CASE REPORT

Equine Colitis "X", Still an Enigma?

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Summary

Colitis "X" is a sporadic diarrheal disease of horses with clinical signs of dehydration, electrolyte imbalances and "shock"-like features. Macroscopic and microscopic findings include signs of disseminated intravascular coagulation, necrosis of colonic mucosa and presence of large numbers of bacteria in the devitalized parts of the intestine. Recently published work suggests that the causative agent may be *Clostridium perfringens*, Type A, but the bacteria are recoverable only in the preliminary stages of the disease. Excess protein and lack of cellulose content in the diet is thought to be the trigger for the multiplication of the clostridial organisms. The pathological findings are pathognomonic, but clinically, a number of differential diagnoses have to be considered, such as intestinal accidents, salmonellosis, heavy metal intoxication and occlusive verminous arteritis.

Résumé

Est-ce que la colite "X" du cheval représente toujours une énigme?

La colite "X" est une maladie diarrhéique sporadique équine, qui se manifeste par des signes de déshydratation, de débalancement électrolytique et de choc. Les observations macroscopiques et microscopiques incluent de la coagulation intravasculaire disséminée, une nécrose de la muqueuse du côlon et la présence d'une flore bactérienne luxuriante, dans les parties dévitalisées de la muqueuse du côlon. Une publication récente mentionne *Clostridium perfringens* du type A comme agent étiologique possible, mais on ne peut l'isoler qu'au début de la maladie. Un excès de protéine et un manque de cellulose dans la diète seraient à l'origine de la multiplication des clostridies. Les lésions macroscopiques sont pathognomoniques mais, du point de vue clinique, le diagnostic différentiel doit tenir compte des conditions suivantes: accidents intestinaux, salmonellose, empoisonnement par les métaux lourds et artérite vermineuse occlusive.

Introduction

A sporadic, often peracute, foul-smelling and mostly fatal diarrheal disease of horses was already described in 1919 as "transport disease" (1) and was later referred to as colitis "X" (2), "exhaustion shock (3), "acute colitis syndrome" (4), "hemorrhagic edematous colon" (5), "post stress diarrhea" (6) and "equine intestinal clostridiosis" (7). The disease has been and continues to be a particular problem for the clinician, as proven by the occasional case reports (8, 9 and others, see 7).

The nonspecific clinical signs — sudden onset of the disease, profuse, watery diarrhea and rapidly developing signs of shock — require that a considerable number of differential diagnoses and therapeutic measures have to be considered. Confirmation of the diagnosis and exclusion of others rest frequently with the post-mortem examination.

The purpose of the paper is to review the pertinent literature and to describe the salient features using one randomly selected case from the records of the Department of Veterinary Pathology in Saskatoon as an example.

Case History

Clinical findings — A six year old female Quarter Horse was reported to have severe diarrhea for two days. The horse was treated with intravenous fluids, chloramphenicol and steroids. Clinical examination showed a severely depressed animal with only moderate dehydration. The animal died despite the treatment, and was submitted for necropsy with the tentative diagnosis of acute salmonellosis. Clinicopathological laboratory findings became available at the time of death. The following observations were made: PCV 68; leukopenia, about 4 000 WBC with relative increase of lymphocytes; blood pH 7.3 (acidemia); HCO_3 20 mmol/L; sodium 125 mmol/L; chloride 95 mmol/L; potassium 2.0 mmol/L; BUN 24 mg/dL; total protein 7.5 g/dL (elevated).

Gross necropsy findings — The animal was moderately dehydrated and had several circumscribed hematomas on the left rib cage (T2-4). The intestinal tract was filled with a foul smelling, watery content from the duodenum to the colon. Mild edema of the jejunal and ileal mucosa and submucosa was evident. The large colon, particularly the ventral colon, had an extreme degree of edema both in mucosa and submucosa; the mucosa was thickened, appeared necrotic and contained multiple hemorrhagic ulcers (Figure 1). The cecum and the small colon contained only watery ingesta and presented a few petechial hemorrhages, but no ulcers. Mesenteric lymph nodes appeared to be quite small. All other organs had no remarkable lesions, save for considerable congestion and edema in the left ventricle. There were no signs of an intestinal accident (volvulus and the like) and the aorta and the mesenteric arteries were free from parasitic tracts.

Histological findings — Myocardial scars were associated with arteriosclerosis of the coronary artery supplying this area. Multiple hyaline thrombi in

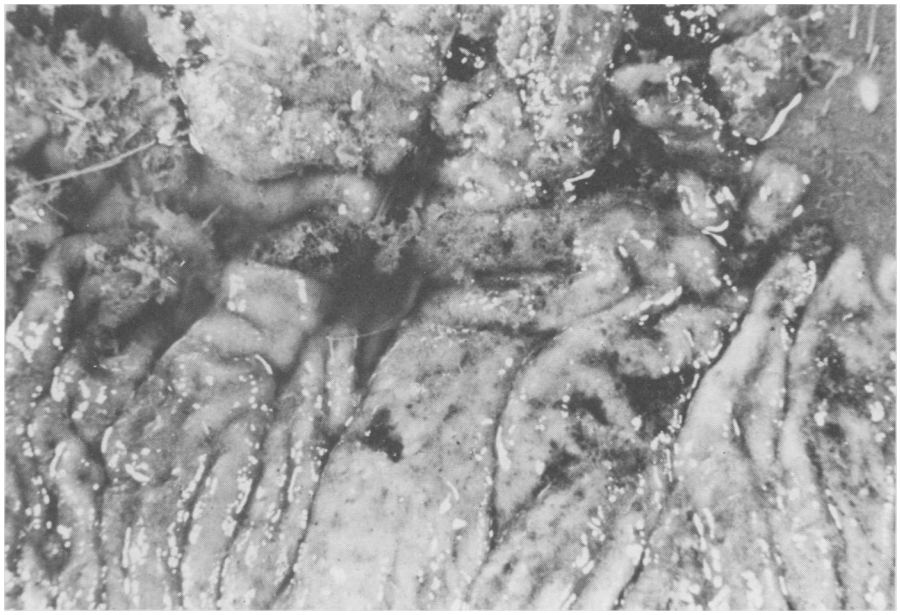

FIGURE 1. Necrosis and thickening of mucosa in the ventral colon with numerous smaller and larger ulcers.

lungs and kidney (Figure 2), suggestive of disseminated intravascular coagulation (DIC) were found in all smaller vessels. The liver had a mild mononuclear perivasculitis and pericholangitis. The mucosa of the jejunum was infiltrated by mononuclear cells and a few eosinophilic leukocytes; findings in the ileum were similar, but there were more eosinophils. The colonic mucosa was completely necrotic in some regions (Figure 3). In the area of the lamina propria and underneath, considerable accumulations of polymorphonuclear leukocytes (PMN were present and blood vessels contained hyaline thrombi (Figure 3). The submucosa showed cystic dilation of the interstitial tissue (Figure 3), with presence of pink-staining slightly fibrillar material located in the cysts. Many bacteria were seen in the mucosa (Figure 4), except for some clusters of Gram-positive streptococci on the surface. However, most bacteria were Gram-negative, and a silver stain (Warthin-Faulkner) revealed presence of numerous comma-shaped, slightly curved agents in the mucosa and in the submucosa (Figure 5).

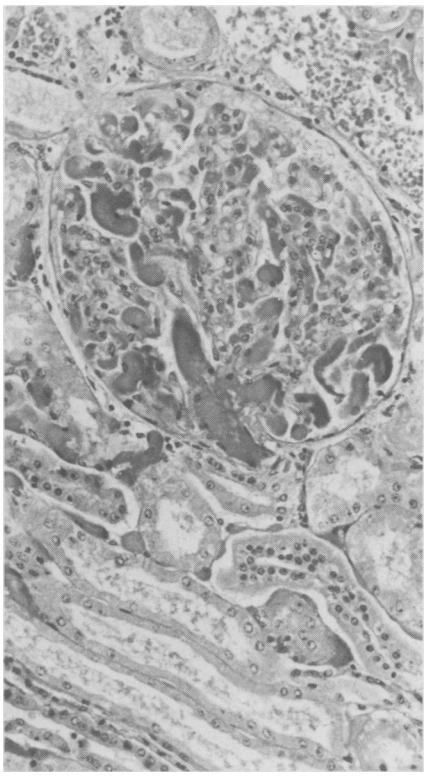

FIGURE 2. Hyaline thrombi, suggestive of disseminated intravascular coagulation in renal glomeruli. H & E. X160.

Bacteriological findings[1] — Large colon: 3+ nonhemolytic *E. coli*; 3+ *alpha*-strep; 2+ *gamma*-strep; small colon: 2+ nonhemolytic *E. coli*; 2+ *gamma*-strep; jejunum: 2+ nonhemolytic *E. coli*; 2+ *gamma*-strep; liver: few nonhemolytic *E. coli*, 1+ *gamma*-strep; salmonella not isolated.

On the basis of gross and histologi-

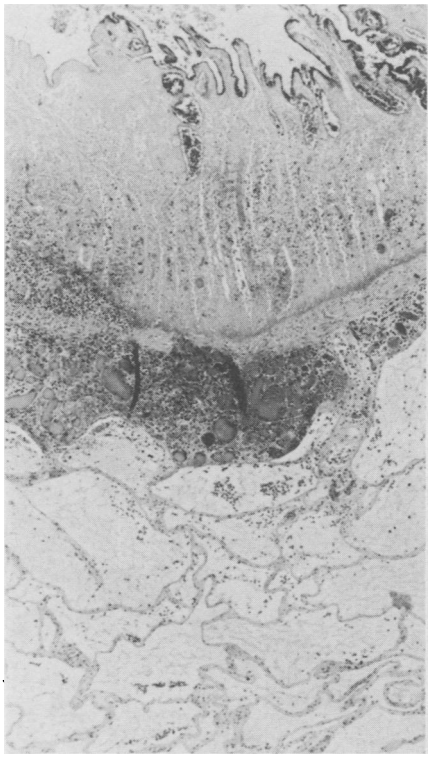

FIGURE 3. Necrosis of colonic mucosa, polymorphonuclear leukocytes and disseminated intravascular coagulation in lamina propria and submucosal edema. H & E. X25.

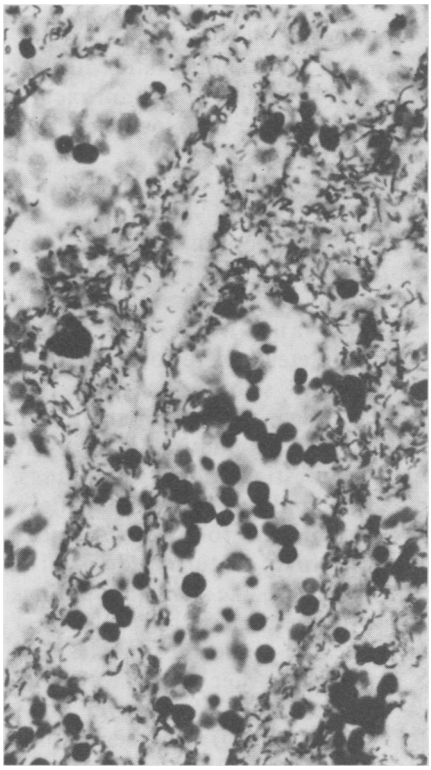

FIGURE 4. Comma-shaped bacteria in colonic mucosa. Warthin-Faulkner. X400.

[1]Courtesy of Diagnostic Laboratory, Department of Veterinary Microbiology, Western College of Veterinary Medicine.

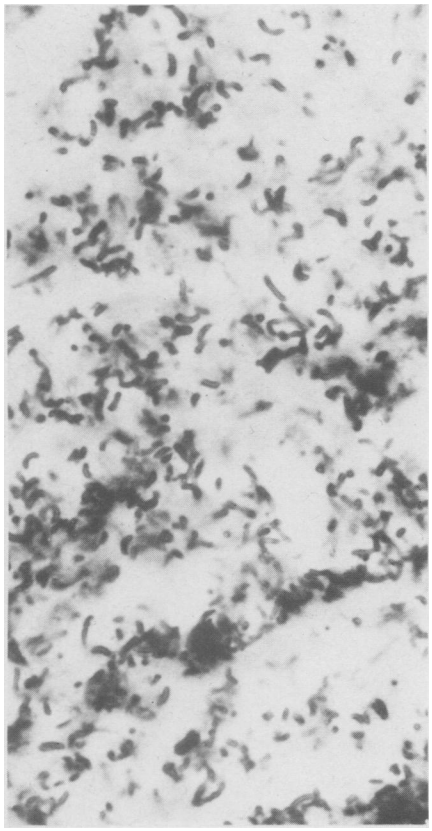

FIGURE 5. Bacteria in submucosal colonic tissue. Warthin-Faulkner. X1000.

cal findings, a diagnosis of colitis "X" was made. The immediate cause of death was thought to be endotoxemia and DIC, together with loss of electrolytes into the gut.

Discussion

The major lesions in the horse of this report were associated with the colon. Massive necrosis of the mucosa had occurred, and numerous Gram-negative bacteria were found both in mucosa and submucosa. Hyaline thrombi, suggestive of disseminated intravascular coagulation (DIC), were found in intestine, kidneys and lungs. All these findings point towards a primary enteritis followed by endotoxemia which, in turn, led to DIC. Thus, the shock-like signs and findings have to be regarded as the result rather than the cause of the intestinal lesions, as suggested earlier (3). Intraperitoneal application of *Aerobacter aerogenes* endotoxin (10) caused endotoxic shock in horses but no lesions in the large intestine. Similar observations were made after intravenous injection of *E. coli* lipopolysaccharide endotoxin (11).

The hypothesis that colitis "X" is a stress-shock related disease is further weakened by the fact that histories fail to give evidence of "stress" more often than not (12; personal observations). Probing into the history, one is frequently able to obtain evidence of sudden changes of diet, particularly diets rich in protein and low in cellulose content. In one incidence, 20 horses developed signs of colitis "X" and five animals died (personal observation) after feeding on mouldy silage. Such observations, and reports on occurrence of colitis "X" after oxytetracycline treatment (13, 14) suggest a disturbance of the normal intestinal flora as the primary event. It appears that the flora may have shifted towards a larger proportion of Gram-negative bacteria, thus allowing for liberation of large amounts of ecto- or endotoxins which may cause intravascular coagulation (15), and start the cascade of events that lead to rapid devitalization of the intestine, dehydration, loss of electrolytes and death.

Recent work (7) suggests that *Clostridium perfringens*, Type A, may play an important, if not the principal role, in colitis "X". Wierup (7) found high counts of *Cl. perfringens* (up to 10^7/g feces) in the initial stages of the disease. *Clostridium perfringens* was detected only in exceptional cases in the intestinal contents and feces of healthy horses, and then only in very low numbers (7) and this species of bacteria has been classified as belonging to the group of allochthonous (nonindigenous) microbes of the intestine (16).

Clostridium perfringens counts rise dramatically during the early stages of the disease in horses, but regress to normal levels within days (7). Thus, it is quite possible that one might not find any clostridia at the time of necropsy if the animal had been kept alive by energetic supportive treatment (fluids, electrolytes). Immunological investigations indicated that sick and experimental horses which were exposed to *Cl. perfringens* orally, were immunologically stimulated by the extracellular antigens (7). Not surprisingly, Wierup (7) proposed to use the name "equine intestinal clostridiosis" instead of colitis "X". Wierup's findings have been confirmed by another group of researchers (17) who were able to produce intestinal lesions similar to those of colitis "X" by a single, intravenous application of a crude extract of *Clostridium perfringens* A-toxin.

The failure to isolate or demonstrate *Clostridium perfringens* in many instances, like the one described in this paper, may be related to the fact that the isolation attempts were made too late. On the other hand, there is, at least hypothetically, the possibility that other Gram-negative bacteria and their ecto- or endotoxins may be responsible for the clinical and pathological lesions. Thus, it appears that the name, colitis "X", is probably the most valuable one at this time. The disease is a clearly defined entity, with pathognomonic lesions on necropsy. Any name that makes reference of particular etiology, assumed or thought to be proven, confuses the issue until it is unequivocally established that there is one only single etiological factor.

As far as differential diagnoses are concerned, the list to be considered is long. The similarity of colitis "X" symptomatology to occlusive verminous arteritis and acute salmonellosis is obvious. Both conditions can be excluded on necropsy, as is the case with other intestinal accidents (torsions, intussusceptions, etc.). Necrotizing colitis may be the result of heavy metal intoxications, thus a toxicological examination may be indicated in cases where there is a remote possibility of ingestion of mercury-treated grains or access to other heavy metals.

The treatment of colitis "X" has been reviewed (4,12) and consists chiefly of massive parenteral fluid therapy. In addition, large doses of corticosteroids are recommended (18) whereas the use of antimicrobials is controversial because they may exacerbate the condition (12).

It follows from the etiological considerations above, that a critical evaluation of feed is probably the most important aspect of the prevention of this disease. Further etiological studies, particularly in regard to the role of *Clostridium perfringens* and the composition of feeds (protein *vs* cellulose content), appear to be indicated.

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BOOK REVIEW

Canine Medicine and Therapeutics. Edited By E.A. Chandler, J.M. Evans, W.B. Singleton, F.G. Startup, J.B. Sutton and W.D. Travernor. Published by The C.V. Mosby Company, Linn, Missouri. 1979. 441 pages. Price $69.50.

This book is a multi-author, multi-editor effort having been written by 22 authors who were selected for their expertise in specific fields. An editorial board of past presidents and currently serving officers of the British Small Animal Veterinary Association has demanded and received consistent and high caliber material from the authors.

The book is aimed primarily at the practising veterinarian but final year veterinary students should find the book a valuable source of information.

The text is broken into 18 separate chapters covering all the body systems plus chapters on autoimmune diseases, specific infections, endoparasites, poisoning and behavioural problems. Many chapters have extensive reference and further reading lists while others do not; however, a comprehensive index allows rapid location of relative material on specific problems. Within each chapter the material is presented in a clear and concise way with disease entities handled under the headings of etiology, pathology, clinical signs, diagnosis and treatment. Drugs are given by their generic name and not by the British trade names. Good use has been made of diagnosis, photographs and charts but not to the point of making the text into a glossy picture book.

The use of multiple authors and critical editing has resulted in a text that is up to date, to the point and easy to read but at the same time presenting enough in-depth material to help keep the busy practitioner and senior veterinary student abreast of the latest in canine medicine. *A.G. Binnington.*