Digital Dermatitis: A Histopathological Evaluation and Some New Aspects in the Pathogenesis of a Multifactorial Disease

Leist, G., Rudolph, R.
Institut für Veterinär-Pathologie der Freien Universität Berlin, Straße 518 Nr. 15, 14163 Berlin, Germany
Natterman, H.
Institut für Mikrobiologie und Tierseuchen der Freien Universität Berlin, Luisenstr. 56, 10117 Berlin, Germany

Abstract

Tissue samples of skin affected by digital dermatitis were studied histopathologically together with post-mortem findings and anamnestic datas to achieve better understanding of this disease. There are hyperplastic, ulcerative, proliferative and combined forms distinguishable. The epidermal cells show signs of degeneration, hypertrophy and hyperplasia, combined with differing extensions of cell destruction by bacteria and spirochetes. Dermal reactions contain arteriosclerosis-like plaques, activation of endothelial cells, thrombosis and different patterns of perivascular infiltration. It is concluded that epidermal lesions are a sequel of dermal malperfusion. Partial or total ischaemia leads to hyperplasia and ulceration, respectively. Endotoxins of gram negative bacteria taking part in other diseases in the same cattle are strongly presumed as causing agents. This indicates a multifactorial pathogenesis.

Introduction

Digital dermatitis (DD) was first described in 1974 by Mortellaro in Italy. Since the early 1980's this hyperplastic, ulcerative or proliferative inflammation of the skin was found in other countries in Europe, North and South America, Africa, Australia and parts of Asia. In northern parts of Germany 59% of dairy farms had an average prevalence of 12.5% of the examined animals per farm for DD. Heifers around parturition are especially affected, mostly during the housing period but likewise in hot summer months on pasture. There are two seasonal peaks; January to March and June to July (Metzner, Dopfer, Pijl & Kehler, 1995). A lot of predisponding factors are discussed; breed, state of lactation, milk yield, amount of exercise and management have a great influence on the susceptibility of DD. Dietz *et al.* (1995) found all examined samples positive for Bacteroides levii, while most were positive for *B. melaninogenicus* and Prevotella bivia, *Fusobacterium necrophororum*. was cultured from only 10% of the samples. Together with the other bacteria the spirochetes, having been proved not to be *Borrelia burgdorferi* (Grund, Natterman & Horsch, 1995), are presumed to be the causing agents. Until now, there were only few histological examinations performed, with only orientating character (Dopfer, 1994). The pathogenesis of DD is still unclear. This evaluation has the intention to give a detailed description of pathological changes in the skin, a description of a possible pathogenesis with the aim of achieving methods of therapy and prophylaxis in the future.

Materials and Methods

Ten cattle, killed or having died from different organic diseases and showing skin-alterations in the plantar aspect of the claws, were autopsied and bacteriologically examined. Skin-samples from these animals and another 150 native tissue sections from skin lesions suspected of being altered by DD were fixed in 4% buffered formalin and embedded in hydroxyglycolmethacrylate (Kulzer® Technovit 8100). These 150 samples came from 49 farms utilizing various types of housing. The samples were cut into sections and stained with haematoxylin-eosin, PAS modified by pre-treatment with diastase for showing glycoproteins, lipids in membrane coating vesicles, intercellular cementing sub-

Adapted from the Proceedings, XIX World Buiatrics Congress, Edinburgh, Scotland; July 8-12, 1996.

stance and basal lamina. Giemsa stain was used to differentiate the inflammatory cells, Ladewig's fibrinstain to show thrombosis and differences in keratinization. Miller's elastica stain was used for detection of elastic and collagenous fibres and silver staining by Movat was used for more detailed performance of basal lamina.

Results

The diagnosis found by necropsy ranged from enteritis, bronchopneumonia, paratuberculosis, abscesses, glomerulonephritus, gut-infarction, peritonitis, endometritis, mastitis to parasitosis with all showing signs of septicaemia. In all cases, bacteriological examination revealed infection by Gram-negative bacteria known as "producing" endotoxins. The DD-lesions could macroscopically be classified into hyperplastic, ulcerative, proliferative and mixed forms.

Hyperplastic form

The epidermis shows slight to severe hypertrophy and hyperplasia (up to 20-fold) by developing rete ridge formations. Deep parts of the stratum basale show increased mitotic figures. There are signs of degeneration detectable as slightly swollen isoprismatic cells with enlarged nuclei. The loose chromatin possesses some small condensed clods besides the nucleolus resembling apoptotic bodies, sometimes compressed by nuclear oedema. Few cells show reticular degeneration's or dyskeratosis. There appears slight to moderate spongiosis with some spongiotic vesicles. Intracellular granules corresponding to the membrane coating vesicles (MCV) appear deceased, the PAS-reaction mostly fails, as in the intercellular substance of the keratinized cells. Some of the keratinocytes present fragmented tonofibrils. The number of keratohyalin granules decreases, accompanied by big intracellular basophilic vesicles. Suprapapillary keratinocytes often consist of a homogenous eosinophilic substance, also described as horn-like bodies. The horny layers are characterised by parakeratosis with reduced tissue continuity. The produced horn implies a lack of maturation. Some cases are slightly colonised by micro-organisms between the hornscales with some destruction of these cells. Different bacteria-types can be distinguished: long or short, thick rods and varying coccus types. There are no spirochetes detectable. The basal cells possess projections through the basement membrane in connection with elastic fibres and thus fixation in the connective tissue. This sometimes seems extended but not damaged, caused by a slight oedema in the dermis that is separating collagenous fibres. The dermal papillae show slight extravascular exudate with few lymphocytes and rare neutrophils. The capillaries contain only few red and white blood cells, but there are increased numbers of mast cells in the perivascular area. Slight infiltration appears around dermal blood vessels consisting of few lymphocytes, single macrophages, neutrophilic granulocytes and only scattered plasma cells. Perivascular mastcells are increased in number with rounded or triangular shape, filled with different amounts of granules. The endothelial cells exhibit large round to oval nuclei, increased cytoplasm, protruding into narrowed lumina. In medium-sized and greater arteries the arterial intima is afflicted by arterio-sclerosis-like plaques, with fragmentation of the lamina elastica interna and collagen-formation in the media. In some cases sludge phenomenon, fibrin-deposition and cellular agglutination on the endothelial cells is seen, leading to thrombosis with blood congestion. In walls of arterioles and small arteries, obstructed either by thrombosis or by greater plaques, there appears angiogenesis.

Ulcerative form of digital dermatitis

Adjacent to a hyperplastic skin area the horny layers are destructed by micro-organisms. Total loss of the stratum corneum leads to invasion of spirochetes into "living" layers of the stratum spinosum, using the intercellular space and destroying the embraced keratinocytes. This often is followed by ulceration of dermal papillae with emigration or erythrocytes, neutrophils and eosinophils into the epidermis, producing a crust together with cellular detritus, hornsquamas, plant-particles, dust and in great excess bacteria and spirochetes. This ulceration seems to spread up to total destruction of the epidermis and in some cases extending to the deepest layers of the stratum reticular of the dermis. In these cases granulation tissue is formed containing a lot of inflammatory cells and thrombus. The dermal reactions are more severe than in the hyperplastic form. The changes in the underlaying keratinocytes and dermal reactions are more severe compared with the hyperplastic form. Additionally there appear increased numbers of plasma cells, neutrophils and eosinophils in the perivascular infiltration and in the papillary vessels and connective tissue. Great arteries in deep parts of the dermis often are obstructed by thrombosis or plaques and show increased necrosis with increased angiogenesis. The collagenous fibres run in more curved bundles, with some swelling and few fragmentation's. The elastic fibres are shortened, curled and disorientated. In the skin, organs alterations are detectable that increase from hypertrophy of hair follicles and sebaceous glands to metaplastic keratinisation of the latter and degenerative processes in the hair root, up to total destruction of these appendages. This development seems strongly correlated with the hypertrophy and destruction of the epidermis, leading to prolonged hair growth followed by alopecia.

Proliferative form (hairy-wart-like lesions)

"Hairy" projections consist of dermal papillae, covered by 2-4 layers of basal and spinosal cells. Suprapapillary cells are not affected by microbial destruction, their horny layers are prolonged. The interpapillary spinosal cells are to a great extent destroyed by spirochetal invasion. Often the spirochetes reach the papillae, spread via capillaries or extravasal and clot together, but only few penetrate into subepidermal tissue. There appears only very low cellular immunoreaction in these vessels, macrophages and neutrophils with phagocytosed material are destroyed. The other signs of epidermal degeneration and dermal reactions are the same as described in the hyperplastic form.

All three forms of DD sometimes contain arteries affected by vasculitis in different stages. Some show intact neutrophils lying perivascular and in the vessel wall, others nuclear dust following leukocytoclasia. These changes can sometimes be seen in combination with sporadic plasma cell participation.

Discussion

The major problem with skin diseases are that multiple influences are combined with only few mechanisms of clinically tangible reactions. Therefore it is very important to perceive all pathological disturbances in the cutanous integument. Healthy skin is very resistant to bacterial infection because of the quality of keratinisation, production of intercellular substances containing glycolipids and proteins and of a marginal layer on the border of keratinisation. The latter two products are very resistant to a lot of detergents and reducing agents, even proteinases of micro-organisms (Matoltsy, 1975; Mulling 1993). Production of IL-1 and TNFα by epidermal cells is a further protective system. Epidermal cells are shown to possess receptors for IL-1, which makes them react as immunocompetent cells (Groves, Sherman, Mitzutani, Dower & Kupper, 1994). This implicates that in DD these protective systems are disturbed, underlined by the disorders in epidermal cell differentiation, missing glycolipids and proteins in the MCVs and the intercellular cement. Regarding the dermis, malperfusion of the adjacent tissues is the sequel of arteriosclerosis, activation of endothelial cells, thrombosis and the oedema in the connective tissue, resulting in total or partial ischaemia. Epidermal cells lack in supply of nutrients and growth factors. For example reduced epidermal growth factor leads to reduced lifetime and early terminal differentiation of keratinocytes *in vitro* (Rheinwald & Green, 1977). Hypercholesterolaemia or endotoxins induce arteriosclerotic lesions and activation of endothelial cells. The latter seem to be more important in cattle, often suffering of gram negative infectious diseases like mastitis, endometritis, pasteurellosis, retentio secundinarum and slight to severe disorders of the intestinum with endotoxaemia. Breider (1994) proved that lipopolysaccharides of Pasteurella haemolytica and *E. coli* induce secretion of inflammatory mediators by endothelial cells. These are Interleukin-1 and TNFα leading to activation of inflammatory reactors and initiating the coagulation cascade. Sequels are perivascular infiltration by lymphocytes and macrophages, disturbed permeability of endothelial cells with vascular oedema, endocytosis and transcytosis of lipoproteins followed by formation of arteriosclerotic plaques. Destruction of endothelial cells, basement membrane and increased incorporation of lipoproteins is followed by hyperplasia of basal lamina-like material formed by adjacent endothelial cells and smooth muscle cells (Simionescu, Sima, Dobrain, Tirziu & Simionescu, 1993). This exists likewise in DD as onion-like basal lamina-like material in the vessel walls leading to further narrowing of the vascular lumen. On the other hand, increased coagulation leads to thrombosis. The blood flow is reduced, but blood pressure of greater prestenosal arteries is increased. Circulating immunecomplexes may be trapped between endothelial cells and the basement membrane, leading to vasculitis because these antigens cannot be sufficiently eliminated. The sequel of the malformation of the epidermis is a predisposition for bacterial invasion: decreased maturation makes it possible for "presumable" Bacteroides-species to destroy the horny layers, whereas spirochetes profit by the loss of sufficiently produced intercellular substance. The various clinical forms of DD are results of different pathological mechanisms: partial ischaemia leads only to hyperplasia, total ischaemia to infarct with severe necrosis of the poststenosal tissues, with adjacent partial ischaemia caused by collateral blood flow. Furthermore the epidermal pictures are a sequel of epidermal proliferation-rate and the destruction by micro-organisms. It can be concluded that DD is a consequence of other organic diseases leading to a predisposition for secondary infection of the skin.

References

Breider, M.A., & Yang, Z. (1994). Tissue factor expression in bovine endothelial cells induced by *Pasteurella haemolytica* lipopolysaccharide and interleuken-1. Veterinary Pathology, 31 (1), 55-60. Dietz, O., Natterman, H., & Seibert, J. (1995). Zur Ätiologie der Dermatitis digitialis des Rindes. In P.F.Kenezevic (Ed.), Orthopädie bei Huf-und Klauentieren. 2. Internationaler Kongreß für Orthopädie bei Huf-und Klauentieren, Wien, 6-9. Oktober 1993, (pp. 171-175). Stuttgart, Germany: F.K. Schattauer Verlagsgesellschaft mbH. Döpfer, D. (1994). Epidemiological investigations of digital dermatitis on two dairy farms. Unpublished Inaugural-Dissertation, Tierärztliche Hochschule, Hannover, Ütrecht. Groves R. W., Sherman, L., Mitzutani, H., Dower, S.K., & Kupper, T.S. (1994). Detection of Interleukin-1 receptors in human epidermis. Introduction of the type II receptor after organ cul-

ture and in psoriasis. American Journal of Pathology, 145(5), 1048-1056. Grund, S., Natterman, H., & Horsch, F. (1995). Zum elektronenmikroskopischen Spirochäten-Nachweis bei der Dermatitis digitalis des Rindes. Journal of Veterinary Medicine, B, 42, 533-542. Matoltsy, A.G. (1975). Desmosomrs, filaments and keratohyaline granules: Their role in the stabilisation and keratinization of the dermis. J. Invest. Dermatol., 65, 127-142. Metzner, M., Döpfer, D., Pijl, R., & Kehler, W. (1995). Dermatitis digitalis des Rindes: klinisches Bild, Epidemiologie und Maßnahmen. Praktische Tierarzt, 76(collegium veterinarium XXV). 46-50. Mülling, C. (1993). Struktur, Verhornung und Hornqualitat in Ballen, Sohle ind weisser Linie der Rinderklaue und ihre Bedeutung fur Klauenerkrankup. Unpublished Inaugural-Dissertation, Freie Universitat, Berlin, Germany. Rheinwald, J.G., & Green, H. (1977). Epidermal growth factor and the multiplication of cultured human epidermal keratinocytes. Nature, 265, 421-424. Simionescu, N., Sima, A., Dobrian, A., Tirziu, D., & Simionescu M. (1993). Pathobiochemical changes of the arterial wall at the inception of atherosclerosis. In E. Vollmer & A. Roessner (eds.), Recent progress in atherosclerosis research, (Vol. 87, pp1-45): Springer-Verlag.

Abstract

Outbreak of fibrinous pneumonia in recently weaned beef calves in southern Queensland

LF Taylor

Aust Vet J (1998) 76: 21-24

Objective To describe an outbreak of fibrinous pneumonia in 331 recently weaned beef calves on two properties in the Miles district in southern Queensland.

Description of the herd The affected calves came from three groups: 88 recently weaned calves purchased at Casino NSW saleyards on 29 April 1994, 91 recently weaned calves purchased at Inverell NSW saleyards on 11 May 1994 and 152 homebred calves weaned on 18 May 1994 off the owner's cows. All calves were Hereford and Hereford cross.

Investigation The two groups of purchased calves (the Casino-Inverell weaners) were mixed together and moved to another recently purchased property on May 19 after handling on May 18. The homebred weaners were not mixed with the Casino-Inverell weaners, but had nose-to-nose contact for one night via a 3 m gateway while yarded on May 18. By May 25, an outbreak of acute undifferentiated bovine respiratory disease was evident among all 331 calves and two were dead. The morbidity risk in all three groups was 90%, suggesting the three groups of calves were equally susceptible. Five calves died during the outbreak, giving a crude mortality rate of 1.5% (5/331), with necropsy of three calves showing they died of fibrinous pneumonia. Treatment of all calves with a single injection of 20 mg/kg of long acting oxytetracycline lead to rapid clinical improvement in affected calves, and appeared to prevent further mortality. Mortality clustered, with three of the four dead purchased calves coming from one vendor of the Inverell sale.

Conclusions Fibrinous pneumonia can occur after weaning in beef calves in Australia. It is highly contagious among groups of recently weaned calves.

For Your Library

Building the Successful Veterinary Practice

Volume 3: Innovation & Creativity

Thomas E. Catanzaro

Publication Date: April 20, 1998

For Immediate Release

Fueled by innovation and creativity, the full potential of a veterinary practice can be realized. But the rigors of veterinary school leave most veterinarians with such talents suppressed and with diminished opportunity to achieve complete success.

Innovation and Creativity—volume 3 and the key to the series *Building the Successful Veterinary Practice*—can help every veterinarian to:

- Rediscover the delight of risk-taking and original thinking.
- Use these rediscovered talents to:

-achieve new ideas and approaches in veterinary care.

-integrate these ideas and approaches with leadership skills (volume 1) and specific plans and actions (volume 2) to start or improve any veterinary practice and realize its full potential for professional fulfillment and monetary reward.

Anecdotes, pithy quotations, commonsense advice, diagrams, and exercises to stimulate innovation and creative behavior (drawn from experience of the author or his clients; other respected professional consultants, writers, and speakers; and other notable individuals) mark this cornerstone to the *Building of the Successful Veterinary Practice* series and key to fulfillment for veterinary practitioners.

About the Author: *Thomas E. Catanzaro, DVM, MHA, FACHE, DiplACHE,* is founder and CEO of Catanzaro & Associates, Inc., a consulting firm dedicated to the business and team building of veterinary practices. He has taught leadership courses to veterinary practitioners throughout the United States and Canada for more than 16 years and has consulted for the past decade, visiting more than 1,200 veterinary facilities. He previously was hospital services director for the American Animal Hospital Association and is the first veterinarian to achieve board certification in the American College of Healthcare Executives (ACHE).

376 pp., 7 x 10, illus., paperback, ISBN 0-8138-2984-4, $34.95. Available through ISU Press. Price subject to change without notice. *Sixty-day examination copies available to U.S. instructors.* Complimentary copies available to reviewers. For more information contact Beverly Fisher, Publicity Coordinator, ext. 624. Visit our Web site at http://www.isupress.edu

Also available . .

Building the Successful Veterinary Practice, Volume 1: Leadership Tools. Provides a straightforward, step-by-step guide for turning any veterinary practice into an efficient, profitable business. *1997, 180 pp., 7 x 10, illus., paperback, ISBN 0-8138-2819-8, $24.95*

Building the Successful Veterinary Practice, Volume 2: Programs and Procedures. Shows how to apply specific applications of leadership skills and tools explained in volume 1 plus new programs and procedures. *1998, 372 pp., 7 x 10, illus., paperback, ISBN 0-8138-2399-4, $44.95*

Iowa State University Press
2121 S. State Avenue
Ames, Iowa 50014-8300

Orders: 1-800-862-6657
515/292-0155
Office: 515/292-0140
Fax: 515/292-3348

Buy the three volume set at the special price of $94.95

Abstracts

Brucellosis in adult beef cattle of Mexican origin shipped direct-to-slaughter into Texas

W. H. Brown and J. Hernández de Anda

J Am Vet Med Assoc (1998) 212: 705-707

Using serologic testing, results of this study indicate that prevalence estimates of brucellosis (BR) in adult beef cattle are significantly different among states and regions of Mexico. The overall prevalence estimate of BR in cattle of Mexican origin shipped direct-to-slaughter into Texas was 0.32%. The prevalence estimate of BR in cattle from the state of Chihuahua (0.10%) was significantly different from prevalence estimates in cattle from the states of Nuevo Leon (0.32%), Zacatecas (0.34%), Durango (0.47%), Chiapas (1.81%), Tamaulipas (2.71%), Aguascalientes (7.89%), and Campeche (12.24%). Furthermore, prevalence estimates of BR in cattle were significantly different among the northern (0.22%), south-central (3.18%), and south coastal (9.42%) regions of Mexico. Results of this study should make producers, veterinarians, and animal health authorities in border states aware of the continued need for collaboration and sharing of information to control and eradicate BR in the US-Mexico border region.

Preliminary observations on the pathogenesis of experimental bovine spongiform encephalopathy (BSE): an update

G. A. H. Wells, S. A. C. Hawkins, R. B. Green, A. R. Austin, I. Dexter, Y. I. Spencer, M. J. Chaplin, M. J. Stack, M. Dawson

Veterinary Record (1998) 142, 103-106

Further preliminary observations are reported of an experiment to examine the spread of infectivity and the occurrence of pathological changes in cattle exposed orally to infection with bovine spongiform encephalopathy. Calves were dosed at four months of age and clinically monitored groups were killed sequentially from two to 40 months after inoculation. Tissues were collected for bioassay, for histopathological examinations and for the detection of PrP. Previous reported observations have included the presence of infectivity in the distal ileum of cattle killed after six to 18 months, the earliest onset of clinical signs in an exposed animal after 35 months, and diagnostic histopathological changes in the brain, in association with clinical disease, after 36, 38 and 40 months. In spite of the relative inefficiency of the bioassay of scrapie-like agents across a species barrier the new observations confirm that the onset of clinical signs and pathological changes in the central nervous system (CNS) occur at approximately the same time. The earliest pathological change, the presence of abnormal PrP 32 months after inoculation, coincided with the earliest detected infectivity in the CNS and occurred shortly before there was evidence of typical spongiform changes in the brain 36 months after inoculation. Infectivity has now been demonstrated in the peripheral nervous system, in the cervical and thoracic dorsal root ganglia 32 to 40 months after inoculation and in the trigeminal ganglion 36 to 38 months after inoculation. At the time of writing evidence of infectivity in other tissues is confined to the distal ileum, not only after six to 18 months but also after 38 to 40 months, but these findings may be supplemented by the results of further mouse assays. Nevertheless, they are in general agreement with current knowledge of the pathogenesis of scrapie.