UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES
DEPARTMENT OF VETERINARY AND ANIMAL SCIENCES

Congenital idiopathic megaoesophagus in a 5 week old female Gordon Setter puppy

C.B. Becker[1] & H.E. Jensen[2]

[1] DVM, Ph.d. student and ECVP resident, Special Pathology, Department of Veterinary and Animal Sciences, University of Copenhagen, Denmark

[2] Professor, ECVP diplomate, Special Pathology, Department of Veterinary and Animal Sciences, University of Copenhagen, Denmark

Introduction

Megaoesophagus (oesophageal ectasia), is defined as a dilation of the oesophageal lumen or parts thereof, resulting from atony and flaccidity of the oesophageal musculature. The condition may occur in several animal species, including dogs, cats, horses, ruminants and rodents, and may be either congenital or acquired. In most species, the pathogenesis of the congenital condition remains rather obscure. In dogs, however, a link to an organ specific sensory dysfunction has been documented, due to a defect in the distention sensitive vagal afferent system innervating the oesophagus[1]. Congenital idiopathic megaoesophagus (CIM) has been well documented with regards to clinical presentation, diagnostic imaging and treatment options, however, descriptions of the histopathological manifestations of this disease in dogs are scant.

Aim of study
To evaluate the clinical, patho-anatomical and histological manifestations in a case of severe canine CIM.

Materials and methods

A 5 week old Gordon Setter puppy with congenital idiopathic megaoesophagus (CIM) was examined clinically and pathologically by means of contrast radiography, necropsy and histopathology. Neurons within the myenteric plexus of the oesophageal wall were visualized immunohistochemically using a polyclonal primary anti-peripherin antibody (Invitrogen). Histological samples were compared to control samples of a healthy canine oesophagus.

Results

Clinical: After the introduction to solid food (day 21), the puppy slowly started to deteriorate. The owners noticed a gradual weight stagnation compared to the other littermates despite a veracious appetite (Figure 1), and clinical signs of rhinitis, coughing, recurrent vomiting and regurgitation. The rhinitis cleared within a week, but the weight stagnation continued despite assisted feeding. At 5 weeks of age, the puppy was subjected to contrast x-ray examination, using orally administrated barium sulfate. X-ray images revealed a marked dilation of the oesophagus occupying the majority of the neck and thoracic cavity, with a volume exceeding that of the ventricle (Figure 2A). Due to a poor prognosis, the puppy was euthanized and submitted for postmortem examination.

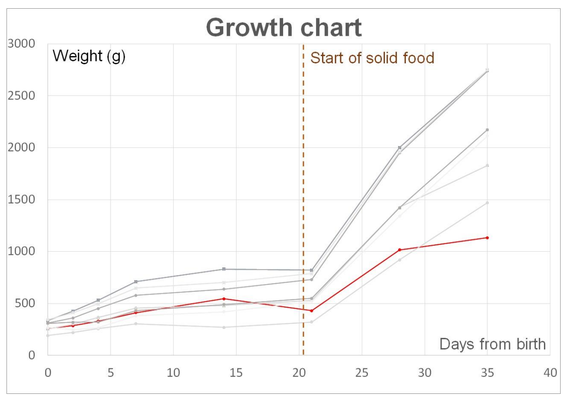

Figure 1. Weight progression over time for the litter.

The line highlighted in red shows the growth pattern of the puppy with CIM. Note the almost complete weight stagnation from day 28, compared to the other puppies of the litter.

Necropsy: During necropsy, a marked dilation of the entire oesophagus was confirmed (Figure 2B), with ventral displacement of the heart and lung. The animal had a body condition slightly below average (WSAVA BCS 3/9), but was otherwise found unremarkable.

Histology: Microscopic analysis revealed generalized muscular atrophy of the external muscle layers of the oesophagus, in combination with moderate interstitial edema (Figure 3A). In the epithelial layer, multifocal erosions and areas of squamous hyperplasia were present. Multifocal mononuclear inflammatory infiltrates were found in the tela submucosa in relation to eroded epithelial areas without signs of reparative changes (Figure 3B).

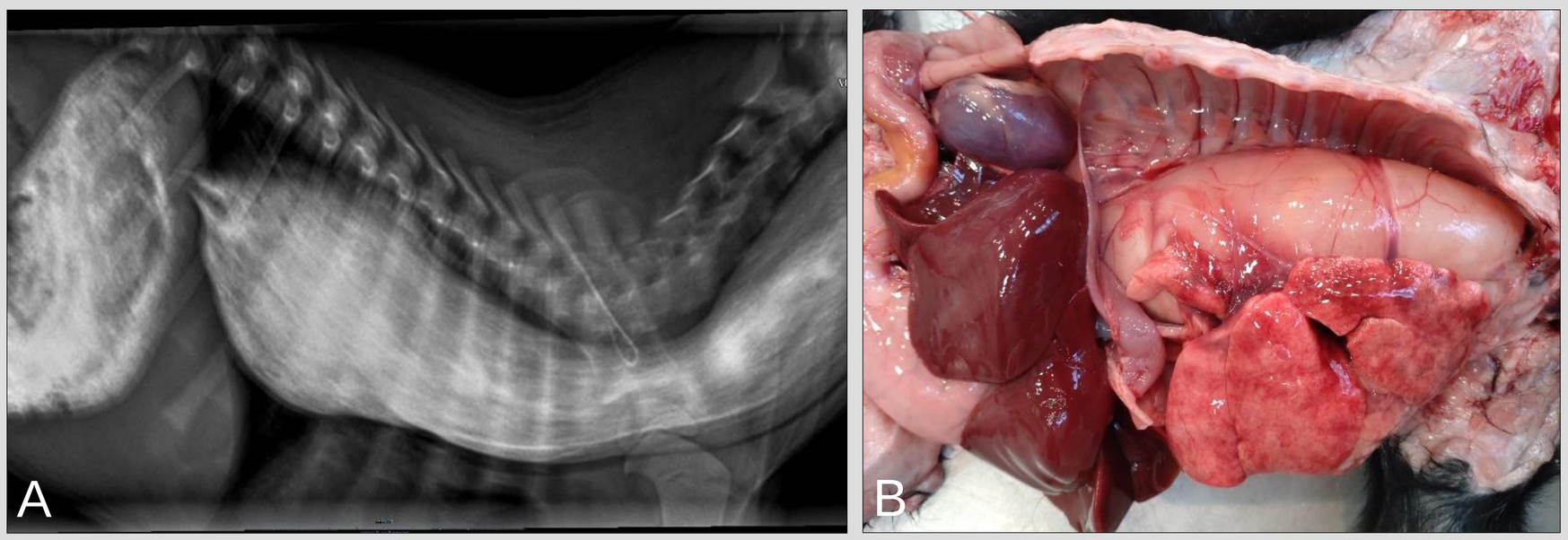

Figure 2. Morphological characteristics of congenital idiopathic megaoesophagus (CIM).

A: Contrast radiographic image, right lateral position. The marked dilation of both the cervical and thoracic part of the oesophagus was appreciated by oral administration of barium sulfate. The oesophageal volume seems to exceed that of the ventricle. **B:** Overview of the thoracic cavity and cranial abdomen at necropsy after removing a part of the thoracic wall,the right lung and heart. The entire length of the oesophagus was severely dilated and the heart and lung were displaced ventrally.

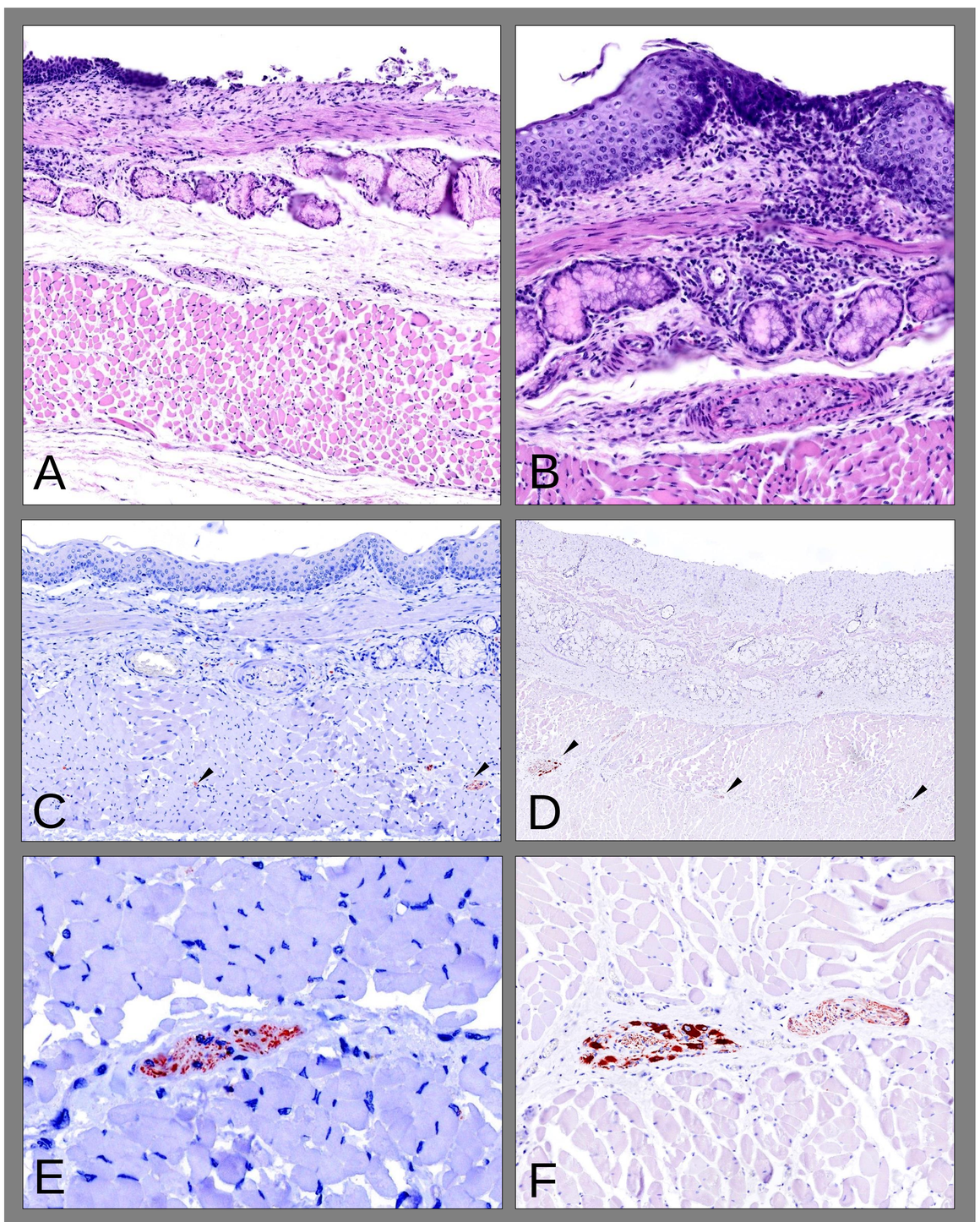

Figure 3. Histological lesions associated with CIM in a puppy compared to normal canine oesophageal morphology.

A: Section from the thoracic part of the megaoesophagus, revealing the generalized atrophy of myocytes in the external muscular layers of the oesophageal wall, along with moderate submucosal edema surrounding the mucous glands, H&E.

B: Mononuclear inflammatory infiltrates in the submucosal interstitium in relation to a mucosal erosion. Note the peripheral, slightly hyperplastic squamous epithelium, H&E.

C+E: Ganglionic structures in CIM are small, with an increased distance between them, and contain little to no ganglion cells. Note the fine granular staining of neuronal axons within the plexi, IHC anti-peripherin antibody.

D+F: Ganglionic structures in the normal canine oesophagus are evenly distributed with a varying size, holding larger structures with multiple peripherin-positive ganglion cells, identified by the intense staining of the cytoplasm, IHC anti-peripherin antibody.

The ganglia of the myenteric plexus, located between the transverse and longitudinal external muscle layers, were (when compared to oesophagus samples from a healthy dog (Figure 5C-F)) reduced in size, and contained a decreased amount, with multi-regional complete absence, of peripherin-positive ganglion cells (segmental aganglionosis). The distance between ganglionic structures was increased (number of ganglionic structures/mm was reduced by 55.5%), fewer ganglia contained peripherin positive cells (66.4% reduction in the percentage of positive ganglia), and the average amount of ganglion cells within these positive ganglia was also reduced (48.5% reduction).

Discussion

Loss of enteric neurons in the myenteric plexus of the oesophagus (aganglionosis) has previously been reported sporadically, including in a case of achalasia in a puppy, in megaoesophagus in Friesian foals, and in genetically conditioned megaoesophagus of mice and rats. Aganglionosis is also one of the hallmarks of human achalasia and Hirschsprungs disease in infants, in which immunohistochemistry is frequently applied to confirm the diagnosis[2]. The presented study is the first to use anti-peripherin antibodies for visualizing oesophageal ganglion cells in any species, and the highly specific and intense staining of the ganglion cell cytoplasm, seems to provide a strong tool for the confirmation of ganglion cell loss and myenteric plexus pathology, as in the present case of canine CIM.

Conclusion
CIM was associated with generalized oesophageal dilation with ventral displacement of the heart and lung. Histological characteristics included oesophageal muscular atrophy, mucosal erosions and inflammation, along with segmental aganglionosis, highlighted immunohistochemically by loss of peripherin-positive ganglion cells within the myenteric plexus.

Acknowledgements

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References

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