Radiographic, MRI, and CT findings in a young dog with Becker-like muscular dystrophy

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DOI: https://doi.org/10.1111/vru.13200

Multimodality features of Becker-like muscular dystrophy in a young dog

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ABSTRACT

An 8-month-old, male, crossbreed dog was presented for macroglossia, reduced mandibular extension, ptyalism, dysphagia and regurgitation. Serum creatine kinase and aspartate aminotransferase activity were markedly increased. Thoracic radiographs showed a gastro-esophageal hiatal hernia, diaphragmatic thickening and asymmetry. Magnetic resonance imaging showed a severely enlarged tongue, symmetric increase in volume of the geniohyoid and mylohyoid muscles and diffuse masticatory hypomyotrophy. Whole body computed tomography was performed to rule-out other musculoskeletal abnormalities and confirmed all radiographic and MRI findings. Muscular histopathology was consistent with Becker muscular dystrophy. Multimodality imaging was helpful to characterize the musculoskeletal abnormalities associated to the disease.

SIGNALAMENT, HISTORY AND CLINICAL FINDINGS

An 8-month-old, intact male, crossbreed dog (body weight 10 kg) was presented for macroglossia, reduced mandibular extension, dysphagia and regurgitation. Clinical examination revealed poor body condition score (i.e. 3/9), ptyalism, intermandibular hard-elastic swelling in the projection area of the tongue's body and root, mandibular deformity, open mouth and decreased mandibular vertical range of motion without crepitus sounds or pain at the mouth opening. The dog showed also inspiratory effort with stertorous breathing, generalized coat dandruff, and bilateral moderate carpal and slight tarsal hyperextension. Biochemistry revealed elevated creatine kinase (39.523 IU/L; reference range 41-378 IU/L), elevated c-reactive protein (1.07 mg/L, reference range 0.01-0.22 mg/L), elevated alanine transferase (426 IU/L; reference range 25-122 IU/L) and aspartate aminotransferase (816 IU/L; reference range 14-59 IU/L). Complete blood count and echocardiography were unremarkable. Based on the clinical findings an underlying muscular dystrophy was suspected.

IMAGING, DIAGNOSIS AND OUTCOME

Thoracic radiographs including left lateral and dorsoventral projections (90 kVP 1.6 mAs, AeroDR SYSTEM 2, Konica Minolta) showed asymmetry of the diaphragmatic profile with an undulated and irregular appearance and herniation of the gastric fundus into the caudal mediastinum through the esophageal hiatus.
Magnetic resonance of the head (1.5T, GE Medical System, SIGNA Creator) was performed including transverse and sagittal T2-weighted (TR 3907-5556 ms, TE 76-82 ms, slice thickness 3 mm, interval 0,3 mm); transverse T1-weighted (TR 514 ms, TE 12,4 ms, slice thickness 3 mm, interval 0,3 mm), STIR (TR 7782 ms, TE 57 ms, TI 140, slice thickness 3 mm, interval 0,3 mm) and T1-weighted post-contrast sequences (gadoteric acid, Claricyclic, GE Healthcare, Oslo, Norway, 0,2 mL/Kg). The tongue was markedly and symmetrically enlarged obliterating most of the oral cavity, folded in a "V-shape" with secondary lateral bowing of the mandibular bodies causing severe widening of the intermandibular space. There was symmetric enlargement of the geniohyoid and mylohyoid muscles and moderate bilateral diffuse masticatory hypomyotrophy. The affected muscles and the tongue were heterogeneously hyperintense on T2-weighted and STIR sequences, heterogeneously enhancing on T1-weighted postcontrast series. Based on the radiographic and magnetic resonance findings a whole body computed tomography (CT) was

performed (GE Optima 660, Milan; 100 kV, 240 mA, 2,5 mm slice thickness in standard algorithm with reconstruction interval 1.25 mm, tube rotation 0,8 s) to rule out additional musculoskeletal or pelvic abnormalities. Intravenous contrast medium (iohexol, Omnipaque 350 mgI/mL, GE healthcare S.r.l., Milan, Italy) was injected into the left cephalic vein through an 18 g intravenous catheter at a flow rate of 2 ml/s by a double-head power injector (Medrad envision CT injector, Medrad Italia, Cava Manara, Italy) with a dose of 2 ml/kg. All the affected masticatory muscles and the tongue showed heterogeneous enhancement on post-contrast series. The diaphragm was diffusely thickened, asymmetric with a marked undulating appearance and mild heterogeneous enhancement, deforming the adjacent liver profile. The CT confirmed a gastro-esophageal hiatal hernia, regional swelling of the gastroesophageal junction and mandibular and retropharyngeal lymph nodes were slightly enlarged, bilaterally.
Based on clinical and imaging findings, a tentative diagnosis of muscular dystrophy was made.

Muscular biopsies of the lateral head of the Triceps Brachii, Vastus Lateralis and Biceps Femoris were taken. Immunohistochemical analysis was assessed with several monoclonal antibodies against the rod domain (DYS1) and carboxy terminus (DYS2) of dystrophin and against beta-sarcoglycan, gamma-sarcoglycan and beta-dystroglycan. All the muscular samples shared similar findings. Variability in myofiber size, presence of fibers with increased and decreased enzymatic activity and signs of fiber regeneration were described. Most fibers had normal staining for the rod domain of dystrophin but staining for the carboxy terminus of dystrophin was undetectable in most of the fibers. The presence of atrophic angular fibers, clustered into small groups, indicated signs of peripheral neuropathy. Neuromuscular morphologic abnormalities combined with immunohistochemistry results were consistent with the diagnosis of a Becker-like muscular dystrophy (BMD).

Unfortunately, due to the progressive deterioration of his clinical conditions, the dog was euthanized at about 8 months of age.

DISCUSSION

In humans, Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are X-linked inherited recessive degenerative muscle disorders caused by a mutation in the gene that encodes the protein dystrophin that is essential for the maintenance of muscle fiber integrity during contraction [3, 16]. Canine X-linked muscular dystrophy (CXMD), shown to be genetically homologous to human DMD, has been found in several breeds but best characterized in Golden Retrievers[10]. Canine muscular dystrophy with a molecular phenotype of BMD has been reported in Japanese Spitz dogs[1,8], in a Labrador Retriever[2] and in a Border Terrier dog[7]. BMD is a milder clinical form of muscular dystrophy where the protein dystrophin is present but reduced in the amount or abnormal [6, 9,1,]. Clinical signs, usually evident at a juvenile age, may include weakness, gait abnormalities, exercise intolerance, marked muscle atrophy and difficulty in food prehension due to hypertrophy of the tongue and inability to fully open the mouth[17]. Mastication and swallowing problems in these patients are also due to weakness of orofacial muscles. As previously reported in a canine muscular dystrophy model, the tongue and the diaphragm are the first muscles that undergo early degeneration at a neonatal age[16,18]. The most relevant clinical sign in our patient was dysphagia, which occurred at an early age, as previously described in Japanese Spitz dogs with BMD[8]. Creatine kinase and serum AST were markedly elevated, a finding considered essential in diagnosing Duchenne-like muscular dystrophy in dogs and that can be documented as early as 1-2 days of age[19].

To the authors' knowledge this is the first report describing a multimodality imaging approach to characterize musculoskeletal changes secondary to muscular dystrophy in dogs.

Due to the dog's young age, clinical signs and markedly increased muscular enzyme activities, the primary clinical differential diagnosis for macroglossia and masticatory hypomyotrophy included muscular dystrophy, canine masticatory myositis, inflammatory myopathies and, less likely, a neoplastic process. In human and veterinary medicine MRI provides a high soft tissue contrast, allowing excellent assessment of striated muscles. Similar to this case, in canine masticatory myopathy the muscles affected are the temporal, masseter, pterygoideus and rostral digastricus muscles. At an early stage the disease is characterized by edema and swelling of these muscles, pain at muscles palpation, and restricted jaw movements. In the chronic phase masticatory muscles atrophy and fibrosis develop, eventually resulting in the inability to open the mouth, prehend food and swallow[13,5,12]. In this case the tongue, mylohyoid and geniohyoid muscles were severely increased in volume, and the masticatory muscles were moderately hypotrophic, resulting in decreased jaw movements, although the patient was not painful. MRI was able to rule-out cranial nerves abnormalities. Although the MRI findings could not differentiate between muscular dystrophy and masticatory myositis, the morphovolumetric abnormalities of the tongue and extra-lingual muscles have never been described in masticatory myositis. The mandibular and hyoid alterations were hypothesized to represent an abnormal growth of the tongue and extra-lingual muscles, compatible with a chronic progression of the muscular disease[15].

The most consistent findings in thoracic radiographs later confirmed on CT scans were diaphragmatic thickening and gastroesophageal hiatal hernia. The diaphragm was markedly thickened with an undulating appearance, likely due to the muscular hypertrophy. This has been reported in other dogs with DMD and BMD as a unique radiographic feature[4]. Hiatal hernia has also been reported in dogs with muscular dystrophy and is presumed to be related to the primary myopathy of the diaphragm[4]. CT examination was able to rule-out pelvic conformational changes and hyperlordosis, previously described in golden retriever dogs with Duchenne-muscular dystrophy.

Clinical signs, laboratory and imaging findings were similar to previously described cases of CMDX and suggested the diagnosis of muscular dystrophy. Histopathology and immunohistochemistry of the muscle biopsies were typical and confirmed the dystrophic phenotype of BMD. Although human patients with BDM develop clinical signs at a later age, our case was immature and was euthanized soon after diagnosis because of the poor prognosis and the progressive inability to eat and swallow.

In conclusion, multimodality imaging has been helpful for a complete characterization of the musculoskeletal abnormalities secondary to Becker-like muscular dystrophy. In young dogs with dysphagia, mastication and swallowing difficulties muscular dystrophy should be considered among the differential diagnoses.

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