Acta vet. scand. 1999, *40*, 85-88.

# A Case of Trisomy 22 in a Live Hereford Calf

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**Christensen K, Juul L: A case of trisomy 22 in a live hereford calf. Acta vet. scand. 1999, 40, 85-88.** – A case of the rare genetic trisomy 22 in a live calf is described. The calf had low blood thyroxine level and low growth rate. It had several defects including brachygnathia superior, strabismus convergence, aortal cusp insufficiency and hypertrophy of clitoris. Chromosome analysis was performed on cultured blood lymphocytes and fibroblast cells. In all counted metaphases 61 chromosomes were present. The extra chromosome was identified as a chromosome 22 by R-banding. The defects of the calf have similarities with cases of partial trisomy 3p25-pter in human. This section of the human chromosome 3 corresponds to sections of cattle chromosome 22.

***cattle; genetics; defect; congenital; Down's Syndrome; anomaly.***

## Introduction

The aetiology of congenital malformations in cattle is often obscure. However, chromosome aberrations have in some cases been identified as the causal factor. These cases have often been due to trisomy of either autosomal chromosomes or sex chromosomes. Malformations due to autosomal trisomy have mostly been described in connection to trisomy of chromosome 17 or 18 (*Herzog et al.* 1977 and 1982a, b). Other trisomies have only been identified one or few times. In addition, several unidentified trisomies have been found in malformed calves (*König et al.* 1980, *Tschudi et al.* 1975). Trisomy of autosomal chromosomes is almost always lethal due to either embryonic death or perinatal mortality (*Herzog & Höhn* 1991, *Herzog et al.* 1977 and 1982a).

This article describes additional findings to those of *Mayr et al.* (1985) and *Agerholm & Christensen* (1993) in a live calf with trisomy 22. The similarities with human trisomy syndromes are compared using known homology between human and cattle chromosome 22.

## Materials and methods

A 12-month-old female Hereford calf with poor thrift and low growth rate was sent to the Veterinary clinics at the Royal Veterinary and Agricultural University. The calf was examined clinically and blood samples for bovine virus diarrhea (BVD) and blood chemistry were taken (PCV, RBC, WBC, differential cell count, total protein, serum albumin, kidney-/liver-/muscle-profiles, iron, cortisol, thyroxine (T4), formolgel and glutaraldehyde). Faeces was analysed for gastrointestinal, lung and liver parasites. X-ray photos were taken of the skull and cranial part of thorax. An ultrasound scanning of the heart was performed. Due to physical abnormalities of the calf a chromosome analysis was also performed.

Chromosome analysis was performed according to the methods of *Christensen & Pedersen* (1990) using conventional whole blood lymphocyte cultures and skin fibroblast cell cultures derived from an ear clip; with and without bromodeoxyuridine (BrdU) in the medium for the final 7 h before harvest. The chromosome

preparations were stained with Giemsa or Acridine orange giving R-bands on BrdU incorporated chromosomes (cf. *Detrillaux et al.* 1973). Numbering of the chromosomes was made according to ISCNDA (1989): International System for Cytogenetic Nomenclature of Domestic Animals (*Di Berardino et al.* 1990). The 5-year-old mother and the father, a 3-year-old bull, were not available for chromosome analysis.

## Results

The calf's dam had previously given birth to 3 normal calves. The proband female Hereford calf was born without complications after a normal pregnancy period. It weighed 28 kg at birth and 120 kg at 12 months of age (both values are subnormal). The calf had been submitted to the veterinary clinics due to slow growth and poor thrift. The clinical examination revealed a severe brachygnathia superior (2 cm) and hyper-salivaion, and a high degree of strabismus convergence. Except a hypertrophic clitoris and super numeral nipples (7 in total), no further macroscopic abnormalities were found. X-ray photos of the cranial part of the thorax showed no pathological findings. Normal contractility of the heart was seen in the ultrasound scanning, but a mild degree of aortal regurgitation (aortal cusp insufficiency). The size of the heart was normal.

Blood chemistry showed low thyroxine (T4) level with a value half of normal (52 nmol/l versus 105 nmol/l). Alkaline phosphatase (ALP) was not as high as expected for a young animal. No other specific changes were seen.

BVD virus was not isolated. No parasites were found in the faeces.

The number of chromosomes was counted in 15 metaphases from lymphocyte culture and 10 from fibroblast culture. All metaphases had 61 chromosomes and the extra chromosome was identified by R-banding to be number 22 in 5 cells. The R-banded karyotype is shown in Fig. 1.

## Discussion

Previously, trisomy 22 in cattle has only been described in 2 cases. *Mayr et al.* (1985) detected a viable female calf with trisomy 22. This calf had an umbilical hernia, an urachus defect, and a slight inferior brachygnathism. The hernia was corrected surgically, and the brachygnathism disappeared, as the calf grew older. Later, the heifer gave birth to a normal calf (*Mayr et al.* 1987). *Agerholm & Christensen* (1993) found trisomy 22 in a 2-day-old calf which was euthanised due to many malformations. The calf had malformations of both the splanchnocranium and the interventricular septum. Furthermore, *Sakai et al.* (1991) described a trisomic calf with skin fragility, mild superior brachygnatism, and cryptorchidism. The authors supposed the trisomic chromosome to be number 22, but a specific identification was not made. The pathological findings in the calves with trisomy 22 described until now show heterogeneity, which indicates that calves presumed to be trisomy 22 can be quite different. – The amount of chimerism should be taken into account when evaluating the heterogeneity, as it is well known from human trisomy cases that quite many are chimeric having some proportion of normal tissue which makes them survive. In the present case only lymphocytes and fibroblast cells have been investigated. Therefore it can not be excluded that the animal might contain cells with normal karyotype. Trisomy studies of more tissues await identification of strong repeat probes for cattle chromosome 22, which can be used on interphase cells. The most common trisomy in humans is trisomy 21 (Down's syndrome). It is well established that the frequency of human trisomy 21 increases with the age of the mother. This is due to an age dependent increase in the meiotic non disjunction rate (*Lilienfeld & Benesch* 1969). The described case of trisomy 22 was the dam's fourth delivery. It is therefore possible that it

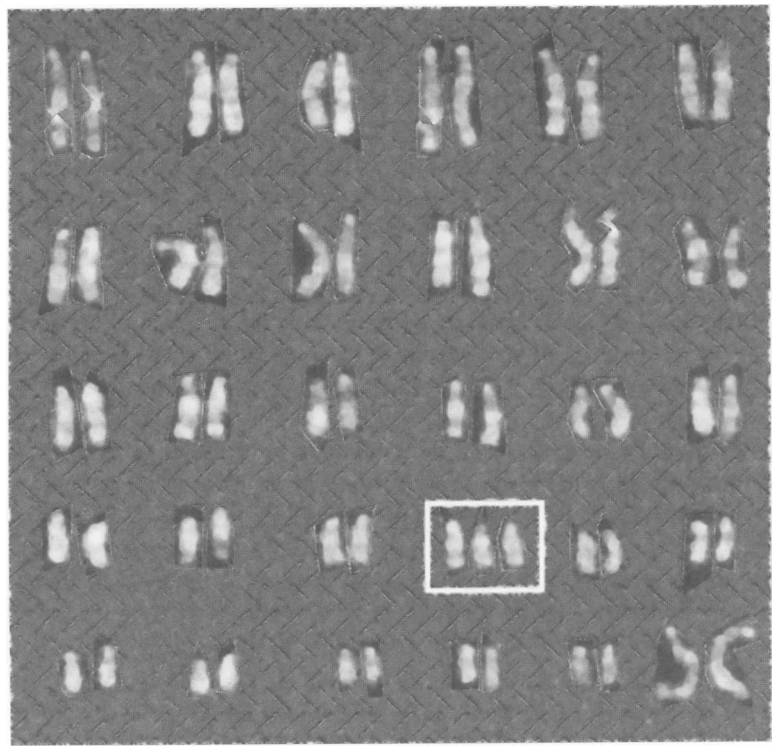

Figure 1. R-banded metaphase chromosomes from a calf with trisomy 22. The trisomic chromosomes are indicated in a box.

was related to ageing of the mother. But from the few sporadic cases that have been described in cattle, no age effect has so far been proved.

The development of bovine chromosome specific markers have progressed rapidly and Zoo FISH has now established homology between cattle and human chromosomes (e.g. *Chowdhary et al.* 1996). They found that the large human chromosome 3 paints the small cattle chromosome 22, and no other human chromosome paints this chromosome. A database queries (http://www.informatics.jax.org/) of identical genes on human chromosome 3 and cattle chromosome 22 gave 4 marker genes; GPX1 and RHO on human chromosome 3q11-24 and LTF and RAF1 on human chromosome 3p21-25. The sections of identity detect which partial human trisomic chromosome 3 might be of interest for homology studies. By studying published cases of partial trisomy 3 in humans, we found that the partial human trisomies 3p25-pter (*Kotzot et al.* 1996, *Reiss et al.* 1986) have defects similar to our case of cattle trisomy 22. Among the similarities can be mentioned cardiac defects, moderate retarded growth, a general disproportionate face and super-numeral nipples. In the cases where the partial human trisomy involves the chromosome 3q arm no similarities were revealed. Due to the heterogenity of the presumed trisomy 22 cases in cattle, it is premature yet to name it as a syndrome.

## Acknowledgement
We thank Mrs. I. H. Christensen for the chromosome preparations and Dr. J. Koch, Department of Clinical Studies, for the ultrasound scanning of the cardiac function.

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## Sammendrag
Et tilfælde af den sjældne kromosomdefekt trisomi 22 hos en levende kalv er beskrevet. Kalven havde lavt blod-thyroxine-niveau og lav vækstrate. Den havde adskillige defekter såsom brachygnathia superior, strabismus convergens, aortal cusp insufficiens og hypertrofi af clitoris. Kromosomanalyse blev gennemført på lymfocyt og fibroblast cellekulturer. I alle talte metafaser var der 61 kromosomer. Det ekstra kromosom blev identificeret som kromosom 22 ved R-bånds farvemetoden. Kalvens defekter har ligheder med defekter hos tilfælde af partiel trisomi 3p25-pter hos mennesker. Denne sektion af det humane kromosom 3 svarer til sektioner af kvægets kromosom 22.

*(Received October 17, 1998; accepted January 27, 1999).*

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