CASE REPORT

Congenital bilateral anterior nasal atresia in 16 half-sibling Holstein-Friesian calves

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Case report  Cases of bilateral anterior nasal atresia, sometimes referred to as arhinia or partial arhinia, are extremely rare in cattle and have only been reported as single events. This report describes the birth of 16 Holstein Friesian calves over a 3-month period, all affected with bilateral atresia of the nares and anterior nasal cavity, with 2 calves having additional severe deviation of the nasomaxillary bones and nasal septum. One affected calf was born with an anatomically normal twin. Parentage testing demonstrated that a single Holstein Friesian bull sired all cases tested.

Conclusion  This is the first report of multiple cases of bilateral anterior nasal atresia in cattle with evidence that demonstrates a heritable condition.

Keywords  arhinia; congenital conditions; dairy cattle; Holstein; nasal atresia


Bilateral anterior nasal atresia is defined as abnormally closed or absent nostrils, whereas arhinia is congenital absence of the nose and partial arhinia is congenital absence of a portion of the nose.1–3 It is an extremely rare condition, with only two individual reported bovine cases4,5 and 36 reported cases in humans.6,7 The human cases mostly have occurred sporadically as single events, but in a few instances as multiple events within related families.6,7 A variety of other congenital anomalies may accompany nasal atresia and arhinia. It has been reported in association with cyclopia in one bovine case and with choanal atresia, cleft palate, microphthalmia, hypotelorism or hypertelorism, and midface hypoplasia in human cases.6,8

The pathogenesis of nasal malformation is complex and not clearly understood. Although a few human cases have been associated with chromosomal abnormalities, most people with arhinia have a normal karyotype and limited molecular studies have failed to identify an associated genetic mutation.6,7 Authors of a recent report, in which human arhinia was associated with hypogonadism, suggested that it may result from gonadotropin deficiency affecting gonadotrophin-releasing hormone neuron formation or migration.8

During a 3-month period, 16 Holstein-Friesian calves with apparent bilateral anterior nasal atresia were born on a 550-cow purebred commercial dairy farm. Six affected calves were initially observed and photographed by the herd owner who reported the problem to the herd veterinarian, who subsequently initiated investigation of a further 10 cases.

The calves presented with bilateral atresia of the nostrils and bony nasal cavity. The nostrils were absent in all cases and replaced by small, non-functional indentations of glabrous skin present in the region of the external nares (Figure 1). The nasal planum and rostral upper jaw, including incisive maxillary and nasal bones, were present but showed variable malformation. Two calves also had craniofacial dysostosis. The calves were able to stand and walk normally, but were not able to suckle and as a result were euthanased. Examination of the photos of the initially affected calves indicated that they were similarly affected to those that underwent veterinary examination. The prevalence in male and female calves was similar. One affected calf was a twin to a normal calf. The sires and dams of all calves born during this period were anatomically normal.

The dams of the affected calves had grazed improved subtropical pasture after being dried off and prior to calving had been fed a total mixed ration of maize silage, sorghum silage, wheat, barley, soybean meal and/or palm kernel. The preventative medicine program on the farm included an annual clostridial and leptospirosis (7-in-1) vaccination and vaccination for bovine ephemeral fever. The dams of all calves had been on the affected farm for a minimum of 2 years and there was no history of clinical illness during gestation in the dams of the affected calves.

In all cases the gross pathology showed that the rostral bony nasal cavities were incompletely formed and non-patent. This was associated with variable malformation of the nasal planum and subjacent bony structures from mild to moderate narrowing of the upper jaw, resulting in a tapered and pointed facial profile (Figure 2). Of the 10 calves subjected to veterinary examination, 2 had severe nasal cavity asymmetry caused by deviation of the nasomaxillary bones and nasal septum (Figure 3). One of these calves additionally had bilaterally smaller than normal olfactory lobes and an incompletely formed rostral cranium, with absence of the cribriform plate and hypoplasia/aplasia of the nasal chonchae. Apart from this calf, the brains and craniums of all the other affected calves examined were grossly normal.

Histological examination of the tissue from the nasal cavities of the 2 calves with nasal deviation showed dysplastic arrangements of nasal and turbinate anatomical structures with distortion of trubinate architecture. However, all component tissues, including bone, cartilage, connective tissue, glands and epithelium were histologically normal.
normal (Figure 4). Examination of long bone physeal tissue from one of these calves showed normal growth plate anatomy.

Parentage testing of 90 calves born over the same period, as well as 10 of the affected calves, was conducted at The University of Queensland’s Animal Genetics Laboratory using internationally standardised DNA microsatellite markers.9,10 A single sire was shown to be responsible for the 10 congenitally malformed calves tested. Samples from the 6 initially affected calves reported to have similar if not identical congenital malformations were unavailable because the calves had been euthanased and disposed of by the farmer. The bull responsible for the malformed calves also sired 14 clinically normal calves. The remaining calves produced during this period were sired by two other bulls and all were clinically normal. If the observed condition was caused by an environmental factor, then it would have been expected that at least some of the affected calves would have been sired by the two other bulls. The difference between the observed and expected was tested using an odds ratio test and was found to be highly significant (P = 0.001), supporting the conclusion that the observed condition was likely to be a heritable congenital malformation.

**Discussion**

This is the first report of multiple cases of bilateral anterior nasal atresia in cattle. It is recognised that fetal malformation in cattle can be associated with a number of environmental, nutritional and infectious disease factors.11 However, demonstration that all 10 affected calves included in the parentage analysis were sired by the same bull demonstrates a genetic aetiology. The frequency of affected and unaffected calves sired by this bull suggests that the likely mode of

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**Figure 1.** Clinical manifestations of bilateral anterior nasal atresia in calves. (A) Rostral view: bilateral atresia of the nostril in a mild case with minimal accompanying malformation of the nasal planum. (B) External gross pathology demonstrating the atretic nostril filled with glabrous skin but minimal deformation of the nasal planum and rostral muzzle.

**Figure 2.** (A) Lateral view of calf showing atresia of the nostril in a mild case with minimal deformation of the muzzle or skull. (B) Paramedian section of the skull demonstrating normal mid and caudal nasal cavity and cranial morphology.
inheritance was autosomal dominance with reduced penetrance. The finding that sex did not affect frequency of this condition, and the birth of twins (one with nasal atresia and the other clinically normal), further support this conclusion. However, other explanations are possible. For example, the progenitor bull in this case may be the germline mosaic for the putative autosomal dominant mutation, something that is well recognised in humans and animals, or other modifier loci may be involved in abnormal trait expression.

Embryology of the nose in humans demonstrates that the primitive nasal cavity develops from the nasal pit after the disappearance of the oronasal membrane. The walls of the future nostrils form from

Figure 3. Gross pathology of severely affected atypical case of bilateral anterior nasal atresia from a calf exhibiting nasomaxillary deformation and malformation of the cribriform plate and olfactory bulbs. (A) Rostral view showing bilateral atresia of the nostrils with the rostral bony nasal cavities incompletely formed and non-patent. (B) Lateral view: severe lateral deviation of the nose. (C) Nasal cavity cross-section (rostral view): deviation and dysplasia of nasal turbinate tissue and right displacement of the nasal septum. (D) Ventral view: deviation of the hard palate in a calf with severe nasal cavity asymmetry.
surface ectoderm as the nasal placodes, which invaginate to form nasal pits, fill with epithelial plugs that are reabsorbed allowing nostril patency. The embryology of the anterior face in humans was extensively described by Albernaz et al. in 1995, who postulated that arhinia may result from several pathogeneases, including failure of the medial and lateral nasal processes to grow; overgrowth and premature fusion of the nasal medial processes resulting in an atretic plate; or abnormal migration of neural crest cells. Congenital nostril atresia is likely caused by failure of reabsorption of the epithelial plugs and is considered the likely pathogenesis in the present bovine cases. However, the presence of non-patent bony structures subjacent to the atretic nostrils means that premature or aberrant fusion of the nasal medial processes that form the frontonasal process must also be considered. The fact that craniofacial dysostosis, including lateral deviations, caudal skull and cerebral malformations, was present in only a small subset of affected calves suggests that this was a secondary phenomenon. Thus, abnormal neural crest migration or failure of embryological mechanisms that form the caudal nasal cavities, which is a separate developmental process from the rostral nasal cavity, is not likely part of the principal pathogenic mechanism present in the affected calves. Unfortunately, paramedian sagittal sections through the nasal pits were not available for examination, which may have provided more insight into the pathogenic mechanism of the nasal atresia in these calves.

Chronic ingestion of cyanogenic glycosides (perhaps associated with intake of maize or sorghum silage) has been reported to cause arthrogryposis, but there have been no reports of malformation of the nares and nasal cavity. Maternal vitamin A deficiency during pregnancy is also known to produce ocular and nasal malformations. In mice, vitamin A deficiency caused by retinaldehyde dehydrogenase mutations results in choanal atresia in the offspring, similar to isolated congenital choanal atresia in humans. Transplacental infection with Akabane virus can cause a range of congenital malformations, including hydrancephaly and arthrogryposis, but again, malformations of the nares and nasal cavity have not been reported. Bovine viral diarrhoea virus infection of immunologically susceptible early-pregnant females has also been associated with a wide range of congenital malformations, but there are no reports of malformations of the nares and nasal cavity.

The congenitally malformed calves on this farm showed no evidence of arthrogryposis and showed none of the characteristic clinical signs of hydrancephaly or cerebellar hypoplasia. Also, given that all pregnant cows were managed together on this farm, it seems extremely unlikely that chronic ingestion of cyanogenic glycosides or vitamin A deficiency or an outbreak of either Akabane virus or bovine viral diarrhoea virus infection would have only affected the calves sired by just one of the three bulls mated to this herd. Although we were unable to conclusively determine the mechanism of heritability for anterior nasal atresia in this cohort of calves, the DNA parentage verification is ample evidence for a conclusion that bilateral anterior nasal atresia is likely to be a heritable congenital defect in the Holstein breed.

References


Blackwell’s five-minute veterinary practice management consult 2nd edition is a 783 page hardcover or electronic book. Each of the 14 major sections has between 13 and 24 chapters. Additionally, there is a comprehensive abbreviations section, glossary and an effective index. This edition differs from the 1st edition in that it is available as an e-book, and includes the new Section 9, Technology Management.

Although much of the 1st edition is still highly applicable, the 2nd edition has superseded it, with many of the chapters improved and the addition of the new section on technology management.

Both editions focus on companion animal practice and the US scene, the 2nd edition less so than the first. However, the information is translatable to Australian practitioners and specific chapters are included for equine practice, not for profit hospitals, house-call and mobile practices. For the mixed practitioner, the 3rd edition of Bovine Medicine (Ed. P. Cockcroft)* has highly complementary additional material for management and development of progressive cattle practice.

The style of the writing is concise and easy to understand. The information is well-ordered, comprehensive and current (for instance, we all know how quickly technology changes). Like other books of the Blackwell’s five-minute consult series, chapters are presented in a repeating format.

The target audience for this book is primarily new and current practice owners, managers, administrators, veterinary and support staff. The reviewer uses it as a key reference text for Bachelor and DVM veterinary student business curriculum. The book’s concise 1–2 page chapters and availability as an electronic book make it ideal for use as an on-line resource for students. As such, the 2nd edition of Blackwell’s five-minute veterinary practice management consult is a recommended purchase for any person or stakeholder in veterinary business (staff, owners, leaders and operational managers), veterinary school and veterinary nursing institution libraries.

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Adele is a veterinarian and academic with a background in practice ownership, production animal, equine and companion animal practice.

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