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Polioencephalomalacia in Cattle

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ABSTRACT

Polioencephalomalacia (PEM) of ruminants is a neurological disorder, characterized by cerebrocortical necrosis. PEM has been involved with thiamine deficiency, sulfur intoxication and other less common factors include lead poisoning and water-deprivation-sodium ion toxicosis. In this study, the clinical signs, pathological findings and etiopathogenesis of PEM in ruminants are reviewed.

Key words: Poliencephalomalacia, cattle, pathogenesis

INTRODUCTION

Polioencephalomalacia (PEM) or cerebrocortical necrosis is a neurologic disease of ruminants characterized by necrosis of cerebral cortex (Loew *et al*., 1969; Summers *et al*., 1995). PEM affects young ruminants, usually 2 to 7 months/sheep and from weaning at 6 to 18 months/cattle. Adults animals can also develop it although more sporadically. Several causes have been associated with this disease, including thiamine deficiency, sulfur intoxication, acute lead poisoning and water deprivation-sodium ion toxicosis (Pandher, 2000). Sudden changes in diet (from poor to good pasture, or supplementation, or sudden increase in carbohydrates), administration of oral antibiotics and/or coccidiostats (Amprol plus), water deprivation and even eating carcasses has also been incriminated as triggering factors (Radostits *et al*., 2007). The diagnosis of PEM usually is based on clinical signs, history of the herd management and laboratory analysis (levels of blood lactate, pyruvate and thiamine, glycemia, transketolase activity in red blood cells) (Edwin *et al*., 1979; Horino *et al*., 1994). Differential diagnosis includes rabies, Aujesky disease (Callan and van Metre, 2004), BHV-5 (Aquino Neto *et al*., 2009), cerebral babesiosis (Everitt *et al*., 1986), enterotoxemia (Filho *et al*., 2009), hepatic encephalopathy (West, 1997), plant poisoning and tetanus (Summers *et al*., 1995).

CLINICAL SIGNS AND PATHOGENESIS

PEM is characterized by progressive neurological signs including blindness, ataxia, listlessness, proprioceptive deficits, circling, recumbency, muscular incoordination, t nystagmus, head pressing against solid objects, convulsions, coma and death. Symptoms seem to be associated with increased intracranial pressure that accompanies brain edema and necrosis of neurons. Death usually occurs 2-3 (sometimes up to 12) days after the onset of signs. Treatment with thiamine may have an effect if started early. The mainly causes and mechanisms involved in the developing of PEM are described below.

Thiamine deficiency: Thiamine (vitamin B1) is an important coenzyme in several pathways of intermediate metabolism of carbohydrates and energy in organisms. This vitamin is essential for brain function and its deficiency causes decreased levels of thiamine diphosphate (ThDP), an indispensable cofactor for several key enzymes in cell energy metabolism, especially pyruvate and oxoglutarate dehydrogenases and transketolase. In ruminants, thiamine is produced by ruminal bacteria and protozoa under normal environmental conditions. Disruptions in the normal rumen microbial population can promote a thiamine-deficient state. Thiamine deficiency is related to overeating, acute impaction, grain engorgement, founder and grain overload (Harmeyer and Kollenkirchen, 1989). Acidosis can promote proliferation of thiaminase II producing bacteria (*C. sporogenes* and *Bacillus* sp.) (Brent, 1976). This enzyme destroys thiamine, producing a thiamine analog that inhibits thiamine-dependent reactions of glycolysis and decarboxylations (Brent and Bartley, 1984). It has been known that thiamin analogs in the presence of a cosubstrate are responsible for PEM development. PEM can also be caused by thiaminase I (Edwin and Jackman, 1970). Several drugs including promazines, levamisole, benzimidazoles act as a cofactor to thiaminase I. This enzyme is also present in different plants such as horsetail (*Equisetum arvense*), bracken fern (*Pteridium aquilinum*) (Vetter, 2009), prostrate pigweed (*Amaranthus blitoides*)(Ramos *et al*., 2005), small flowered mallow (*Malva parviflora*) (Main and Butler, 2006), kikuyu grass (*Pennisetum clandestinum*) (Bourke, 2007), Medicago sativa (Meyer, 1989) and Nardoo fern (*Marsilea drummondii*) (Pritchard *et al*., 1978). Amprolium, an anticoccidial drug can promote PEM in cattle, acting as a thiamine antagonist. This drug inhibits thiamine metabolism and ThDP biosynthesis leading to neuronal cell loss (Rindi *et al*., 2003; Chornyy *et al*., 2007). Experimental studies in calves showed that oral administration of amprolium (600 mg/kg/day) promotes neurological signs and pathological findings of cerebrocortical necrosis. Blood and tissue thiamine levels decreased, especially in cerebrum and cerebellum (Kasahara *et al*., 1989; Horino *et al*., 1994).

Sulfur-associated polioencephalomalacia: This disorder has been more recently and frequently described in the literature. The excess of sulfur in diet is one of the related causes of sulfur-associated PEM. The major dietary sulfur sources are alfafa hay, molasses, beet pulp, barley malt sprouts, calcium sulphate, ammonium sulphate, sodium sulphate and grain-processing products (corn gluten meal, brewers grain) (NRC, 2001). The recommended maximum rate of sulfur on diet is 0.5% for cattle eating more than 40% forage (Klasing *et al*., 2005). On the other hand, when dietary sulfur is as low as 0.35% cattle on diets containing less than 15% forage, cattle can develop PEM. Younger beef cattle and lactating cows seem to be more susceptible to excess sulfur intake (Sager *et al*., 1990; Kung *et al*., 1998; Loneragan *et al*., 1998). Experimentally, diets with high concentrations of sulfate has been reproduced PEM. It was demonstrated that the onset of clinical signs presents in animals with sulfur-related PEM coincided with excessive ruminal sulfide production (Gould, 1998). The sulfite produced during the reduction of sulfate to sulfide cleaves thiamine at the methylene bridge; thus, high sulfide levels could cause the brain lesions associated with PEM.

Acute lead poisoning (plumbism): Lead (Pb) is a highly toxic heavy metal found in all parts of the environment. There are different forms of lead: metallic lead, inorganic lead and lead compounds (or lead salts) and organic lead (containing carbon). The main sources of lead include batteries, discarded crankcase oil, asphalt, paint and solder. These products can contaminate

pastures or feeds during storage and processing (Van Beek *et al*., 1992; Lemos *et al*., 2004). The lead is rapidly absorbed in the gut and distributed to blood and tissues (Humphreys, 1991). The nervous tissue is especially sensitive to the effects of lead. Several experiments with rodents exhibited the direct neurotoxic actions of lead by apoptosis (programmed cell death), excitotoxicity affecting neurotransmitter storage and release and altering neurotransmitter receptors, mitochondria, second messengers, cerebrovascular endothelial cells and both astroglia and oligodendroglia (Liu *et al*., 2010). The duration to exposure depends of the chemical form of the lead. Lead sulphate and particulate lead promotes temporary, but very high exposure and poisoning after the ingestion of battery fragments. On the other hand, exposure to metallic lead is extended because it is retained in the rumen (Sharpe and Livesey, 2004). One studied demonstrated that tissue Pb was significantly higher in calves on a milk diet compared to tissue from calves on a grain and hay diet (Zmudzki *et al*., 1984). Neurological signs typically occur after a single ingestion of a material containing a large quantity of lead (Oskarsson *et al*., 1992). The affected animals can present blindness, facial tremors, progressive recumbency and chewing gum seizures (Osweiler *et al*., 1985).

Water deprivation-sodium ion toxicosis: PEM can occur sporadically in cattle subjected to water restriction. This disorder can be due to blood sodium imbalance in cases of water deprivation followed by unrestricted imbibition (Carmalt *et al*., 2000). The water restriction can be caused by broken pumps, overturned water tubs, frozen water and moldy bottles, for example. Access to salt or salt-containing water exacerbates the effects of water restriction (Sandals, 1978). The increase in serum concentration of sodium leads to water movement from the brain intracellular space to the extracellular compartment. Large shifts in brain water content can decrease brain volume and predispose to vascular damage and irreversible neurologic injury. High concentrations of sodium in the central nervous system can also impede anaerobic glycolysis with consequent inhibition of sodium export. The affected animals reveal right lateral recumbency, rumen tympany, convulsions, opisthotonus, horizontal nystagmus, champing of the jaws, generalized tremors, abdominal pain and polydipsia. Some animals can also present diarrhea and blindness (Senturk and Huseyin, 2004). The recommend limit of salt is 4% in feed and 0.3% in water (Pearson and Kallfelz, 1982).

PATHOLOGICAL FINDINGS

Lesions vary accordingly to the intensity and duration of disease. In the early phase of the disease, the damaged tissue autofluoresces under ultraviolet (360 nm) illumination. Progressively, the affected tissue becomes swollen and soft and undergoes cavitations (Markson and Wells, 1982). Gross lesions include flattening of cerebral gyri, hemorrhages, necrosis to cavitations in the gray matter of the occipital and temporal regions (Fig. 1) and herniation of the cerebellum in some cases (Summers *et al*., 1995). Interstitial and bullose emphysema are visualized in the lung. In the histopathological analysis of cerebral cortex, the neuropil exhibits spongiosis, neuronal necrosis, hemorrhages, perivascular edema and vascular hyperplasia. Cavitations and accumulation of Gitter cells are seen in grey matter. Interlobular interstitial and alveolar emphysema and mononuclear cell infiltration can be detected in the lungs (Kul *et al*., 2006). Brains of animals that survived for a longer period of time have reduced sizes and feature areas almost totally devoid of cortex and sometimes with small cysts. In these areas only a thin layer of the cortex or the meninges cover the white substance (Summers *et al*., 1995).

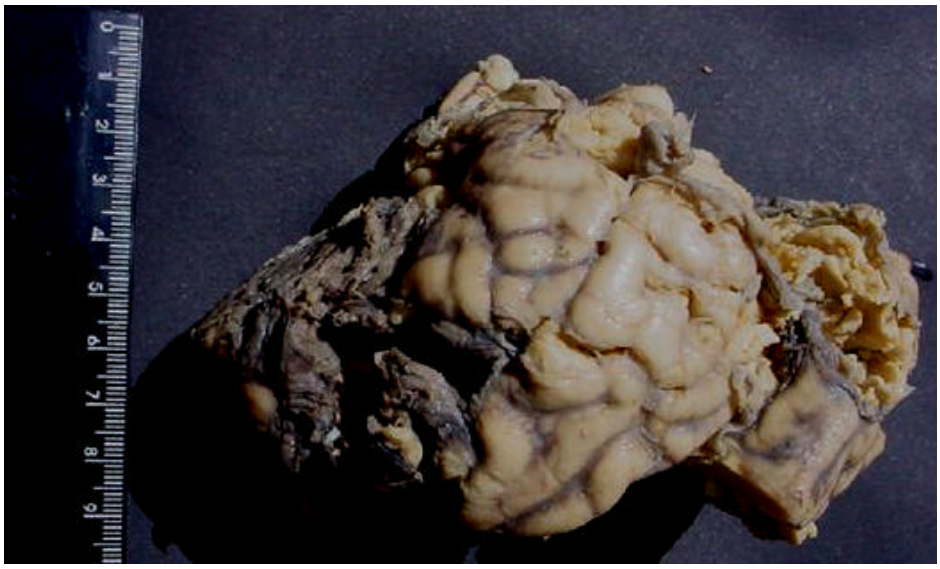

Fig. 1: Locally extensive cavitation (malacia) located in the cerebral cortex, frontal lobe

CONCLUSION

The poliencephalomalacia is an entity related to multiple factors, which causes neurological changes in ruminants. The diagnosis of PEM is based on clinical signs, laboratory analysis and history of the herd management. Gray matter necrosis to cavitation in occipital and temporal regions are considered pathognomonic changes for PEM.

REFERENCES

Aquino Neto, H.M., A.U. Carvalho, E.J.F. Filho, P.M. Ferreira and E.F. Barbosa-Stancioli *et al.*, 2009. Meningoencephalitis by *Bovine herpesvirus* 5 in Minas Gerais State: Clinical case report. Arq. Bras. Med. Vet. Zootec., 61: 1-5.

Bourke, C.A., 2007. A review of kikuyu grass (*Pennisetum clandestinum*) poisoning in cattle. Aust. Vet. J., 85: 261-267.

Brent, B.E. and E.E. Bartley, 1984. Thiamine and niacin in the rumen. J. Anim. Sci., 59: 813-822.

Brent, B.E., 1976. Relationship of acidosis to other feedlot aliments. J. Anim. Sci., 43: 930-935.

Callan, R.J. and D.C. van Metre, 2004. Viral diseases of the ruminant nervous system. Vet. Clin. North Am. Food Anim. Pract., 20: 327-362.

Carmalt, J.L., K.E. Baptiste and J.M. Naylor, 2000. Hypernatremia in neonatal elk calves: 30 cases (1988-1998). J. Am. Vet. Med. Assoc., 216: 68-70.

Chornyy, S., J. Parkhomenko and N. Chorna, 2007. Thiamine deficiency caused by thiamine antagonists triggers upregulation of apoptosis inducing factor gene expression and leads to caspase 3-mediated apoptosis in neuronally differentiated rat PC-12 cells. Acta Biochim. Polonica, 54: 315-322.

Edwin, E.E. and R. Jackman, 1970. Thiaminase I in the development of cerebrocortical necrosis in sheep and cattle. Nature, 228: 772-774.

Edwin, E.E., L.M. Markson, J. Shreeve, R. Jackman and P.J. Carroll, 1979. Diagnostic aspects of cerebrocortical necrosis. Vet. Rec., 104: 4-8.

Everitt, J.I., J.A. Shadduck, C. Steinkamp and G. Clabaugh, 1986. Experimental *Babesia bovis* infection in Holstein calves. Vet. Pathol., 23: 556-562.

Filho, E.J., A.U. Carvalho, R.A. Assis, F.F. Lobato and M.A. Rachid *et al.*, 2009. Clinicopathologic features of experimental *Clostridium perfringens* type D enterotoxemia in cattle. Vet. Pathol., 46: 1213-1220.

Gould, D.H., 1998. Polioencephalomalacia. J. Anim. Sci., 76: 309-314.

Harmeyer, J. and U. Kollenkirchen, 1989. Thiamin and niacin in ruminant nutrition. Nutr. Res. Rev., 2: 201-225.

Horino, R., T. Itabisahi and K. Hirano, 1994. Biochemical and pathological observations on sheep and calves dying of experimental cerebrocortical necrosis. J. Vet. Med. Sci., 56: 481-485.

Humphreys, D.J., 1991. Effect of exposure to excessive quantities of lead on animals. Br. Vet. J., 147: 18-30.

Kasahara, T., S. Ichijo, S. Osame and T. Sarashina, 1989. Clinical and biochemical findings in bovine cerebrocortical necrosis produced by oral administration of amprolium. Nippon Juigaku Zasshi, 51: 79-85.

Klasing, K.C., J.P. Goff and J.L. Greger, 2005. Mineral Tolerance of Animals. 2nd Edn., The National Academies Press, Washington DC., pp: 372-385.

Kul, O., S. Karahan, M. Basalan and N. Kabakci, 2006. Polioencephalomalacia in cattle: A consequence of prolonged feeding barley malt sprouts. J. Vet. Med., 53: 123-128.

Kung, Jr. L., J.P. Bracht, A.O. Hession and J.Y. Tavares, 1998. High sulfate induced polioencephalomalacia (PEM) in cattle-burping can be dangerous if you are a ruminant. Proceedings of the Chr. Hansen's Technical Symposium, Pacific Northwest Nutrition Conference, Oct. 13-15, Vancouver, BC, Canada. http://ag.udel.edu/anfs/faculty /kung/H2S.htm.

Lemos, R.A., D. Driemeier, E.B. Guimaraes, I.S. Dutra, A.E. Mori and C.S. Barros, 2004. Lead poisoning in cattle grazing pasture contaminated by industrial waste. Vet. Hum. Toxicol., 46: 326-328.

Liu, J., D. Han, Y. Li, L. Zheng and C. Gu *et al.*, 2010. Lead affects apoptosis and related gene XIAP and Smac expression in the hippocampus of developing rats. Neurochem. Res., 35: 473-479.

Loew, F.M., O.M. Radostits and R.H. Dunlop, 1969. Polioencephalomalacia (*Cerebrocortical necrosis*). Can. Vet. J., 10: 54-56.

Loneragan, G.H., D.H. Gould, R.J. Callan, C.J. Sigurdson and D.W. Hamar, 1998. Association of excess sulfur intake and an increase in hydrogen sul?de concentrations in the ruminal gas cap of recently weaned beef calves with polioencephalomalacia. J. Am. Vet. Med. Assoc., 213: 1599-1604.

Main, D.C. and A.R. Butler, 2006. Probable *Malva parviflora* (small flowered mallow) intoxication in sheep in Western Australia. Aust. Vet. J., 84: 134-135.

Markson, L.M. and G.A. Wells, 1982. Evaluation of auto-fluorescence as an aid to diagnosis of cerebrocortical necrosis. Vet. Rec., 111: 338-340.

Meyer, P., 1989. Thiaminase activities and thiamine content of *Pteridium aquilinum*, *Equisetum ramosissimum*, *Malva parviflora*, *Pennisetum clandestinum* and *Medicago sativa*. Onderstepoort J. Vet. Res., 56: 145-146.

NRC., 2001. Nutrient Requirements of Dairy Cattle. 7th Edn., National Academies Press, Washington, DC., USA., ISBN: 0309069971, pp: 381.

Oskarsson, A., L. Jorhem, J. Sundberg, N.G. Nilsson and L. Albanus, 1992. Lead poisoning in cattle transfer of lead to milk. Sci. Total Environ., 111: 83-94.

Osweiler, G.D., T.L. Carson, W.B. Buck and G.A. van Gelder, 1985. Clinical and Diagnostic Veterinary Toxicology. 3rd Edn., Kendall Publishing Company, Dubuque, IA.

Pandher, K., 2000. Polioencephalomalacia in cattle. Kansas Vet. Q., 3: 1-2.

Pearson, E.G. and F.A. Kallfelz, 1982. A case of presumptive salt poisoning (water deprivation) in veal calves. Cornell Vet., 72: 142-149.

Pritchard, D., G.W. Eggleston and J.F. Macadam, 1978. Nardoo fern and polioencephalomalacia. Aust. Vet. J., 54: 204-205.

Radostits, O.M., C.C. Gay, K.W. Hinchcliff and P.D. Constable, 2007. Veterinary Medicine: A Textbook of the Diseases of Cattle, Sheep, Pigs, Goats and Horses. 10th Edn., WB Saunders Co., London, Toronto, ISBN-10: 0702027774.

Ramos, J.J., L.M. Ferrer, L. Garcia, A. Fernandez and A. Loste, 2005. Polioencephalomalacia in adult sheep grazing pastures with prostrate pigweed. Can. Vet. J., 46: 59-61.

Rindi, G., C. Patrini, A. Nauti, R. Bellazzi and P. Magni, 2003. Three thiamine analogues differently alter thiamine transport and metabolism in nervous tissue: An *in vivo* kinetic study using rats. Metab. Brain Dis., 18: 245-263.

Sager, R.L., D.W. Hamar and D.H. Gould, 1990. Clinical and biochemical alterations in calves with nutritionally induced polioencephalomalacia. Am. J. Vet. Res., 51: 1969-1974.

Sandals, W.C., 1978. Acute salt poisoning in cattle. Can. Vet. J., 19: 136-137.

Senturk, S. and C. Huseyin, 2004. Salt poisoning in beef cattle. Vet. Hum. Toxicol., 46: 26-27.

Sharpe, R. and C. Livesey, 2004. Discarded lead-acid batteries: A preventable cause of lead poisoning in cattle. Vet. Rec., 154: 512-512.

Summers, B.A. and J.F. Cummings and A. De Lahunta, 1995. Veterinary Neuropathology. In: Principles of Neuropathology, Duncan, L. (Ed.). Mosby, Missouri, pp: 1-67.

Van Beek, H., I.J.R. Visser, G. Vos, W. van Delft and G. Fennema *et al.*, 1992. Lead intoxication in cattle: A case report. Food Additives Contam., 9: 357-364.

Vetter, J., 2009. A biological hazard of our age: Bracken fern [*Pteridium aquilinum* (L.) Kuhn]-a review. Acta Vet. Hungarica, 57: 183-196.

West, H.J., 1997. Clinical and pathological studies in cattle with hepatic disease. Vet. Res. Commun., 21: 169-185.

Zmudzki, J., G.R. Bratton, C. Womac and L.D. Rowe, 1984. The influence of milk diet, grain diet and method of dosing on lead toxicity in young calves. Toxicol. Applied Pharmacol., 76: 490-497.