



NEOPLASTIC DISEASE

Embryonal Rhabdomyosarcoma of the Oesophagus in a Young Dog

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Summary

A 15-month-old great Dane dog, showing clinical signs related to hypertrophic osteopathy, was diagnosed radiographically with a mass in the region of the thoracic oesophagus. Exploratory thoracotomy revealed an extensive, highly vascularized and locally invasive oesophageal mass and the presence of nodules in adjacent lung lobes. The dog was humanely destroyed intra-operatively. Histological examination revealed that the mass was an embryonal rhabdomyosarcoma. This is the first report of rhabdomyosarcoma of the oesophagus of a dog. Rhabdomyosarcoma should be considered a differential diagnosis when a mass adjacent to the oesophagus is diagnosed.

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Primary oesophageal tumours are rare and account only for 0.5% of all neoplasms in dogs (Ridgway and Suter, 1979). Tumours may primarily arise from the oesophagus or, alternatively, para-oesophageal tumours may invade the oesophagus (Ridgway and Suter, 1979). Soft tissue sarcoma is the most common primary oesophageal tumour (Withrow, 2013) and thyroid carcinoma is the most common para-oesophageal tumour (Ridgway and Suter, 1979). The purpose of this report is to describe a rhabdomyosarcoma of the oesophagus in a young dog.

A 15-month-old male great Dane dog was presented with a 2-month history of pyrexia, lethargy, inappetence and weight loss. Haematological and serum biochemical examinations and abdominal radiographs performed by the referring veterinarian were within normal limits. The dog was treated empirically with amoxicillin, meloxicam and metoclo-

pramide without significant improvement. Because of the persistent pyrexia, antibiotics were changed to doxycycline after 1 week; this resulted in a partial and temporary clinical improvement. A few days before referral, the dog developed generalized stiffness and the distal forelimbs became diffusely swollen. At this time the body temperature was 40.8°C. Radiographs of the distal limbs showed the presence of periosteal reactions surrounding the bones of the phalanges, ulna and radius. These changes were consistent with hypertrophic osteopathy (Fig. 1). Subsequent thoracic radiographs revealed a large soft tissue opacity in the caudal mediastinum that was predominantly on the left side and between the diaphragm/liver and the caudal border of the cardiac silhouette (Fig. 2). Iodinated contrast medium (50 mgI/kg, Omnipaque™ 300 mgI/ml, GE Healthcare, Oslo, Norway) was administered orally to visualize the thoracic oesophagus. The caudal part of the oesophagus was displaced dorsally, suggesting the presence of a mass. The main differential diagnoses

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Fig. 1. Dorsopalmar radiograph of the right forefoot. There is palisading new bone formation (arrows) over the complete lateral cortex of the 5th metacarpal bone and the lateral and medial aspects of the 2nd phalanx of the first digit.

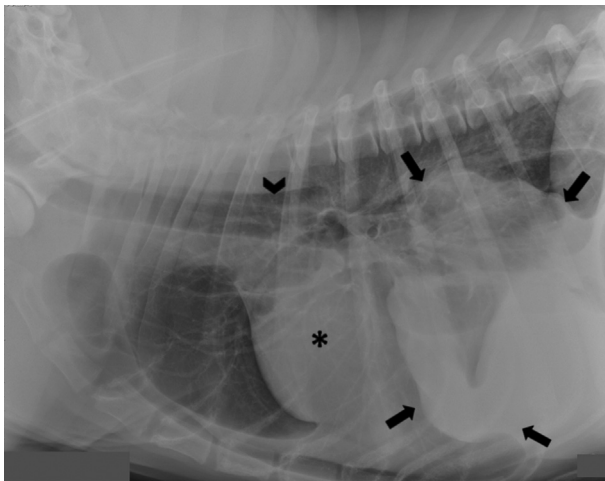


Fig. 2. Left lateral thoracic radiograph. There is a soft tissue opacity (arrows) in the caudal to caudoventral aspect of the thorax, causing border effacement of the caudal margin of the cardiac silhouette (asterisk) and the diaphragm. The oesophagus is partially filled with air (arrowhead).

were a para-oesophageal abscess, a granuloma (related to a foreign body or *Spirocerca lupi* infection) or neoplasia. Because of the young age of the dog, the (temporary) improvement on antibiotics and the fact that the dog liked to chew sticks and had never been to a region endemic for *S. lupi*, a para-oesophageal abscess was presumed to be the most likely diagnosis. A preoperative computed tomography scan was advised, but the owners declined.

A caudal sternotomy was performed, revealing an oesophageal mass ($25 \times 20 \times 12$ cm) in the caudal mediastinum, attached to the accessory and the left and right caudal lung lobes. The mass surrounded the vagus nerve. An incision into the mass revealed the absence of a lumen. Incisional biopsy samples were taken from the vascularized and fragile tissue. Small nodules (<3 mm) were noticed in the caudal lung lobes and on the ventral mediastinum. Because of the impossibility of complete removal and the short life expectancy, the owners opted for intra-operative humane destruction. Permission for necropsy examination was declined.

Tissue samples of the oesophageal mass were fixed in 10% neutral buffered formalin, processed routinely and embedded in paraffin wax. Sections ($5 \mu\text{m}$) were stained with haematoxylin and eosin (HE). Immunohistochemistry (IHC) was performed with Dako Envision™ and System HRP-labelled polymer™ anti-mouse secondary reagent (Dako, Glostrup, Denmark). Primary antibodies used were specific for cytokeratin (monoclonal mouse anti-human cytokeratin clone AE1/AE3, 1 in 50 dilution, Dako), desmin (monoclonal mouse anti-human desmin clone D33, 1 in 200 dilution, Dako), sarcomeric actin (monoclonal mouse anti-sarcomeric actin clone alpha-Sr-1, 1 in 100 dilution, Dako) and vimentin (monoclonal mouse anti-vimentin, clone Vim 3B4, 1 in 400 dilution, Dako). Antigen retrieval was performed with a microwave technique using citrate buffer (pH 6.0) except for vimentin labelling, for which proteinase K was used. The chromogen used was 3,3'-diaminobenzidine (Dako) and counterstaining was performed with HE.

Microscopical examination revealed a non-encapsulated, moderately cellular neoplastic mass containing two cell populations. The dominant population consisted of sheets of round to polygonal cells with indistinct cell borders and abundant eosinophilic cytoplasm, with centrally placed, round to oval nuclei with a distinct basophilic nucleolus and finely stippled chromatin. Intermingled between these cells were spindle-shaped cells with indistinct cell borders, arranged in streams. These had a moderate amount of slightly granular, eosinophilic cytoplasm with occasional cross-striations and a centrally placed oval

nucleus with a distinct, basophilic nucleolus and finely stippled chromatin. Mitotic figures ranged from 2 to 5 per $\times 400$ field. No atypical mitotic figures were present. There was moderate anisocytosis and anisokaryosis. Both populations contained many bi- and trinucleated cells. In the multinucleated spindle-shaped cells, the nuclei were arranged in rows (Fig. 3). IHC was positive for expression of vimentin, desmin and sarcomeric actin and negative for cytokeratin (Fig. 4). Based on the histopathological evaluation and the IHC, a diagnosis of embryonal rhabdomyoblastic rhabdomyosarcoma was made.

Rhabdomyosarcomas are rare in dogs and arise from striated muscle, striated muscle progenitor cells or primitive mesenchymal cells (Caserto, 2013). They are divided into several subclasses (i.e. embryonal, botryoid embryonal, spindle-shaped embryonal, alveolar and pleomorphic rhabdomyosarcoma).

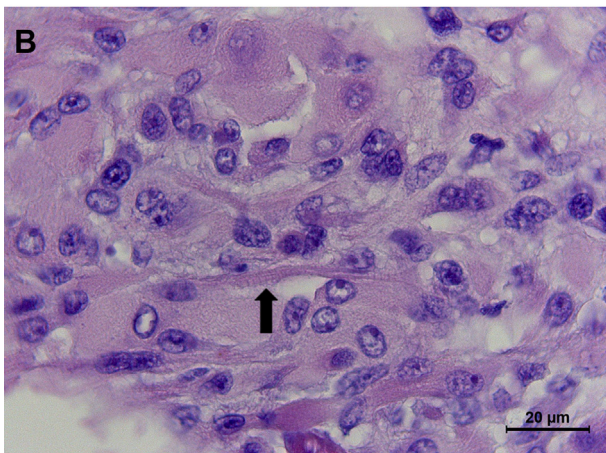
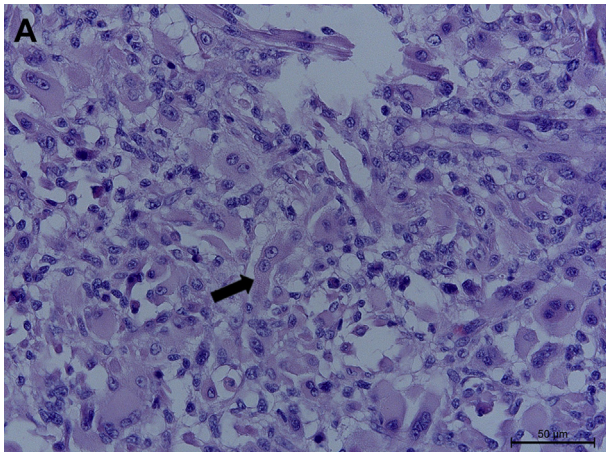


Fig. 3. Embryonal rhabdomyosarcoma of the oesophagus. Neoplastic cells are round to polygonal with abundant eosinophilic cytoplasm. Some neoplastic cells form myotubes with cross-striations (arrow) and multiple nuclei. HE.

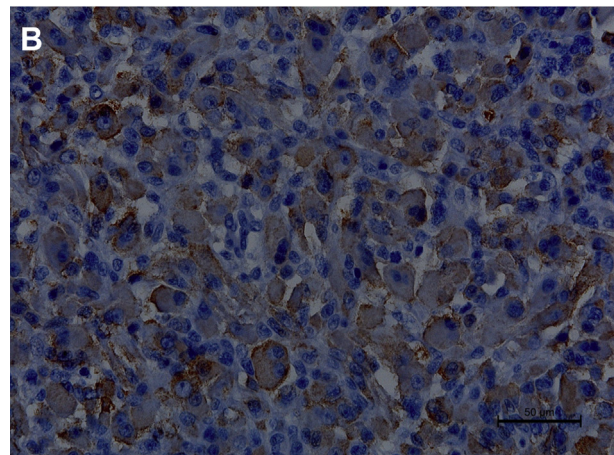
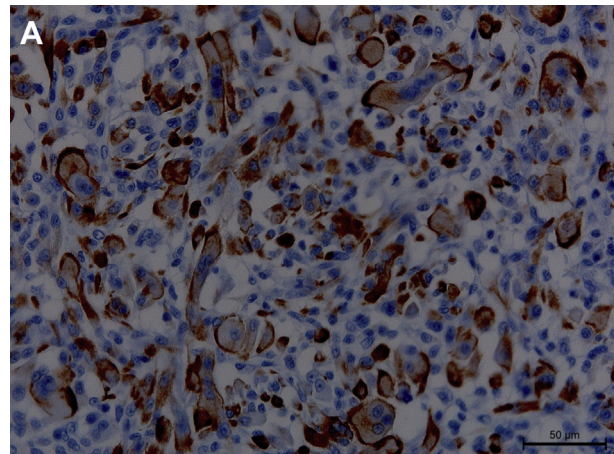


Fig. 4. Embryonal rhabdomyosarcoma showing expression of (A) desmin and (B) sarcomeric actin. Mainly tubular cells label strongly for desmin expression. Many of the neoplastic cells are positive for sarcomeric actin. IHC.

Of all rhabdomyosarcomas in dogs, embryonal rhabdomyosarcomas occur in 23% of cases. Rhabdomyosarcomas may occur in any part of the body and embryonal rhabdomyosarcomas are most commonly reported in the head and neck region (Caserto, 2013).

Only a few cases of oesophageal rhabdomyosarcomas have been described in man. All occurred in adolescents and people over 50 years old, with most in the older population (Ortega and Malogolowkin, 1991). The most commonly described oesophageal rhabdomyosarcomas in man are pleomorphic (Shah *et al.*, 1995; Batoroev and Nguyen, 2006), while embryonal oesophageal rhabdomyosarcoma has only been reported in an aged man (Willén *et al.*, 1989). The single oesophageal rhabdomyosarcoma reported in an animal occurred at the gastro-oesophageal junction of a 12-month-old rat and was of pleomorphic type (Inoue *et al.*, 2009).

In dogs, embryonal rhabdomyosarcomas are diagnosed in juveniles as well as in adults. Rhabdomyosarcomas are often locally invasive and have the potential to metastasize to regional lymph nodes, lungs and spleen. Embryonal rhabdomyosarcomas metastasize in 50% of the cases and metastases are more commonly reported in juvenile compared with adult dogs (Caserto, 2013). In man, oesophageal rhabdomyosarcomas are known to be highly aggressive (Shah *et al.*, 1995; Batoroev and Nguyen, 2006), which was also seen in the current case, as the mass invaded adjacent lung lobes. Although the small nodules in the caudal lung lobes and on the ventral mediastinum were not examined, it is likely that these were metastases.

Although only the upper third of the oesophagus in man consists of striated muscle (Henrikson *et al.*, 1997), oesophageal rhabdomyosarcomas are only described in the mid- to caudal oesophagus. It has been hypothesized that oesophageal rhabdomyosarcomas originate from undifferentiated mesenchymal cells (Ortega and Malogolowkin, 1991). In dogs, the oesophagus has striated muscle fibres throughout the length of the oesophagus (Bacha and Bacha, 2012), making both a rhabdomyosarcoma from preformed striated muscle and from striated muscle progenitors possible at any site along its length.

In the present case, the diagnosis of hypertrophic osteopathy led to the finding of the oesophageal mass. Hypertrophic osteopathy is a rare disease, most often seen in dogs with thoracic masses of infectious or neoplastic origin. Concurrent abdominal lesions, such as rhabdomyosarcoma of the urinary bladder and carcinomas, have been described infrequently (Cetinkaya *et al.*, 2011). Hypertrophic osteopathy is characterized by non-oedematous soft tissue swelling and diffuse periosteal new bone formation affecting the distal limbs and resulting in mild to severe lameness. Although several theories have been suggested (Cetinkaya *et al.*, 2011), the pathogenesis is not yet fully understood.

In conclusion, to the authors' knowledge, this is the first report of a canine oesophageal rhabdomyosarcoma, which was locally invasive, with probable pulmonary metastases. In the absence of clinical signs related to the tumour, the presence of hypertrophic osteopathy led to thoracic radiography and the discovery of a thoracic mass. In dogs, rhabdomyosarcoma should be considered in the differential diagnosis of a mass related to the oesophagus.

Conflict of Interest Statement

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