Congenital Chondrodystrophy of Calves in Scotland

G. J. Gunn[1], D. Scott[2], B. Thorpe[3], N. Loveridge[4], J. Goldie[5]
[1]SAC Veterinary Services, Drummondhill
Stratherrick Rd., Inverness, Scotland IV2 4JZ
[2]Rowett Research Institute, Bucksburn Aberdeen
[3]Roslin Institute, Edinburgh
[4]Bone Research Group, Medical Research Council, Cambridge
[5]SAC Advisory Services, Dumfries, Scotland

Abstract

A distant congenital anomaly of calves within the Scottish beef herd was identified by Scottish Agricultural College Veterinary Services before 1985. The condition involved primarily head and limb abnormalities, due to chondrodystrophy, with a wide range in severity within herds. Similar problems have been described in beef calves in Canada and more recently the Republic of Ireland. Outbreaks appear to be linked in some way to silage feeding. To date the etiology of these outbreaks remains undetermined.

This paper includes a brief clinical and pathological description of the condition as seen in Scottish herds, outlines the suspected extent of the problem, speculates on the potential cost to the industry and makes a preliminary report of the findings from a project which tested the hypothesis that manganese deficiency, acting as an independent factor. The need for further research into the relationship between silage manganese and bone manganese levels in the fetus is highlighted.

Keywords: bovine, congenital, chondrodystrophy, manganese, histopathology

Introduction

Over the last 15 years there has been a growing awareness of a distinct, recurrent, congenital anomaly occurring in the Scottish beef sucker herd (Ross, 1987) (Logue, Gibb and Spence, 1988) (Gunn, 1992). More recently the same problem has also been identified in some groups of dairy heifers. Preliminary investigations coordinated by Scottish Agricultural College, Veterinary Services (SAC VS) Centre, Inverness provided the following clinical picture (Gunn, 1992 & 1993). Affected animals showed disproportionate dwarfism and associated changes included deformity of the limbs and head. The most severely affected calves died at birth due to dystocia and many severe cases were never able to stand. In most clinical cases the proximal limb joints showed restricted movement but a range between restriction and laxity of movement was observed for the more distal joints. There was frequently doming of the cranium and brachygnathia superior. Consistent and distinctive histopathological features of chondrodystrophy were observed.

Reports of similar deformities of calves have been made elsewhere in the world. A congenital skeletal deformity syndrome associated with red clover silage feeding was reported on cow-calf ranches in Western Canada (Ribble and Janzen, 1987) (Ribble, Janzen and Proulx, 1989). More recently (Mee, 1995) reported on disproportionate dwarfism of beef calves in the Republic of Ireland and there have been similar reports from France (personal communications).

From a survey of Scottish veterinary practices completed during 1992, respondents could identify more than 150 herds which had had outbreaks but it was estimated that a large number of less serious outbreaks remain unreported (Gunn, 1993). Preliminary investigations suggested that there was an epidemiological link to silage feeding but the nature of this link had not been elucidated. Economic losses on affected farms could be very serious, undermining farm incomes already on a fragile economic base. With evidence for a nutritional link to fetal development, serious economic losses and obvious attendant welfare implications, further investigation was justified. Literature searches and personal communications indicated that manganese deficiency was a possible factor; for example Valero *et al*, 1990. We have completed a preliminary study which tested the hypothesis that manganese deficiency was the cause of this problem and hopefully provides some indication of the direction for future research.

Materials and Methods

Four SAC VS Centres were involved in collecting material commencing in 1992; Inverness, Dumfries,

Presented at the XIX World Buiatrics Congress, Edinburgh, Scotland, July 8-12, 1996.

Edinburgh and St. Boswells. At each a nominated veterinary investigation officer with previous experience in investigating outbreaks of congenital chondrodystrophy in cattle used a gross post mortem protocol to collect material from affected calves. Specified tissues were frozen at minus 20 degrees Celsius or fixed in 10% formal saline and sent to Inverness where a single operator confirmed the gross diagnosis and selected material for detailed examination. An identical protocol was used to collect material from age matched unaffected calves from routine post mortem submissions for use as control specimens. All calves were neonates, less than 96 hours of age except for one 6 month old affected calf.

Histopathology

Tissues from the following sites were cut and stained using haematoxylin and eosin (H&E) and examined by a single histopathologist: (i) Skull (ii) Lumbar vertebrae (iii) Tracheal cartilage (iv) Rib (v) Proximal Tibia (vi) Scapula (vii) Proximal Humerus

Sections from each humerus were assigned a score. Scores ranged from zero where there were no lesions to four where lesions were estimated to be severe. Additional bone sections, from the right humerus of affected neonatal calves, collected during the preceding investigation and already confirmed as suffering from chondrodystrophy, were submitted for reprocessing, histopathological assessment and scoring by the same operator. In both studies clinical status was unknown to the operator.

Bone Biology

Sections of proximal humerus from both chodrodystrophic and normal calves were examined and the epiphyseal growth plate total and proliferative zone widths assessed by morphometry. Total glycosaminoglycan (GAG) and chondroitin sulfate content were measured by Alcian Blue staining (Farquarson *et al*, 1994)

Biochemistry

Manganese levels for the right humerus and for the liver from each calf was measured using ICP-mass spectrometry on perchloric acid digests. Silage samples from affected farms were analyzed by SAC for a wide range of trace elements and minerals including manganese and the recognized interference factors iron, calcium and phosphates.

Costs

An estimate for the cost of an outbreak was derived from a significant, but not unusual, outbreak recorded for a 120 cow beef suckling herd in Dumfries & Galloway during 1993 when 24 calves died at birth or had to be euthanatized. A further 17 calves were affected to varying degrees but survived. An associated cost of £250 was assigned to each dead animal and an estimated average loss of £200 assigned to each affected calf at the time of sale.

Results

Histopathology

A total of 21 affected calves and 8 unaffected calves were examined for this study.

All the controls showed similar histopatholgy; the phases contained well defined zones of proliferating and hypertrophying chondrocytes, minor abnormalities were detected but none were consistent within a growth plate or across growth plates.

In grossly affected calves histopathological changes showed a range from severe to absent. The changes were characterized by partial to complete absence of fully hypertrophied chondrocytes in the physis, articular/epiphyseal complex and around the epiphyseal ossification centre. In some examples the proliferating chondrocytes were very poorly organized, the columns were not aligned. The number of proliferating cells in the physis appeared reduced in some individuals. No defects of matrix mineralization were detected. In the 6 month old deformed calf, all the phases and articular epiphyseal complexes appeared normal.

Temporal scoring involved samples from a total of 51 calves, including normal calves.

Clinically normal calves had a mean score approaching zero. The scoring system indicated that the changes were most severe in spring born calves with a mean score of 2.3 for April born animals falling to 0.5 for both July and August born animals.

Bone Biology

No statistical differences could be detected between the two groups of calves (two sample t-test). The measurement used in Tables 1 and 2 is mean integrated absorbance (MIA) x 100.

Table 1. Epiphyseal Growth Plate Levels of Total Glycosaminoglycans (MIA x 100)

Statistic	Zone					
	Proliferative		Transitional		Hypertrophic	
	Case	Control	Case	Control	Case	Control
Number	13	7	13	7	13	7
Minimum	55.7	47.7	48.5	52.0	26.2	46.4
Median	65.2	78.6	64.2	73.5	51.4	51.6
Maximum	79.9	91.9	88.8	83.2	66.9	56.9
Mean	65.9	72.8	65.9	70.9	49.8	51.0
SE	2.5	6.2	3.6	4.3	3.5	1.3

Table 2. Epiphyseal Growth Plate Levels of Chondroitin Sulfate (MIA x 100)

Statistic	Zone					
	Proliferative		Transitional		Hypertrophic	
	Case	Control	Case	Control	Case	Control
Number	13	7	13	7	13	7
Minimum	46.3	39.3	35.5	44.4	20.8	39.4
Median	54.3	64.0	55.0	62.5	40.0	40.5
Maximum	66.3	76.9	66.3	70.4	52.1	49.7
Mean	54.9	60.6	53.7	60.1	39.2	41.8
SE	1.9	5.0	2.7	3.5	2.7	1.4

Table 3. Epiphyseal Growth Plate Measurements (μm)

Statistic			Zone	
	Total Width		Proliferative Zone Width	
	Case	Control	Case	Control
Number	12	7	12	7
Minimum	285	326	153	168
Median	437	419	235	252
Maximum	564	548	292	342
Mean	453	441	232	263
SE	22	29	11	23

Tissue Biochemistry

No statistical differences detected between the two groups (two sample t-test).

Table 4. Summary Results for Tissue Manganese Estimations (Dry Matter ppm)

Summary Statistic	Number	Minimum	Median	Maximum	Mean	SE Mean
Bone - Control	7	0.83	1.11	1.40	1.07	0.08
Bone - Affected	15	0.23	0.95	7.33	1.44	0.44
Liver - Control	6	2.68	3.86	17.29	5.98	2.29
Liver - Affected	16	3.31	5.79	12.99	6.31	0.64

Biochemical Analysis of Silage

Silage samples were collected from nine problem farms. The mean dry matter content was 229 g/kg (range 164-385) with a mean manganese level of 108 mg/kg DM (range 57-186). The mean calcium content was 4.4 g/kg DM, mean phosphate content was 3.4 g/kg DM and mean ash content, as a proxy variable for iron, was 92 g/kg DM (range 71-102).

Costs

The total cost of an outbreak to the farmer, in the example, was calculated to be £9600 for that year.

Discussion

The cost example is included to emphasis the devastating impact that this condition can have on a cattle unit. If there were only 100 cases in any year then the cost could easily approach £1M per annum. Although on many units losses might not be so extensive this was by no means the worst outbreak encountered. The example is both superficial and conservative (the true cost would be much greater if feed costs, throughput costs and opportunity costs such as farm labor were included). In most instances the problem recurs over several years and the cost multiplies. The authors are aware that many cases remain unreported so overall the estimate of £1M per annum is probably realistic.

Where histopathological lesions were present they were recorded at all sites to varying degrees. Results confirmed that the spring born cases were suffering from a congenital chondrodystrophy, however, often no lesions could be identified in calves born after June although calves demonstrated significant clinical deformity. The results for the six month old calf were similar; there was clinical disease but growth plates appeared to be normal. These results would support the concept that the insult only causes the endochondral defect during the winter months and therefore might be associated with silage feeding. It appears that with removal of the 'agent' the bone lesions repair but are never able to recover lost length and so affected calves display disproportionate dwarfism for the rest of their lives.

No differences in bone and liver manganese levels could be detected between the case and control groups of calves. However, means for both groups fell below suggested normal bone levels for young calves; 1.46 ppm DM (Rojas *et al*, 1965) and 1.51 ppm DM (Howes and Dyer, 1970). Similarly liver levels were low compared with normal mean levels described in the literature; 11.84 (Rojas *et al*, 1965), and 7.96 ppm DM (Howes and Dyer, 1970). These manganese levels were similar to those seen in calves from cows fed diets deficient in manganese and showing skeletal defects resembling those described here (Rojas *et al*, 1965; Howes and Dyer, 1970; Doige *et al*, 1990; Staley *et al*, 1994).

A comparison of total growth plate width and the proliferative zone width for cases and controls failed to detect any differences. Manganese is a co-factor for a number of enzymes involved in the synthesis of components of the organic matrix (glycosaminoglycans) for cartilage and so plays an important role in the development and mineralizations of the growth plate. Manganese deficiency results in reduced sulphation of the bone matrix which in turn results in chondrodystrophy. The Alcian Blue staining technique is an indirect method of measuring manganese availability in the developing calf. It was expected that if manganese deficiency was involved in the disease process that GAGS and chondrotin sulfate levels would be reduced for the case growth plates compared with con-

trol. No significant differences were detected in the GAGS and chondrotin sulfate levels for the proliferative, transitional and hypertrophic zones between groups. These results are consistent with the observation that both case and control groups were deficient in manganese. It would be valuable to repeat these tests on matched calves from non silage fed calves for comparison.

Silage samples collected from farms which had suffered outbreaks of chondrodystrophy were found to contain adequate levels of manganese compared with suggested requirements from the ARC (20-25 mg/kg) and NRC (40 mg/kg). High levels of calcium and/or phosphate in the ration reduce manganese absorption and retention but the levels recorded here were not substantially elevated. Ash levels for silage which are greater than 9% indicate soil contamination which in turn suggests high iron levels. For most of these silage samples ash levels were above 9%.

Bone lesions consistent with manganese deficiency were described in association with low bone and liver manganese levels. However this study raises several important questions. Since control calves also had low manganese levels, are the cases just one extreme end of a normally distributed spectrum that one might expect for any deficiency associated disease? Lesions diminished with the temporal interval between silage feeding and birth but clinically affected neonates, with no lesions, also had low manganese levels - what other factors were involved? If representative silage samples from affected farms contain adequate manganese levels then why are neonatal bone and liver manganese levels so constantly low? Is there a factor interfering with absorption from the gastrointestinal tract of the dam? The high ash content for some silage samples suggest that dietary iron might play such a role. Calcium and phosphate do not appear to be involved. What is the true availability of manganese for Scottish silage? Is manganese deficiency inherent in Scottish beef sucker cow systems? Collectively the results lead the workers to conclude that manganese deficiency, acting as a single factor, was unlikely to have caused the congenital chondrodystrophy described here. However manganese deficiency is not excluded as part of a multiple factorial etiology for this condition.

Acknowledgments

The authors gratefully acknowledge the assistance of many veterinary colleagues within SAC and MAFF for their earlier contributions to research on this subject. In particular they acknowledge the contribution made by Dr. R Munro, MAFF Lasswade, Edinburgh. SAC received funding from the Scottish Office Agriculture Environment Fisheries Department to carry out this project.

References

1. Doige, C.E., Townsend, H.G.G., Janzen, E.D., McGowan, M., 1990. Congenital Spinal Stenosis in Beef Calves in Western Canada. *Vet. Pathol.* 27:16-25 2. Farquarson, C., Whitehead, C.C., Loveridge, N., 1994. Alterations in Glycosaminogycan Concentration and Sulphation during Chondrocyte Maturation. Calcified Tissue International 54: 296-303 3. Gunn, G.J., 1992. Long Bone Deformity of Beef Calves. *Veterinary Record* 130: 107 4. Gunn, G.J., 1992. A Congenital Chondrodystrophy Syndrome of Calves. *Catte Practice* 1: 42-48 5. Gunn, G.J., 1993. Observations on a Congenital Chondrodystrophy of Calves. Society for Veterinary Epidemiology and Preventive Medicine, Exeter, Conference *Proceedings*: 62-69 6. Howes, A.D., Dyer, I.A., 1970. Diet and Supplemental Mineral Effects on Manganese Metabolism in Newborn Calves. *Journal of Animal Science* 32: 141-145 7. Logue, D., Gibb, A., and Spence, J., 1988. Long Bone Deformity in Sucker Calves. *Veterinary Record* 122: 591 8. Mee, J.F., 1995. Nonhereditary disproportionate Dwarfism in a Beef Herd: Clinical and Pathological Features. *Irish Veterinary Journal* 48: 93-105 9. Ribble, C.S., Janzen, E.D., 1987. Congenital Skeletal Deformity Syndrome. *Canadian Veterinary Journal* 28: 160 10. Ribble, C.S., Janzen, E.D., Proulx, J.G., 1989. Congenital Joint Laxity and Dwarfism: A Feed Associated Congenital Anomaly of Beef Calves in Canada. *Canadian Veterinary Journal* 30: 331-338 11. Rojas, M.A., Dyer, I.A., Cassatt, W.A., 1965. Manganese Deficiency in the Bovine. *Journal of Animal Science* 24: 664-667 12. Ross, H.M., 1987. Beef Calf Deformities. SAC Veterinary Investigation Service, Pitlochry, Biennial Conference *Proceedings*: 11 13. Staley, G.P., Van DER Lugt, J.J., Axsel, G., Loock, A.H., 1994. Congenital Skeletal Malformations in Holstein Calves Associated with Putative Manganese Deficiency. J1 S. Afr. *Vet. Ass.* 65(2): 73-78 14. Valero, G., Alley, M.R., Badcoe, L.M., Manktelow, B.W., Merrall, M., Lawes, G.S., 1990. Chondrodystrophy in Calves Associated with Manganese Deficiency. *New Zealand Veterinary Journal* 38: 161-167