FOOD/FARMED ANIMALS

Congenital diplomyelia and hydromyelia in two calves

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SUMMARY

We describe two clinical cases of diplomyelia with hydromyelia in newborn calves. Both animals presented clinical signs of a general proprioceptive ataxia affecting the pelvic limbs. The most clear finding during clinical examination of the animals was an unilateral (case 1) or bilateral (case 2) absent patellar reflex. Only the second case was serologically tested positive for Schmallenberg virus, which is not a very likely aetiology. The cause of the spinal cord lesions in both calves remains unknown.

BACKGROUND

This case is important because it describes the clinical signs of a general proprioceptive ataxia of the pelvic limbs due to diplomyelia and hydromyelia in detail. Moreover, we present clear pictures of macroscopical and microscopical pathological findings of affected spinal cords. Recently, we have encountered many calves with neurological signs in The Netherlands. This case report gives a clear description of diplomyelia and hydromyelia, both of which should be on the list of differential diagnosis when a calve with a general proprioceptive ataxia af the pelvic limbs is presented.

CASE PRESENTATION

Case 1

History

A 24-day-old male Holstein-Friesian (HF) (100%) calf was offered to the clinic of Farm Animal Health, Faculty of Veterinary Medicine, Utrecht University. The reason for the referral by the farmer (the farm is located in the southwest of The Netherlands) was the presence of a static ataxia since the calf's birth. The parturition process of the multiparous dam needed minimal obstetrical intervention from the farmer because the calf was in breach. A few days after calving the farmer noticed an uncoordinated gait of the pelvic limbs. The health certificates of this farm were Bovine Viral Diarrhea Virus (BVDV) and Bovine Herpes Virus-1 (BHV-1) unsuspected, Leptospirosis free, Johne's disease status B (positive animals are culled), *Salmonella* suspected and neosporosis unfavourable (several positive cases).

Clinical examination

The calf appeared bright and alert. It showed normal eating and drinking behaviour. Defecation and urination appeared to be normal. The animal was able to stand and lie down without assistance despite presenting an ataxia of the pelvic limbs. In standing position, the pelvis and pelvic limbs tended to lean more to the left but the calf was able to correct this position spontaneously (figure 1). While walking and running, the calf did not fall and hence was able to display normal behaviour combined with the ataxia and paraparesis. Body condition and hygiene were normal for a calf this age without signs of muscle atrophy. No other clinical abnormalities were visible. Physical examination showed no abnormal findings regarding the respiratory system, the circulatory system, temperature, skin/hair/claws, mucous membranes and lymph nodes. During the neurological examination,[1] no abnormal functioning of the cranial nerves was observed. Menace response, pupillary light reflex, palpebral reflex and corneal reflex were all normal. Placed in a corridor with several obstacles, the calf showed no abnormal behaviour or signs of blindness to these objects. The sole abnormality found testing the spinal reflexes was the absence of the patellar reflex on the left side. A re-evaluation (one week later and before euthanasia) of the neurological examination and spinal reflexes resulted in the same results. Based on the findings of the complete physical examination, the following problem definition was defined: a 24-day-old male HF calf with a general proprioceptive ataxia, paraparesis and an absent patellar reflex on the left side. The neuroanatomical localisation was addressed to L4-S3 spinal cord segments due to paraparesis, general proprioceptive ataxia of the pelvic limbs and a decreased patella reflex on the left side. One may argue if an assisted delivery of a calf in breach could have caused a spinal lesion resulting in these clinical signs. Based on ethical grounds and poor prognosis, the calf was euthanased and a necropsy was performed at the Veterinary Pathology Diagnostic Centre, Faculty of Veterinary Medicine, Utrecht University, The Netherlands. No additional diagnostic methods were possible in this case.

Case 2

History

In the second case, a male crossbred (HF x Belgian Blue) calf, which was delivered via caesarean section on day 294 of pregnancy, is described. The first 3 days post partum (pp), the calf was unable to stand straight. After performing standard clinical examination on the calf, the findings of the referring veterinarian were arthrogryposis, a circular gait and undefined signs of ataxia. On day 15 pp, the calf was offered to the clinic of Farm Animal Health, Faculty of Veterinary Medicine, Utrecht University, The Netherlands. The referring farm, located in the south of The Netherlands, was certified free of BVDV, BHV-1 and leptospirosis. The statuses for Johne's disease was status A (highest status), *Salmonella* unsuspected and neosporosis unknown.

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FIGURE 1 Case 1, clinical presentation of the calf with diplomyelia. Broad posture of the pelvic limbs with a tendency to the left.

Clinical examination

In appearance, a bright and alert bull calf had difficulties in standing and walking due to flexion of both metacarpal joints (arthrogryposis). While standing, the calf was drifting to the right, which appeared to be an incoordination of the right pelvic limb. The feed intake, body condition and faeces appeared to be normal. On physical examination, the animal presented a high respiratory rate. The examination of the respiratory system gave no other abnormalities. There were no abnormal signs regarding the circulatory system, temperature, skin/hair/claws, mucous membranes and lymph nodes. Neurological examination[1] showed no abnormal functioning of the cranial nerves; the menace response, pupillary light reflex, palpebral reflex and corneal reflex were normal. In a corridor with several obstacles, the calf showed no abnormal behaviour or signs of blindness to these objects during the walking test. Furthermore, the vertebral column seemed to be broader between T2 and L4, compared with other calves of approximately the same age. Testing proprioceptive reflexes of the calf showed delayed repositioning of all four limbs. The sole abnormality found when testing the spinal reflexes was the absence of the patellar reflex in both of the pelvic limbs. A re-evaluation (one week later and before euthanasia) of the neurological examination and spinal reflexes provided identical findings. In summary, we defined the following problem definition: a healthy 15-day-old male crossbred calf with a general proprioceptive ataxia, paraparesis and arthrogryposis of both front legs. The neuroanatomical localisation was addressed to L4-S3 spinal cord segments due to paraparesis, general proprioceptive ataxia of the pelvic limbs and a decreased patella reflex on both sides. Clinically, arthrogryposis was treated as a separate deficit without being related to the general proprioceptive ataxia affecting the pelvic limbs. However, one may argue if this is justified because several congenital malformations could have the same causative agent. Delayed proprioception of the front limbs is most likely caused by the arthrogryposis of these limbs. Based on the clinical findings, the calf was euthanased and subsequently necropsied at the Veterinary Pathology Diagnostic Centre, Faculty of Veterinary Medicine, Utrecht University, The Netherlands.

INVESTIGATIONS

Serology was performed on blood of the calf at the Animal Health Center (GD Deventer, The Netherlands) for BVD virus antibodies and antigen, Schmallenberg virus antibodies, Bluetongue virus antibodies and *Neospora* antibodies. Both of the tests for Schmallenberg virus antibodies and Bluetongue virus antibodies were positive. According to the farmers' information the dam was vaccinated against Bluetongue virus.

DIFFERENTIAL DIAGNOSIS

Clinical signs of neurological diseases could be classified according to the acronym VITAMIN D.

V: vascular diseases
I: inflammatory diseases
T: trauma
A: anomalies or malformations
M: metabolic/toxic diseases
I: idiopathic diseases
N: neoplasia
D: degenerative diseases[2]

The list of possible differential diagnoses in order of likelihood is determined by the signalment of the animal, combined with the duration, onset and progression of the clinical signs. For instance, degenerative conditions are common in later juvenile stages and throughout adulthood and usually have a slow, insidious onset and progressive course. Given that the neurological signs were present since birth with a static progression, congenital anomalies or malformations are considered to be the most likely causes.[3–5] These include genetic mutations or intrauterine infections with BVDV, SBV, BTV, *Neospora*.[6 7] Trauma could explain these clinical signs, especially after assisted deliveries or dystocia. The calf in case 1 was in breach and was born after assisted delivery. The calf in case 2 was born after a caesarean section, but it is unknown whether the farmer had tried to deliver the calf per vaginam.[8] Vascular problems such as haemorrhagic or ischaemic infarctions around the time of birth would also be considered possible, however, it is less likely given that some gradual functional improvement would be expected following onset.[9 10] Active inflammatory, infectious, degenerative and neoplastic processes should be considered unlikely as such diseases typically worsen over time and rarely remain static.[11] Finally, two remaining differential diagnoses are excluded in these cases. First, metabolic/toxic spinal cord diseases are not recognised in animals. Second, idiopathic spinal cord diseases without detectable lesions do not exist in calves.[2]

OUTCOME AND FOLLOW-UP

Postmortem examination

In both calves, a section of the spinal cord from approximatively the third lumbar vertebra until the sacrum is marked to severely broadened (figure 2). On transverse section, the spinal cord shows locally an almost complete duplication of the spinal cord, more specific, two central canals surrounded by two butterfly shaped gray matters, and two ventral median fissures, all comprised within the same leptomeninges and dura mater (diplomyelia) (figure 3). Each butterfly shaped gray matter is composed of two dorsal and two ventral horns. The ventral gray horns, close

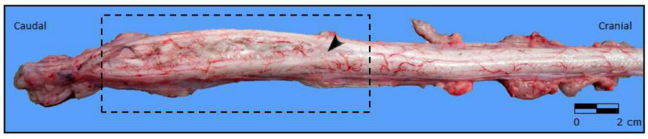

FIGURE 2 Case 1, dorsal macroscopic view of the lumbosacral spinal cord. The spinal cord shows a focal extensive broadening (dotted line) at the level of the segment with diplomyelia and hydromyelia. The location of the severe dilated central canal is marked with the arrowhead.

to the median plane of each duplicated butterfly shaped gray matter, are smaller than the lateral ventral horns. The cranial portion of the broadened spinal cord segment contains focally a severe dilated central canal (hydromyelia) (figure 4; figure 5 transverse section 26–30), with effacement of the dorsal median fissure, and separation of the two dorsal horns of gray matter. No significant changes suggestive for neuronal degeneration are present in the spinal cord.

DISCUSSION

Based on the macroscopic and microscopic pathological findings, both patients were diagnosed with diplomyelia and hydromyelia in the lumbosacral spinal cord. The spinal cord is formed during the gastrulational and neurulational phases in embryological development, several genetic and environmental factors could result in neural tube defects. In pregnant women, a folate deficiency is most known to cause neural tube defects (NTDs). Genetic mutation of genes involved in the folate metabolism are associated with the development of NTDs as well.[12] In mice, over 240 genes are identified to be involved in the development of NTDs.[13] Furthermore, antiepileptic medications during pregnancy increase the risk of NTDs in humans.[14] In veterinary medicine, besides genetic factors, environmental factors such as a vitamin A deficiency, copper deficiency and the ingestion of neuroteratogenic plants during early pregnancy are described to be involved in the development of NTDs.[3]

Congenital abnormalities of the spinal cord mainly originate during the gastrulational and neurulational phases. Diplomyelia

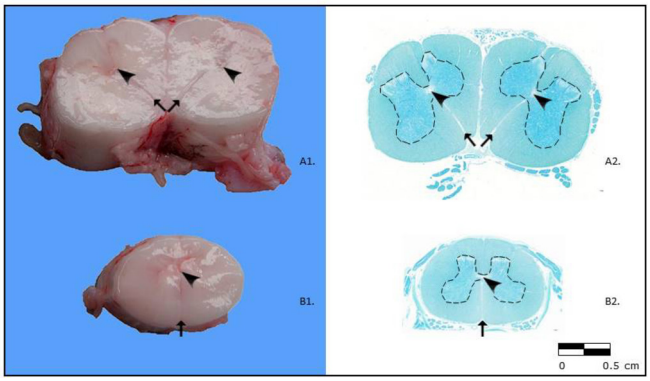

FIGURE 3 Case 1, macroscopic and microscopic view of lumbosacral spinal cord transverse sections. (A1) Macroscopic view spinal cord segment which shows duplication of the central canal (arrow heads) and ventral median fissure (arrows). (A2) Histology (luxol fast blue staining) clearly shows the duplicated central canal, ventral median fissure and butterfly shaped gray matter (dotted line). (B1) and (B2) Macroscopic and microscopic view of the normal segment of the spinal cord respectively, without duplication of the previously mentioned anatomical structures.

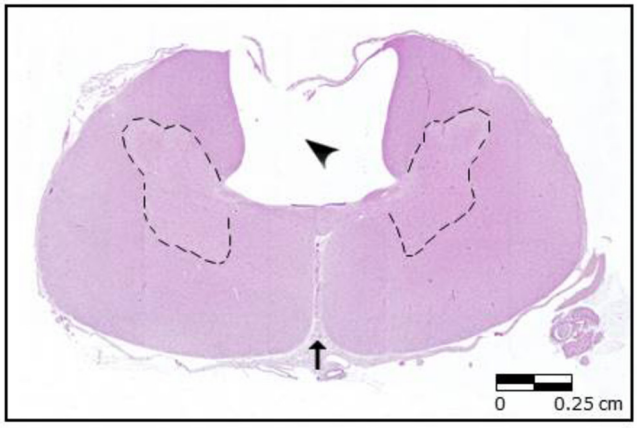

FIGURE 4 Case 1, microscopic transverse section of the lumbosacral spinal cord at the level of the segment with hydromyelia. Histology (haematoxylin and eosin staining) shows a severely dilated central canal (arrow head) (hydromyelia). Each half of the butterfly shaped gray matter (dotted line), especially the dorsal horns, are severely separated. The dorsal median fissure appears absent. The ventral median fissure (arrow) shows no significant abnormalities.

and diastematomyelia are known malformations affecting solely the spinal cord.[15] The difference between both congenital defects is based on the involvement of the vertebrae. Diplomyelia consists in a duplication of the spinal cord without separation of both cords by bony structures, where diastematomyelia is characterised by a duplicated spinal cord with separation of the cords by bony structures.[15]

Congenital malformations in bovines can be caused by a number of infectious agents. BVDV, SBV and BTV are known

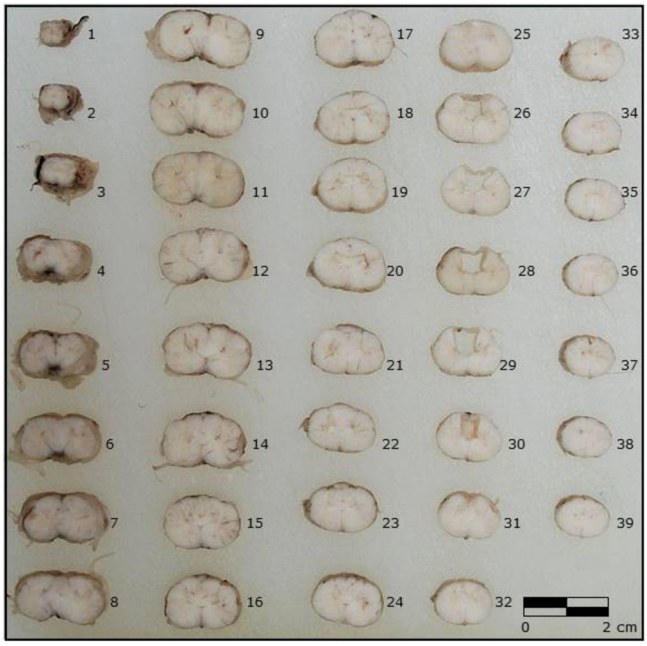

FIGURE 5 Case 2, macroscopic view of successive lumbosacral spinal cord transverse sections, from caudal (1) to cranial (39). Section 1–3: cauda equina region. Section 4–25: segment with the, to a greater or lesser extent, duplication of the different anatomical structures of the spinal cord. Section 26–30: segment with the severely dilated central canal (hydromyelia). Section 31–39: segment without any significant pathomorphological abnormalities.

for causing viral-induced congenital malformations.[6] Furthermore, neosporosis, a protozoan infection, may cause congenital neurological signs.[7] Besides these 4 infectious agents, Akabane virus and Aino virus are also known as causative agents for congenital malformations.[6] Based on the number of reports, spinal cord malformations in general are rare in cattle, where de Lahunta mentions spinal cord malformations in calves as 'very common'.[16] Ohfuji documented a calf with neurological signs that was subsequently diagnosed with spinal dysraphism, a congenital defect of the spinal cord due to an incomplete closure of the neural tube leading to a cavity in the spinal cord.[17] A combination of spinal dysraphism and dicephalia with Arnold-Chiari malformation is described in a stillborn calf by Gülbahar *et al*.[18] In two previous reported cases concerning diplomyelia in calves, the clinical signs differed from this case. In this case, both calves were able to stand and walk where the patients in previous reported cases were not.[4 5] An intrauterine Schmallenberg virus infection could have caused a congenital malformation of the spinal cord of these calves but does not fit with previous reported lesions caused by SBV. Reported lesions caused by SBV include the brain, the vertebral column and joints but most lesions consist of a loss of tissue instead of a duplication of tissue, which is the case in this study.[19] Moreover, a positive serology for SBV antibodies does not discriminate between passive (maternal) or active immunity.

What remains unclear is the effect of the size and functionality of the duplication on the neuronal pathways. Strictly taking the clinical signs into account, the lesion in both cases was located between spinal segments L4 and S3 because of the general proprioceptive ataxia, paraparesis and a reduced patellar reflex. However, at necropsy the duplication had a length of approximately 15–20 cm and was located between the vertebral bodies of L2 and S2. It would be interesting to study the neurological structures involved and to see how the neuronal pathways in these duplications work. De Lahunta describes a case of a calf with diplomyelia which comprehends a unique clinical sign of 'bunny hopping'. It is assumed that bunny hopping is the result of a inability of interneuronal communication to coordinate the gait.[16] In dogs, cattle and pigs, bunny hopping is associated with spinal dysraphism or myelodysplasia, mostly affecting the thoracic spinal cord.[20] In our cases, we have learned that it is debatable whether the calves displayed the sign of bunny hopping. When calves start running, they sometimes use both of the pelvic limbs at the same time to initiate. Both calves in this case displayed this behaviour sometimes. The lack of interneuronal communication because of the diplomyelia and hydromyelia could explain these neurological signs.

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