Case Report Rapport de cas

Congenital hypotrichosis and partial anodontia in a crossbred beef calf

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Abstract — Clinical examination, skin biopsies, skull radiographs, and DNA analysis of a 2-day-old Red Angus-Charolais-Simmental cross bull calf confirmed the diagnosis of congenital hypotrichosis and anodontia defect (HAD), also called anhidrotic ectodermal dysplasia, which is a rare anomaly caused by a deletion in the bovine EDA gene on the X chromosome.

Résumé — Hypotrichose congénitale et anodontie partielle chez un veau de boucherie de race croisée.
L’examen clinique, les biopsies cutanées, les radiographies crâniennes et l’analyse de l’ADN d’un veau mâle de race croisée Angus Rouge-Charolais-Simmental âgé de 2 jours, ont confirmé le diagnostic d’anomalie d’hypotrichose congénitale et d’anodontie (AHA). Cette anomalie rare, connue aussi comme dysplasie ectodermique anhidrotique, est causée par la délétion du gène bovin EDA sur le chromosome X.


A 2-day-old, male, Red Angus-Charolais-Simmental cross calf was presented to the Western College of Veterinary Medicine (WCVM) because of a short hair coat and an inability to stand and suckle. The calf had been placed in a heated box and bottle-fed powdered colostrum along with milk replacer twice daily until presentation. Herd history revealed that no other calves had been born that year or in previous years with a similar phenotype, and the purebred Red-Angus sire had been the predominant herd-sire. The 4-year-old dam of the bull calf was of crossbred Red Angus-Charolais-Simmental descent and her previous calf, full sibling to the bull calf in question, was phenotypically normal. The owner was unable to provide the gestational age of the bull calf; however, it was considered full term, as the herd of origin was approximately halfway through calving and numerous half siblings, recently born, were approximately the same size at birth with no phenotypic abnormalities.

Case description

Physical examination revealed a 31.1 kg, profoundly depressed, recumbent calf with severe hypothermia (32.4°C), an irregular cardiac arrhythmia, and rotary nystagmus. Extremely fine hair

Figure 1. Normal appearing hair in the inner margins of the pinna.

Figure 2. Lack of incisors evident on digital examination. Note the dry muzzle and lack of normal appearing hair on head.

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covered nearly the entire body, such that, ostensibly, normal hair could be found only on the inner margin of the pinna (Figure 1), the distal parts of the extremities, and the tip of the tail. The calf was hypersensitive to palpation of the skin, which was abraded over pressure points: hips, shoulders, carpi, tarsi, and fetlocks. No incisors were evident (Figure 2) and only 1 molar was palpable on the lower right side of the jaw. The prognosis for a normal, productive life was poor; therefore, the calf was donated to the Veterinary Teaching Hospital. Differential diagnoses included viable hypotrichosis caused by *Bovine viral diarrhea virus* (BVDV) infection during midgestation, hypotrichosis with incisor anodontia (HID), or hypotrichosis and anodontia defect (HAD) (1,2).

The calf was placed under an external heat source and given 1 L of whole milk through an esophageal feeder. Septicemia was suspected, so the calf was administered ceftiofur sodium (Excenel; Pharmacia Animal Health, Orangeville, Ontario), 2 mg/kg bodyweight (BW) SC, q24h, and flunixin meglumine (Banamine; Schering-Plough, Pointe-Claire, Québec), 1.1 mg/kg BW, IV, q24h. The nystagmus and arrhythmia were not observed after the calf regained a normal core body temperature.

Serum, ethylenediamine tetra-acetic acid (EDTA)-treated whole blood samples, and a free flow urine sample were submitted for a biochemical panel, complete blood (cell) count (CBC), and urinalysis, respectively. The results showed decreased gamma-glutamyl transpeptidase (GGT) (9 U/L; reference range, 12 to 39 U/L) and hypoproteinemia (37 G/L; reference range, 68 to 87 G/L), which were indicative of failure of passive transfer of maternal antibodies, and a neutropenia (0.759 × 10⁹/L; reference range, 0.95 to 3.8 × 10⁹/L), which was suggestive of peracute inflammation. The urinalysis was unremarkable. Skin biopsies were obtained from the muzzle, lateral flank, and dorsal lumbar regions, using a 6-mm biopsy punch, and were submitted for histopathologic examination. Samples of hair from the ear and heparinized blood were taken for future DNA analysis and sequencing. Despite daily anti-inflammatory and antibiotic treatment, in addition to whole milk feeding through an esophageal feeder every 6 to 8 h, the calf’s condition continued to deteriorate over the next 48 h. Multiple limb joints, including carpi and tarsi, became swollen and effusive; the calf was reluctant to stand and refused to nurse from a bottle. The development of signs consistent with septicemia or endotoxemia was attributed to failure of passive transfer of maternal antibodies due to the poor quality and quantity of colostrum at birth and was not associated with the observed congenital defects. The calf was euthanatized (Euthanyl Forte; Bimeda-MTC, Cambridge, Ontario) and submitted for postmortem examination.

Radiographs of the head, taken post mortem, showed the lack of incisors, the presence of only 4 maxillary premolars, and a single mandibular premolar, for a total of 5 teeth, which eliminated HID as a differential diagnosis. The dental formula for this bull calf was deciduous incisor (DI) 0/0; deciduous canine (DC) 0/0; deciduous premolar (DP) 2/1; deciduous molar 0/0, as opposed to the DI 0/4; DC 0/0; DP 3/3; DM 0/0 (20 teeth in total) for a normal newborn calf (3). No evidence of permanent dentition was found on radiographic examination.

Necropsy revealed hypotrichosis; oligodontia; locally extensive bronchopneumonia, potentially due to repeated esophageal tube feeding; and mild lymphoid atrophy of Peyer’s patches, consistent with the clinical findings of peracute inflammation. There was no evidence on gross postmortem examination of arthritis. Swelling over the carpal and tarsal joints could have been due to skin abrasion over the same joints. Immunohistochemical examination of formalinized skin samples was negative for BVDV. On histopathologic examination, very few normal anagen hair follicles were present and in the small, scattered foci of all biopsies, there was total underdevelopment of hair follicles. Hypoplastic follicles were common, contained smaller than normal hair shafts and fewer than normal adnexal glands (both sebaceous and epitrichial) (Figure 3). Otherwise, dermal collagen and the epidermis appeared normal. All 3 biopsies showed the same changes, but a couple of foci of secondary epidermal necrosis were present in 1 biopsy. A diagnosis of congenital hypotrichosis and anodontia defect (HAD) was suggested, based on the clinical, radiographic, and histological findings, mainly the absence of normal hair covering, along with total lack of incisors and almost complete lack of deciduous premolars, and confirmed with DNA analysis. Sequencing of DNA confirmed
that a nonsense mutation in the *EDA* gene (R244X) was present and was the most likely cause of the phenotype (4).

**Discussion**

Hypotrichosis is a congenital condition in cattle that consists of partial or complete absence of hair follicles, with or without associated developmental defects (2,5,6). Two inheritable disorders that display both hypotrichosis and anodontia have been reported: congenital hypotrichosis and anodontia (HAD) and congenital hypotrichosis and incisor anodontia (HID). Congenital hypotrichosis with incisor anodontia has been attributed to an X-linked incompletely dominant inheritance (1,6). The HAD discussed in this paper has been reported to be due to a rare sex-linked trait produced by an Xq-deletion and partial X inactivation in females (1,6), while it is inherited as a monogenic X-linked recessive trait in males (1,6,7). The bovine condition is phenotypically similar to an X-linked genetic disorder (anhidrotic ectodermal dysplasia, Christ-Siemens-Touraine syndrome) in humans and mice, except that in that condition, there is hypohydrosis in addition to hypotrichosis and anodontia (1,9). Affected humans may also suffer from chronic respiratory conditions due to the absence of mucous glands in the respiratory tract (10). Anhidrotic ectodermal dysplasia is caused by various deletions or mutations of the *EDA* gene located on the X chromosome. Deletions of the *EDA* gene on the X chromosome, including complete removal of exon 3, have been demonstrated in cattle (1,9–11). The *EDA* gene encodes for a trimeric transmembrane protein, ectodysplasin 1 (EDA), which is a member of the tumor necrosis factor-like molecules (10). Ectodysplasin 1 is believed to be involved in the early epithelial-mesenchymal interaction that controls the formation of fetal hair follicles and tooth buds (9). The phenotypic abnormalities in animals affected with *EDA* gene mutation are almost entirely restricted to tissues of ectodermal origin: hair follicles, keratinocytes, sweat glands, and teeth (10,11). However, a hypotrichotic Holstein bull recently diagnosed with an *EDA* gene mutation also demonstrated respiratory lesions similar to those found with anhidrotic ectodermal dysplasia in humans (10). *Bovine viral diarrhea virus* likely did not play a role in this case, as this calf was negative for BVDV and no cases of congenital hypotrichosis associated with anodontia due to the teratogenic effects of BVDV infection have been found (9).

The clinical signs of this newborn crossbred calf are consistent with a mutation of the *EDA* gene causing congenital whole body hypotrichosis, absence of normal apocrine glands, and almost complete anodontia. The origin of the point mutation of the *EDA* gene is unknown, as this is a novel bovine *EDA* mutation. Rare occurrences of congenital hypotrichosis and anodontia defect have also been observed in Holstein, Normandy-Maine-Anjou, and Charolais cattle (1,2,7,9–11).

**References**