 47–51.

Hendrix DV, Gelatt KN (2000): Diagnosis, treatment and outcome of orbital neoplasia in dogs: A retrospective study of 44 cases. Journal of Small Animal Practice 41, 105–108.

Kern TJ (1985): Orbital neoplasia in 23 dogs. Journal of the American Veterinary Medical Association 186, 489–491.

Komaromy AM, Ramsey DT, Render JA, Clark P (1997): Primary adenocarcinoma of the gland of the nictitating membrane in a cat. Journal of the American Animal Hospital Association 33, 333–336.

Labelle AL, Labelle P (2013): Canine ocular neoplasia: A review. Veterinary Ophthalmology 16 Supplement 1, 3–14.

Miyazaki A, Yonemaru K, Hirata A, Yanai T, Sakai H (2015): Histopathological and immunohistochemical features of atypical epithelial tumours of the gland of the third eyelid in seven dogs. Journal of Comparative Pathology 152, 299–303.

Taeymans O (2011): Lymph nodes of head and neck. In: Schwarz T, Saunders J (eds): Veterinary Computed Tomography. Wiley Blackwell, Oxford. 171–174.

Wang FI, Ting CT, Liu YS (2001): Orbital adenocarcinoma of lacrimal gland origin in a dog. Journal of Veterinary Diagnostic Investigation 13, 159–161.

Ward DA (1999): Diseases and surgery of the canine nictitating membrane. In: Gelatt KN (ed.): Veterinary Ophthalmology. Lippincott, Williams & Wilkins, Philadelphia. 609–618.

Wilcock BP (1993): The eye and ear. In: Jubb KVF, Kennedy PC, Palmer N (eds): Pathology of Domestic Animals. Academic Press, San Diego. 441–529.

Wilcock B, Peiffer Jr R (1988): Adenocarcinoma of the gland of the third eyelid in seven dogs. Journal of the American Veterinary Medical Association 193, 1549–1550.

Zwingenberger A, Taeymans O (2015): Neck. In: Penninck D, d'Anjou MA (eds): Atlas of Small Animal Ultrasonography. Wiley Blackwell, Oxford. 55–80.

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