Metastatic malignant pilomatricoma with bone and lung metastasis in a Portuguese Water Dog

Summary: Pilomatricomas consist of neoplastic proliferations of germinative cells of the follicular matrix or hair bulb. Malignant pilomatricomas are considered rare, with only a small number of cases reported in dogs. Here we present a case of malignant pilomatricoma in a Portuguese Water Dog with a 3-year clinical history of recurrent pilomatricomas with evidence of cellular atypia from the first diagnosis. The malignant behavior of the tumour in this animal included bone and lung metastasis. The bone invasion in the C1 vertebra resulted in severe pain and discomfort that finally led to euthanasia after a severe crisis of respiratory distress.

Keywords: malignant pilomatricoma, Portuguese Water Dog, bone and lung metastasis

Introduction

Follicular tumors are a relatively common event in small animal dermatology, more frequently reported in dogs and rarely in cats (Goldschmidt and Shofer 1992; Scott et al., 2001). Separating the structure of the hair follicle in three distinctive areas (infundibulum, isthmus and hair bulb) facilitates characterization of the various tumor types, in which malignant behavior is seldom reported.

A pilomatricoma (pilomatrixoma or calcifying epithelioma of Malherbe) consists of a neoplastic proliferation of germinative cells of the follicular matrix, or hair bulb (Gross et al., 2005; Lopansri and Mihm, 1980). Pilomatricomas occur most commonly in relatively young animals on the proximal legs and dorsal trunk, particularly over the rump and shoulders, and usually present as solitary, well circumscribed, firm to hard dermal and/or subcutaneous masses (Goldschmidt and Shofer, 1992; Neto et al., 2009). Some tumors have a gritty or bony consistency and lesions may be chalky when sectioned (Goldschmidt and Shofer, 1992; Gross et al., 2005; Massone et al., 2005). The overlying epidermis is often atrophic and lesions may be chalky when sectioned (Goldschmidt and Shofer, 1992; Gross et al., 2005; Massone et al., 2005).

Histologically, pilomatricomas are composed of multiple cystic structures of varying size, lined predominantly by small basaloid keratinocytes which resemble the matrix cells of the anagenic hair bulb. Mitotic activity is fairly high but nuclear or mitotic atypia is not present (Goldschmidt and Shofer, 1992; Gross et al., 2005). The neoplastic cells undergo matrical-type keratinization characterized by abrupt transition to large masses of keratinized ‘ghost’ or ‘shadow’ cells that fill the cysts’ lumen (Goldschmidt and Shofer, 1992; Gross et al., 2005; Neto et al., 2009). Ghost cells have a nucleus that does not stain with Hematoxylin&Eosin appearing as acidophilic cells with an apparent central void. They often become mineralized, and osseous metaplasia may occur, particularly in later stages, so that some tumors of chronic duration exhibit a predominance of ghost cells and bone with little residual epithelium (Gross et al., 2005).
A survey of follicular neoplasias diagnosed in the Laboratory of Pathological Anatomy of the Faculty of Veterinary Medicine of the Technical University of Lisbon, between 2005 and 2010, identified 182 cases (Table 1). Pilomatricomas accounted for 31 of these tumors, with a single case of malignant behavior; the one reported here.

Malignant pilomatricomas are considered rare, with only a small number of cases reported in dogs, some of which describing metastatization to the lymph nodes, lungs and bone (Maxie et al. 2007). The aim of the present work is to add a new case to these rare reports of malignant pilomatricoma in dogs (Carroll et al., 2010; Jackson et al., 2009; Johnson et al., 1983; Rodriguez et al., 1995; Sells and Conroy, 1976), this time in a Portuguese breed.

Case Report

In August 2008, Black, a three-year-old Portuguese Water Dog underwent surgery to remove a 3 cm dorsal nodule which was then sent to the Laboratory of Pathological Anatomy of the Faculty of Veterinary Medicine (Lisbon) for analysis. Histopathology reported this nodule to be a pilomatricoma, a proliferation of basaloid cells forming lobules with cystic central abrupt matrical keratinization and numerous ghost cells. Although the mitotic index was low, with less than one dividing cell per ten high power fields, there was some evidence of cellular atypia. Several lobules showed foci of bone formation and necrosis with cholesterol crystal clefts (Figure 1). In some areas, ruptured cysts had triggered inflammation and desmoplasia.

Eighteen months later, Black was again submitted to surgery to remove three small nodules. These new masses were located (i) in the head over the left eye (2 cm), (ii) in the left pectoral region (0.5 cm) and (iii) in the lumbar left area (1 cm). Upon histopathological analysis all three tumors showed characteristics already described for the tumor previously removed, although with clearer signs of malignant behavior, especially in the facial and pectoral nodules, such as indistinct limits and dermal infiltration (Figure 2). The neoplastic cells had a less basaloid appearance, and were larger, with paler nucleus and distinct nucleoli. Single cell necrosis was common and mitotic figures were frequent, accounting for a mean of two dividing cells per high power field. No calcification or bone formation were present in any of these nodules.

Six weeks after the last surgery, Black was presented for orthopedic evaluation due to severe right thoracic limb lameness without evidence of joint pathology distally to the shoulder. Clinical examination revealed a severe cervical pain on manipulation of the neck.

Table 1 - Retrospective survey of the archives of the Laboratory of Pathologic Anatomy of the Faculty of Veterinary Medicine (2005-2010). Follicular neoplasm type, species and sex distribution

<table>
<thead>
<tr>
<th>Type of Neoplasm</th>
<th>Cats</th>
<th>Dogs</th>
<th>Other Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Trichoepithelioma</td>
<td>3</td>
<td>4</td>
<td>29</td>
</tr>
<tr>
<td>Trichoblastoma</td>
<td>6</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>Pilomatricoma</td>
<td>0</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>Malignant pilomatricoma</td>
<td>0</td>
<td>0</td>
<td>0</td>
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*Male; ± Female
Radiographic studies were performed, showing bone proliferation over the left wing of C1 (Figure 3).

In the following weeks, Black's condition worsened. The owners opted for euthanasia after a severe crisis of respiratory distress and pleural effusion.

Upon necropsy, the only mass present in the skin was a nodule, 1.5 cm in diameter, located over the right eye. The left wing of the atlas (C1) was markedly enlarged, its dimensions being 5.5 x 3.5 x 3 cm, slightly projecting into the spinal canal and lightly compressing the spinal cord (Figure 4A). A negligible number of small blood clots were present in the epidural space. The pleural cavity contained around 100 ml of hemorrhagic fluid and both lungs exhibited various nodules, ranging from 0.5 to 4 cm in diameter (Figure 4B).

Sectioning the nodules revealed a white, rough and pasty cut surface with the consistency of calcified tissue. The surrounding pulmonary parenchyma was severely congestive.

Various tissue samples were collected from the necropsy and fixed in 10% buffered formalin. They were submitted for routine histopathological processing, except for the bone tissue, which was previously submitted for 24h to a commercial decalcifying solution (OSTEOMOLL ©, MERCK). Sections obtained from the processed tissue samples were all stained with Hematoxylin&Eosin (H&E). Giemsa stain was additionally applied to the decalcified bone sections.

Histopathological analysis of the nodule over the eye confirmed it was a pilomatricoma. However, although the cells still formed cystic lobules, they were now clearly smaller and more loosely arranged than in the other lesions.

Analysis of the pulmonary nodules revealed them to be similar to this nodule, with wide cystic cavities containing matrical keratin and ghost cells, occasionally surrounded by a thin rim of neoplastic cells. Although calcification was frequent, no bone formation was detected (Figure 5A). Lesions of purulent pneumonia were visible throughout the remainder of the pulmonary tissue.

Histopathology of the C1 mass revealed infiltration of bone trabeculae by neoplastic tissue that stands out due to the pale blue colour of keratinized cells in contrast with the bone tissue staining purple (Figure 5B). In fact, staining with Giemsa contributed to enhance the perception of the keratinized cells also improving the visualization of cellular details that were not so clear in the decalcified tissue stained with H&E.

**Discussion**

Pilomatricomas are most commonly benign tumors that originate from the germinative cells of the follicular matrix, taking the form of dermal and/or subdermal masses composed of multiple cystic structures lined by small basaloid keratinocytes, similar to the matrical cells of an anagenic hair follicle. Reports of malignant pilomatricomas are rare and restricted to dogs, in which metastatization to the lymph nodes, lungs and bone has been previously described (Maxie et al., 2007).

Histologically, malignant pilomatricomas can be distinguished from benign processes due to characteristics such as a low cellular differentiation, fast or erratic growth, high mitotic index, infiltration of neighbouring tissue and, finally, metastatization. In fact, malignant pilomatricomas generally assume a similar clinical presentation to benign pilomatricomas in the skin itself. In certain cases, the iatrotropic stimulus (the motive for owners to seek medical support) may be related not to the primary tumor but to some degree of dysfunction associated with distant...
metastasis (e.g., lameness) (Carroll et al., 2010).

Here we present the case of a Portuguese Water Dog with a clinical history of recurrent neoplastic lesions diagnosed as pilomatricomas, which became progressively more frequent and numerous and eventually invaded both bone and lung, severely compromising the animal’s quality of life. The multiple neoplastic lesions observed upon necropsy and histopathological analysis were attributed to metastasis of one of the previously removed pilomatricomas, namely the one located over the right eye. Black’s severe right thoracic limb lameness was attributed to medullary compression.

To the best of our knowledge, Black’s case is the first case of a malignant pilomatricoma ever to be reported in this particular breed. Although most cases of pilomatricoma described in the literature are related to the benign variant of this neoplasia, there is now a growing suspicion that malignant pilomatricoma may actually be a more common, aggressive and potentially fatal entity than previously assumed (Carroll et al., 2010; Meuten, 2002).

As reports of aggressiveness become more frequent, awareness to the presentation and behavior of these tumors becomes increasingly important to both pathologists and clinicians (Carroll et al., 2010), as a precocious diagnosis and an adequate treatment are essential in improving the patient’s quality of life and extending life expectancy.

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Bibliography