

# Congenital hypospadias and vertebral malformation in a Barbados Blackbelly neonate

Brittany Diehl,<sup>a</sup> Federico Grosso,<sup>b</sup> Marley Iredale,<sup>c</sup> Michael Dark,<sup>d</sup> Catalina Cabrera<sup>a</sup>

<sup>a</sup>Department of Large Animal Clinical Sciences, <sup>b</sup>Department of Small Animal Clinical Sciences <sup>c</sup>Department of Comparative, Diagnostic and Population Medicine, College of Veterinary Medicine, University of University of Florida, Gainesville, FL, <sup>d</sup>Veterinary Diagnostic Laboratories, College of Veterinary Medicine and Emerging Pathogens Institute, University of Florida, Gainesville, FL

## Abstract

A male purebred Barbados Blackbelly, twin to another male, was born with obvious external congenital abnormalities. Male twin was normal. Abnormal lamb had a short torso and spinal column. At 1 week, the lamb was presented with dyspnea and lethargy, and euthanasia was elected. Lamb was submitted for full necropsy and for additional diagnostics. After postmortem, in addition to histopathology, radiographs and computed tomographs were obtained. Lamb had congenital vertebral and occipital malformations, meningitis, hypospadias, and renal malformation. To authors' knowledge, hypospadias and vertebral malformation in the Barbados Blackbelly breed has not been reported. Apparently, Barbados Blackbelly breed harbors closely related genetics, thus vigilant monitoring for genetic malformations is suggested.

**Keywords:** Barbados blackbelly, twin lamb, congenital, hypospadias, vertebral malformation

## Case presentation

A congenitally abnormal, purebred Barbados Blackbelly male lamb was born as a twin to a normal, healthy male lamb. They were born in central Florida to a dam and sire with a history of healthy lamb offspring in previous years; however, this was the first time that they were bred to each other. Owner observed that the lamb had excessively long limbs, a short torso and vertebral column, and external genital malformations (Figure 1). Owner described urination to be occurring from the perineal region. Initially, the lamb was unable to stand and was rejected by the ewe. With some assistance, the lamb was able to stand and nurse from a bottle within the first few hours. Lamb was alert, consuming milk replacer from a bottle, and was able to urinate and defecate. At 1 week, the lamb was presented with lethargy and dyspnea. Due to welfare concerns, euthanasia was recommended and elected. Owner submitted the lamb for a full necropsy and further diagnostics.

## Radiology and computed tomography

Immediately after postmortem, orthogonal radiographs of the skull, vertebral column, thorax and abdomen of the lamb were performed with a digital radiography plate (CXDI-50G digital plate, Canon, Lake Success, NY). Additionally, single medio-lateral radiographs of right thoracic and pelvic limbs were obtained. Lamb had normal vertebral formula with 7 cervical, 13 thoracic, 7 lumbar, 4 sacral, and 5 coccygeal vertebrae. Occipital condyles were subjectively thickened and elongated. Remainder of the skull appeared within normal limits. Cervical vertebrae were substantially larger than the thoracic and lumbar

vertebrae with various sized and shaped vertebral endplates and vertebral bodies.



**Figure 1.** External visualization of the lamb. Note short torso and long appendages.

There was severe narrowing of C2 - C3 and C4 - C5 intervertebral disc spaces with widening of C3 - C4, and especially, C5 - C6 intervertebral disc spaces (Figure 2). Multiple shortened, misshapen and fused thoracic, lumbar, sacral, and coccygeal vertebrae with associated moderate thoracolumbar kyphosis and scoliosis were observed. Thoracic and lumbar vertebrae were markedly widened. Spinous processes of multiple thoracic and lumbar vertebrae were fused and misshapen. Severe mid to caudal thoracic rib crowding secondary to the vertebral malformations (Figure 3) was observed. Sternum was composed

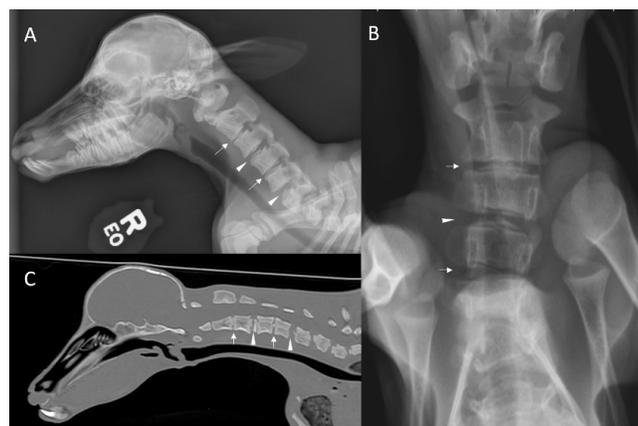
of 7 radiographically normal sternbrae with S5 and S6 fusion. Diffuse increases in pulmonary opacity with decreased visualization of pulmonary vessels were noted, likely, a postmortem finding attributed to pulmonary atelectasis and pulmonary congestion. Otherwise, the thorax appeared normal. In the abdomen, a diffuse loss of peritoneal serosal detail was observed, probably associated with lamb's young age. Gastrointestinal tract contained a mild to moderate amount of gas. Skin margins were irregular in the penile region. No osseous abnormalities were observed in right thoracic and pelvic limbs.

To further assess radiographic changes, a whole-body post-mortem computed tomography (CT) was performed with a 160-slice (Aquilion Prime) multidetector row, helical CT unit (Toshiba Medical Systems, Tustin, CA). Scan was performed in helical acquisition mode with a scan thickness of 0.5 mm, a pitch of 0.8, 100 mA, 120 kVp, tube rotation time of 0.5 seconds, and a 512 x 512 matrix. Radiographic and CT findings were similar: multiple vertebral malformations (Figure 4), abnormally elongated occipital condyles (Figure 5), a normal sternum and a normal appendicular skeleton.

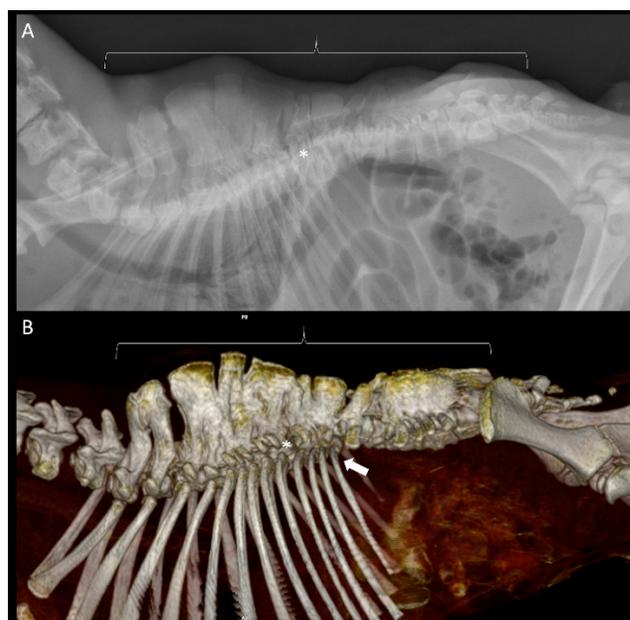
#### Necropsy and histopathology

There was ~ an 8 cm, shallow, linear defect in the integument and urethra between rectum and prepuce base (Figure 6) that divided the scrotum with 1 testis on either side of the defect (hypospadias). Testes, pelvic urethra, bladder and ureters were grossly and microscopically unremarkable. Right kidney was ~ twice the size of the left kidney and was irregularly shaped. Histopathology revealed no prominent lesions within either kidney.

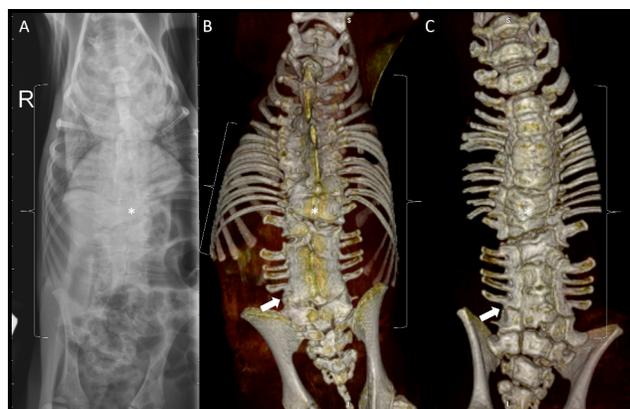
Following removal of head and dissection of masticatory muscles, substantial malformation of the occipital condyles was noticed that caused deformation of foramen deformation and magnum and cerebellum herniation. On dissection of the epaxial and hypaxial muscles, severe irregularity of lumbar vertebrae shape was observed that caused moderate scoliosis and kyphosis.



**Figure 2.** Postmortem lateral radiograph of skull and cervical vertebral column (A), ventrodorsal radiograph of cervical vertebral column (B) and sagittal multiplanar CT reconstruction in a bone window of lamb (C). Note severe narrowing of C2 - C3 and C4 -C5 intervertebral disc spaces (arrows) with widening of C3 - C4 and C5 - C6 intervertebral disc spaces (arrowheads).



**Figure 3.** Postmortem lateral radiograph (A), and lateral three-dimensional CT reconstruction (B) of the thoracolumbar vertebral column of the lamb. Note multiple shortened, misshapen and fused thoracic and lumbar vertebrae (braces) with mid to caudal thoracic rib crowding (wide arrow) and kyphosis (asterisks) secondary to the vertebral malformations, and fused and misshapen spinous processes of multiple thoracic and lumbar vertebrae (braces).



**Figure 4.** Postmortem ventrodorsal radiograph (A), and dorsal (B) and ventral (C) three-dimensional CT reconstructions of thoracolumbar vertebral column of the lamb. Note multiple shortened, misshapen and fused vertebrae (braces) with mid to caudal thoracic rib crowding and thoracolumbar scoliosis (asterisks) secondary to vertebral malformations, and markedly widened multiple vertebrae (wide arrows).



**Figure 5.** Caudal three-dimensional CT reconstructions of lamb's skull. Note thickened occipital and elongated condyles (arrows).



**Figure 6.** Shallow, linear defect in the integument between rectum and prepuce base, consistent with hypospadias

Sepsis was evident, characterized by meningitis and valvular endocarditis. Definitive cause of sepsis was not histologically identifiable. Cerebellum herniation and sepsis were likely the cause of lethargy.

## Genetic analysis

Lamb's hair roots were submitted to the University of California-Davis Veterinary Genetics Laboratory for DNA analysis to test for ovine hereditary chondrodysplasia (spider lamb syndrome). Assay used is an allele specific PCR of the c.1719T>A variant. Results revealed N/N, meaning that the lamb was homozygous for tyrosine in the *FGFR3* gene, indicating 2 normal copies. No sequencing was performed and thus flanking sequence was not evaluated.

## Discussion

Ovine hereditary chondrodysplasia (spider lamb syndrome) is a recessive, semilethal inherited disorder in young lambs resulting in skeletal deformities.<sup>1</sup> This syndrome is a result of a mutation within the gene for fibroblast growth factor receptor 3 (*FGFR3*). Frequently, affected lambs have spinal deformities, long bone defects, and underdeveloped musculature.<sup>1</sup> Although the findings in this lamb were compatible with multiple congenital vertebral malformations and caudal occipital malformation, hereditary chondrodysplasia was considered a less likely differential diagnosis in the absence of proximal ulnar, glenoid, sternbrae and facial abnormalities.<sup>10</sup> Negative genetic testing suggested that this lamb did not have the well-characterized single-nucleotide polymorphism that causes spider lamb syndrome; however, this does not rule out other, spontaneous mutations in *FGFR3*.

Hypospadias can be defined as an imperfect closure of the external urethra in a male<sup>9</sup> and is commonly classified into 4 types: palanetic, penile, scrotal, and perineal.<sup>8</sup> This lamb demonstrated a case of penile, scrotal, and perineal hypospadias. Hypospadias has been described in multiple livestock species, and in humans. It is among the most common congenital malformation in human male neonates, whereas these defects apparently occur as a result of a multifactorial disorder that has been associated with genetic and environmental factors.<sup>6</sup> However, broadly this process of morphogenesis appears to be incredibly complex and is largely not understood. In a survey of the occurrence of congenital defects in sheep, the urogenital system was involved in 22.9% of the cases, and the most common male urinary defects were hypospadias and renal agenesis.<sup>3</sup>

Reported concurrent developmental abnormalities in other animals with hypospadias include other urogenital abnormalities, such as penile aplasia, an incomplete ventral sheath, cryptorchidism, and atresia ani.<sup>5,7</sup> None of these concurrent genitoanal abnormalities were present in this lamb. However, this lamb did present with marked, lumbar vertebral and occipital malformation, and moderate cerebellar herniation. Limbs and the external genitalia may originate from nearby cell lines during embryogenesis.<sup>4</sup> Together with this information, these findings suggest that these congenital malformations may have occurred early in the development (differentiation of the embryo mesoderm). Although hypospadias and associated congenital abnormalities etiology remain unknown, lack of abnormalities in the twin suggests that an infectious or environmental process had no effect; however, it cannot be ruled out. Therefore, it is more likely that this abnormality was initiated within the developmental process of that individual embryo, although it remains unclear if it is product of inheritable genetic mutations.

Barbados Blackbelly sheep breed originated in Barbados, easternmost island of Caribbean chain and West Africa. They are known for their ability to withstand harsh tropical climates and heavy parasite burdens.<sup>2</sup> Currently, to our present knowledge, there are no specific perpetuating congenital abnormalities harboring within the purebred of Barbados Blackbelly lineage. However, the closeness of genetics within the breed makes a case for close monitoring of congenital defects that may be the result of recessive congenital genes. Likewise, due to increasing implications of viruses, plants, and medicinal or chemical products, it is important to continue to be vigilant in our efforts to identify environmental teratogens that may be responsible for congenital defects.<sup>3</sup> Producers of sire and dam of this lamb, were informed, to follow up for potential future congenital defects associated with the lines of sire and dam to avoid perpetuating a flaw within the breed. This was the first occurrence in either of their flocks. To our knowledge, a case of hypospadias and vertebral malformation in the Barbados Blackbelly breed has not been reported.

### Learning points

- Hypospadias and concurrent congenital malformations can occur in several mammalian species, often without a definitive explanation.
- Occurrence of congenital malformations within specific breeds is important to monitor, specifically in those with closely related genetics,
- Complications in embryogenesis should be considered when malformations of the external genitalia and appendages are present,

### Conflict of Interest

Authors disclose no conflicts of interest.

### Acknowledgement

Authors thank the producer for willingness to facilitate further evaluation of the lamb.

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