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Clostridium Associated Necrotizing Hepatitis with Multiple Organ Lesions in a Dog

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Abstract

Clostridium-associated necrotizing hepatitis with multiple organ lesions is a rare and severe condition in dogs. *Clostridium* species, anaerobic bacteria commonly found in the environment, can lead to various infectious diseases in animals. Among these, *Clostridium novyi* type B has been identified as a causative agent of necrotizing hepatitis. This case study presents a 4.5-year-old spayed female Golden Retriever with acute-onset lethargy, decreased appetite, and vomiting. Post-mortem examination revealed liver lesions consistent with *Clostridium*-associated necrotizing hepatitis and significant pathology in the kidneys, heart, and spleen, indicating multi-organ involvement. Histopathological examination further supported the diagnosis, highlighting panlobular hepatocytic necrosis, endospore forming bacilli, and toxin-related damage. While the pathophysiology underlying this condition remains incompletely understood, it is hypothesized that bacterial endospores reach the liver *via* the portal circulation, where they germinate and release toxins. The toxins impact endothelial cells, hepatocytes and other organs causing cellular detachment, necrosis and fluid leakage. Furthermore, systemic dissemination of bacteria may play a crucial role in this process. Bacterial endospores might disseminate through the bloodstream, reaching distant organs, including the kidneys, lungs, heart, and spleen, leading to multi-organ involvement. This case underscores the rarity and complexity of *Clostridium*-associated necrotizing hepatitis in dogs, especially with multi-organ involvement, and highlights the need for comprehensive understanding and further research in this area.

Keywords: *Clostridium* • Necrotizing hepatitis • Multi-organ involvement • Dog • Toxin-related damage

Introduction

Clostridium species are a diverse group of bacteria belonging to the phylum *Firmicutes*. These bacteria are anaerobic, meaning they thrive in environments devoid of oxygen. *Clostridium* species are known for their ability to form endospores, which are resistant structures that allow them to survive harsh conditions. The most common types of *Clostridium* spp. are *Clostridium perfringens*, *Clostridium tetani*, *Clostridium botulinum*, *Clostridium piliforme*, *Clostridium chauvoei*, *Clostridium novyi*, *Clostridium septicum* and *Clostridium difficile*. *Clostridium novyi* (*C. novyi*) is a gram-positive, endospore forming; obligate anaerobic microorganism that is found in soil and feces and is pathogenic to human and animals [1]. There are 4 subtypes (type A-D) of *C. novyi* [2]. *C. novyi* type A causes gas gangrene in man and animals and *C. novyi* type B frequently causes infectious necrotic hepatitis in sheep [2]. *Clostridium haemolyticum* is the causal organism of bacillary haemoglobinuria in cattle [3].

Clostridium-associated necrotizing hepatitis is a rare yet highly severe condition in veterinary medicine, known for its rapid progression and potential life-threatening consequences. *Clostridium* species, anaerobic bacteria commonly found in the environment, are responsible for causing a wide range of infectious diseases in both animals and humans. Among these species, *Clostridium novyi*, particularly *Clostridium novyi* type B, has been identified as a causative agent of hepatic involvement, leading to necrotizing hepatitis. Other species, such as *Clostridium piliforme* and *Clostridium perfringens*, have also been associated with liver pathology in small animals [4].

The pathophysiological mechanisms underlying *Clostridium*-associated necrotizing hepatitis in dogs remain to be fully elucidated. However, an established hypothesis suggests that bacterial endospores in the environment are ingested and reach the liver through the portal circulation. Within the liver, these endospores lay dormant in macrophages until a favorable anaerobic environment develops. This process is commonly associated with the migration of liver flukes in ruminants [5]. Once in the anaerobic environment, the endospores germinate and proliferate, releasing toxins such as alpha toxin and beta toxin. The alpha toxin acts on the actin filament of the cytoskeleton within endothelial cells and the surrounding hepatocytes, leading to cellular detachment, cell death, and leakage of fluid from the damaged endothelial cells [6]. While the Clostridial organism also produces low levels of beta toxin which causes hemolysis and hepatic necrosis, its role in the pathogenesis of *Clostridium novyi* type B is considered minimal [6].

Infectious Necrotic Hepatitis (INH) caused by *Clostridium novyi* type B is well documented in sheep, where it is commonly referred to as "black disease" due to the dark discoloration of subcutaneous tissue caused by intense venous congestion observed in affected animals [7]. Although there are indications that INH may also affect other species, such as cattle, goats, and horses, limited information is available about this disease in non-ovine animals [5].

Despite speculation regarding the potential occurrence of INH in diverse species, including cattle, goats, horses, and dogs, it is crucial to acknowledge that comprehensive information concerning this condition in non-ovine animals remains profoundly scarce and fragmented. Particularly in dogs, the occurrence of this condition is exceedingly rare, with very few cases reported in the veterinary literature [8].

In this case study, we present a unique and critical case of a 4.5-year-old spayed female Golden Retriever, who exhibited acute-onset lethargy, decreased appetite, and episodes of vomiting. The patient's medical history, gross lesions, and histopathological examination raised suspicion of *Clostridium*-associated necrotizing hepatitis, particularly with the presence of *Clostridium* spore involvement of *Clostridium novyi* type B. Notably, the post-mortem examination revealed not only liver lesions but also significant

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pathology in the kidneys, heart, lungs and spleen, indicating multi-organ involvement. The rarity of *Clostridium*-associated necrotizing hepatitis in dogs, combined with the occurrence of multiple organ lesions in this particular case, underscores the uniqueness and complexity of this clinical presentation.

Case Presentation

A 4.5-year-old female Golden Retriever that has been spayed was brought to the NPI Veterinary Teaching Hospital because of sudden and severe lethargy, loss of appetite, and vomiting. The dog had been vomiting leaves and foam for a couple of days before coming to the hospital, but the vomiting stopped on its own. However, the dog still didn't eat properly after the vomiting episodes. On the day of presentation, the dog seemed active in the morning but became increasingly tired and lethargic as the day went on. Eventually, the dog became very weak and uncomfortable.

During the physical examination at the veterinary hospital, the Golden Retriever appeared severely weak and unresponsive, requiring immediate medical attention. The dog's body temperature was lower than normal, indicating a significant decrease in metabolic activity, possibly due to severe illness and circulatory problems.

The examination of the dog's cardiovascular system revealed a weak and difficult-to-detect heartbeat, suggesting severe cardiovascular issues and the possibility of circulatory collapse.

The dog's mucous membranes showed signs of severe anemia. The gums were pale, and the Capillary Refill Time (CRT) was almost non-existent, indicating that the blood wasn't properly perfusing the peripheral tissues. The eyes also showed signs of anemia, with pale conjunctiva and barely visible blood vessels, suggesting reduced oxygen-carrying capacity in the blood.

We faced challenges in finding accessible veins to insert an intravenous catheter. Both the saphenous and cephalic veins were difficult to locate, making it hard to administer essential fluids and medications to stabilize the patient. As the situation worsened, the dog eventually collapsed.

Necropsy findings

Following the dog's demise, a post-mortem examination was conducted, and significant gross lesions were identified (Figures 1-4). The accumulation of blood in the abdominal cavity (Hemoperitoneum) was evident (Figure 1), indicating internal bleeding within the abdomen. Additionally, a hepatic lymph node in the liver displayed signs of hemorrhage. The liver showed enhanced reticulation, with a net-like pattern being more pronounced (Figure 2). The liver's texture was firm, and its surface exhibited alternating white striations and darker areas. The kidney's surface appeared undulating or wavy, and at the anterior pole, there was a notable white depressed scar measuring approximately 3-4 cm (Figure 3). The kidney's texture was observed to be firm and hard. Furthermore, a splenic rupture was identified during the examination (Figure 4).

On histopathological examination, the following findings were observed:

Liver: There was evidence of mononuclear infiltration and fibrosis around the central vein, extending from one central vein to another (Figure 5). The sinusoids around the central vein appeared dilated and distended, accompanied by hepatocyte atrophy. However, the sinusoids around the periportal area showed moderate dilation, and the hepatocytes displayed severe hydropic degeneration (Figure 6). Similarly, there was severe accumulation of inflammatory cells in and around the periportal area, indicative of cholengiohepatitis (Figure 7).

Additionally, massive hepatocytic necrosis and inflammation were observed throughout the liver parenchyma, indicating panlobular involvement. Furthermore, necrotizing hepatocytes with intralesional endospore-forming bacilli (Figure 8) were identified.

Kidney: The kidney showed evidence of massive tubular necrosis, with most of the tubule basement membrane remaining intact (Figure 9). There

Figure 1. Hemoperitoneum.

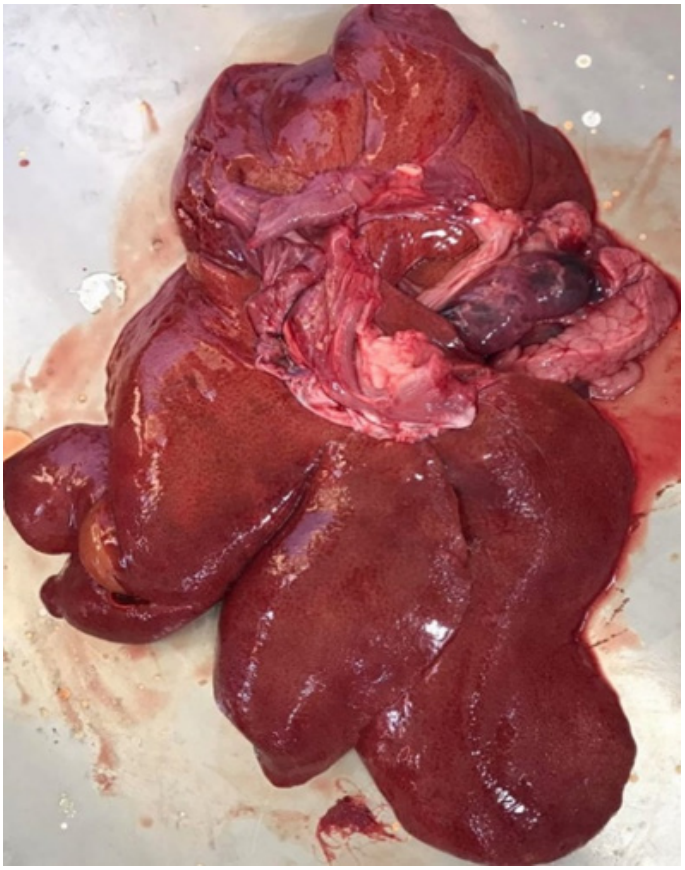

Figure 2. Enhanced reticulation (Liver).

was interstitial nephritis. Additionally, some glomeruli exhibited moderate thickening of the Bowman's capsule, a structure that surrounds the glomerulus.

Furthermore, severe interstitial nephritis and fibrosis (Figure 10) were observed, indicating inflammation and scarring in the spaces between the kidney tubules. Proteinaceous material deposition in the Bowman's capsule (Figure 11) was also noted, suggesting abnormal accumulation of protein in this part of the kidney.

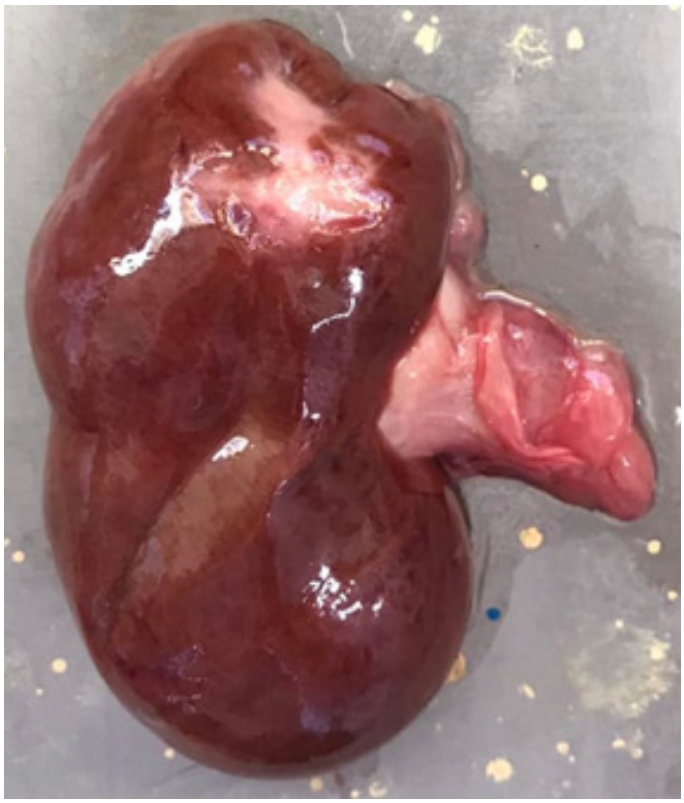

Figure 3. Kidney with undulating surface.

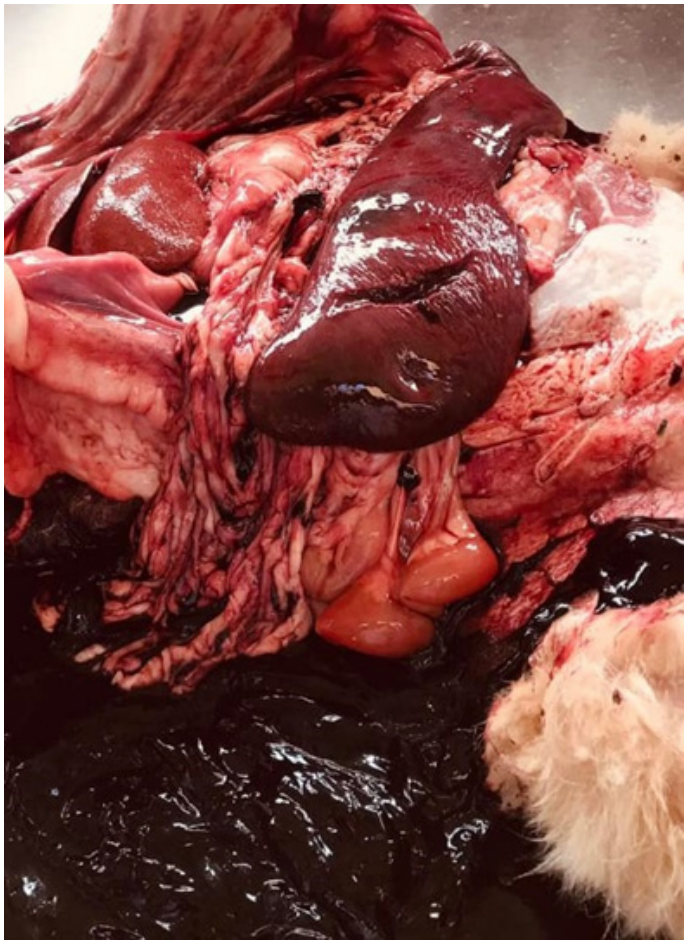

Figure 4. Spleenic rupture.

Atrophy of glomerular ducts was observed in a few glomeruli, along with necrosis of the Bowman's capsule wall (Figure 12). Moreover, glomerulus

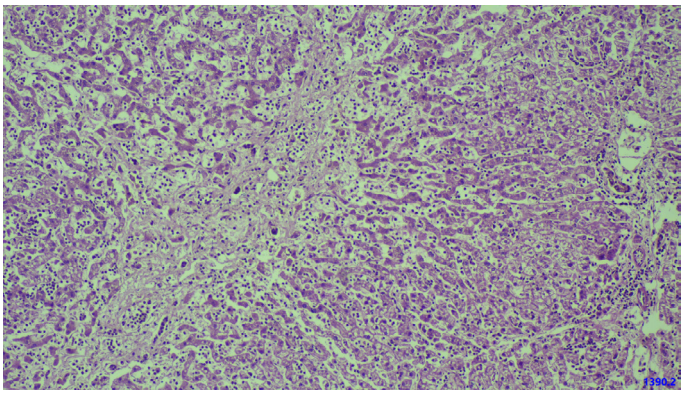

Figure 5. Liver- Mononuclear infiltration and fibrosis around central vein (10X).

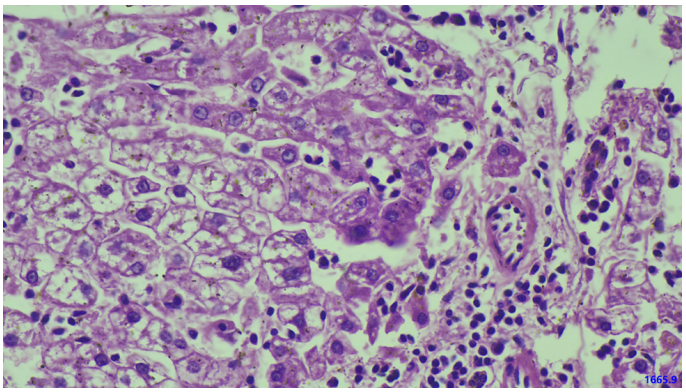

Figure 6. Liver - Hydropic degeneration in hepatocyte around periportal area (40X).

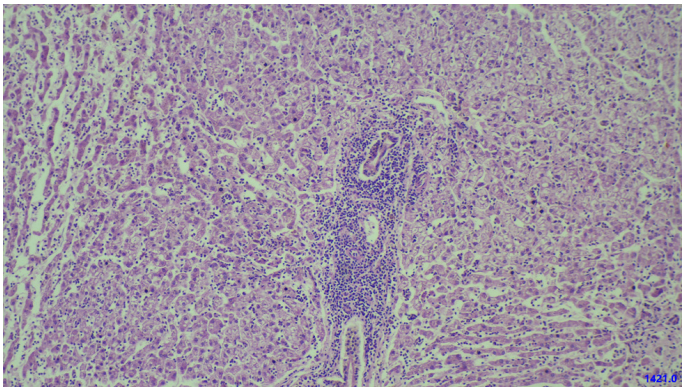

Figure 7. Liver - Cholangiohepatitis (10X).

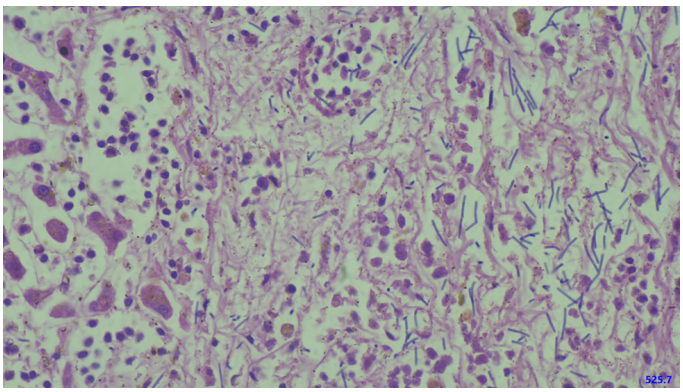

Figure 8. Liver - Iintralesional endospore forming bacilli (40X).

necrosis (Figure 13), involving damage to the functional units of the kidney responsible for filtration, and necrosis of the Bowman's capsule wall were evident, further corroborating the severity of kidney involvement.

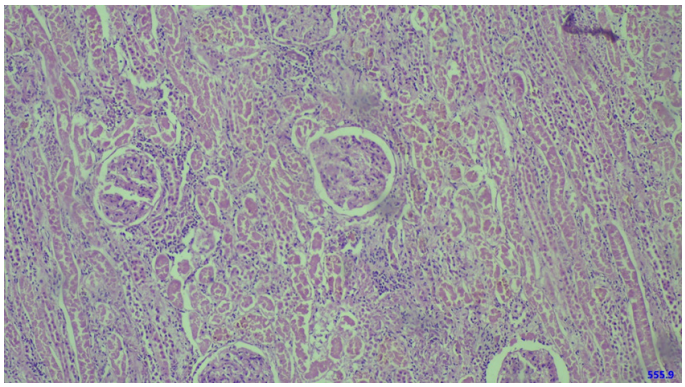

Figure 9. Kidney - Tubular necrosis but basement membrane intact (10X).

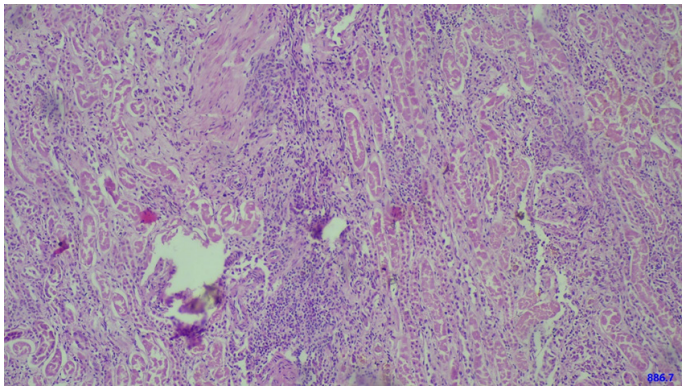

Figure 10. Kidney - Severe interstitial nephritis and fibrosis (10X).

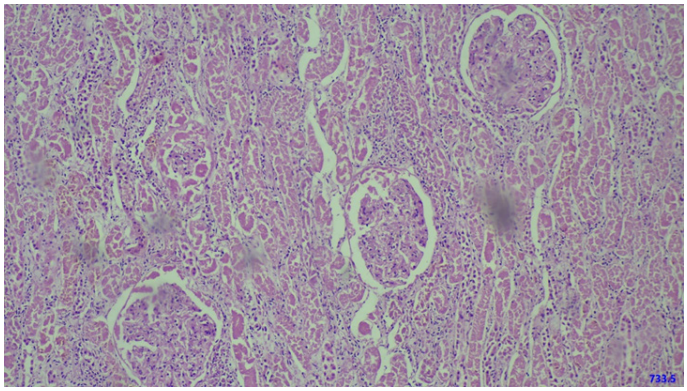

Figure 11. Kidney - Protenious meterial in bowmens capsule (10X).

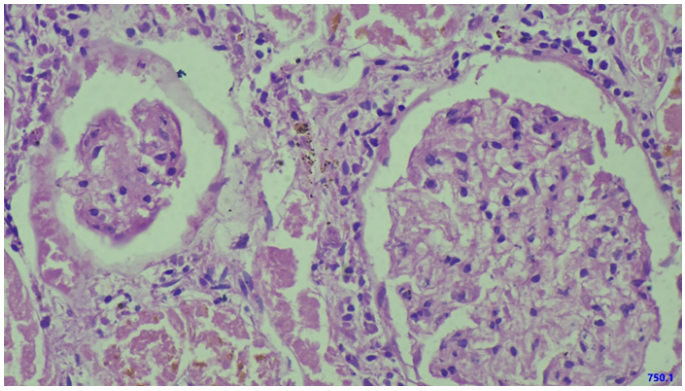

Figure 12. Kidney - Necrosis of bowmens capsular wall (40X).

Heart: The heart showed epicardial inflammation (Figure 14), along with mild myocarditis and edema (Figure 15).

Spleen: The spleen exhibited edema and signs of spleenitis and necrosis (Figure 16). Hemosiderosis (Figure 17) was also observed.

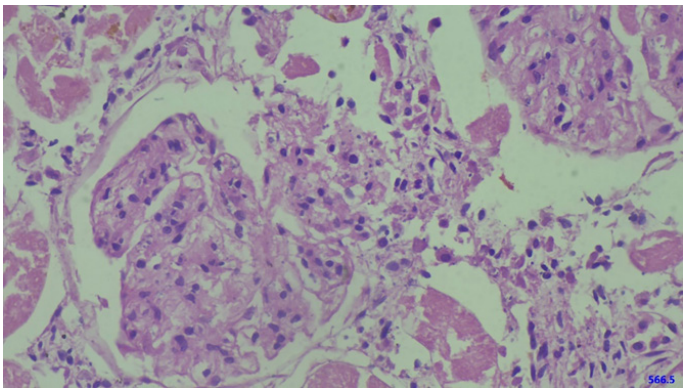

Figure 13. Kidney - Glomerulus necrosis (40X).

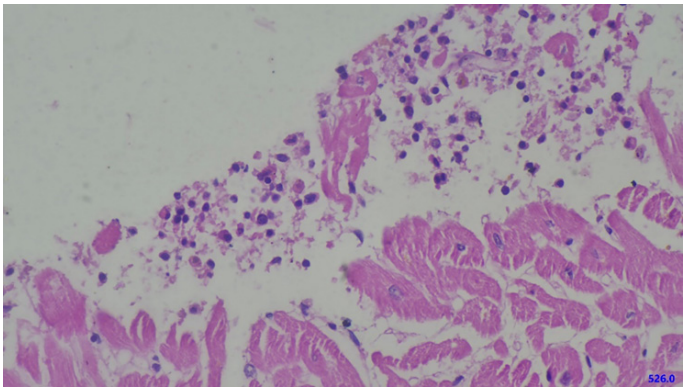

Figure 14. Epicardial inflammation (40X).

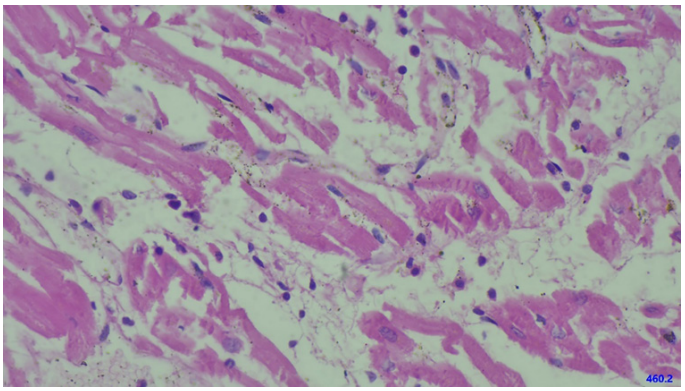

Figure 15. Heart - mild myocarditis and edema (40X).

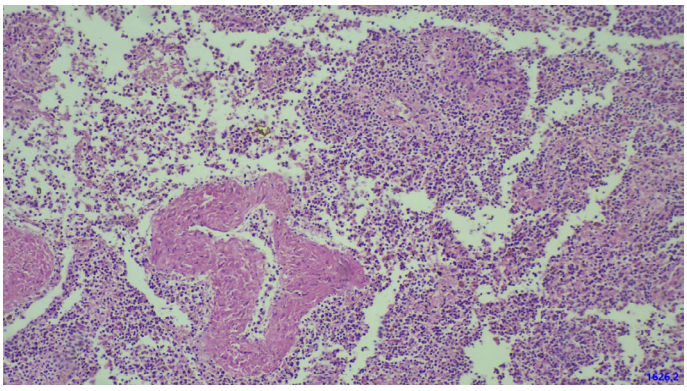

Figure 16. Spleenitis and necrosis.

Lungs: The lung tissue exhibited homogeneous pinkish edematous fluid accumulation in the alveoli, indicating pulmonary edema. There was mild mononuclear cell infiltration, suggesting the presence of inflammatory cells in the lung tissue. The interalveolar septa, the walls separating adjacent

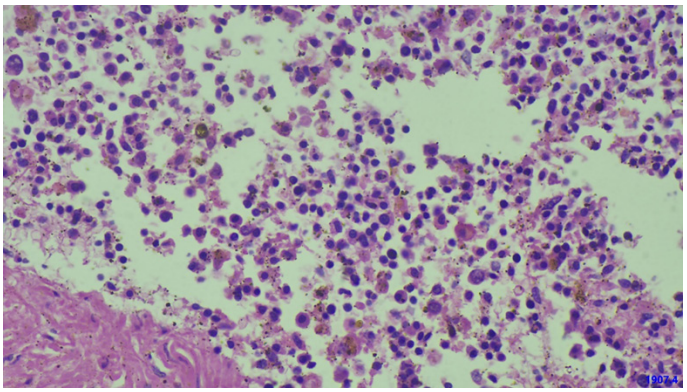

Figure 17. Spleen - Hemosiderosis (40X).

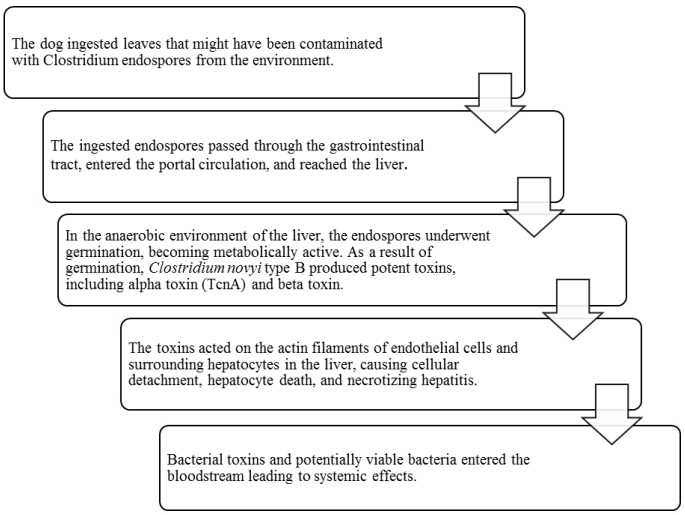

Figure 18. Hypothetical flowchart.

alveoli, appeared congested and distended, likely due to fluid accumulation. Additionally, necrotic bronchus walls were observed, suggestive of bronchiectasis, a condition characterized by the abnormal dilation of the bronchial tubes. Moreover, peribronchial fibrosis and inflammation were evident, indicating scarring and inflammation around the bronchial tubes.

The lung tissue showed accumulation of inflammatory cells within the alveoli, indicating bronchopneumonia, an inflammatory condition affecting the air sacs of the lungs.

The findings from both gross lesions and histopathological slides pointed towards a severe and widespread infection, with characteristic features consistent with *Clostridium*-associated necrotizing hepatitis and multi-organ involvement. The histopathological examination revealed panlobular hepatocytic necrosis and intralesional endospore-forming bacilli, further supporting the diagnosis of *Clostridium* spp. infection, possible *Clostridium novyi* type B associated necrotizing hepatitis as the underlying cause of this critical case (Figure 18).

Discussion

While we have made a presumptive diagnosis based on the patient's medical history, gross lesions, and histopathological examination, it is important to acknowledge that definitive confirmation through PCR or molecular analysis was not conducted. Despite this limitation, the histopathological findings, coupled with the gross lesions, strongly suggest *Clostridium*-associated necrotizing hepatitis with multiple organ lesions, possibly *Clostridium novyi* type B involvement.

The pathophysiology underlying this rare condition in dogs is not fully understood, and the multi-organ involvement observed in this case further adds complexity to the clinical scenario. However, we can hypothesize the possible mechanisms by which the *Clostridium novyi* type B bacterium may have contributed to the development of the observed lesions.

Clostridium species, anaerobic bacteria commonly found in the environment, produce endospores that can remain dormant until they reach a favorable anaerobic environment, such as the liver. In the scenario of this case, ingestion of potentially contaminated seeds initiated the chain of events. The ingested *Clostridium* endospores traversed the gastrointestinal tract, gaining access to the portal circulation, and subsequently arriving at the liver. The most commonly described lesion associated with *Clostridium novyi* type B is secondary to migration of the liver fluke Fasciola hepatica, which causes local hepatic necrosis and damage, thus establishing an anerobic microenvironment [6]. However, metabolic derangements associated with lipid accumulation in hepatocytes, abscessation, and toxin exposure can also incite anaerobic conditions [9]. Within the anaerobic environment of the liver, the endospores underwent germination, transitioning to a metabolically active state. This germination process triggered the production of potent toxins, notably alpha toxin, accompanied by low levels of beta toxin. These toxins impacted the liver, where alpha toxin targeted endothelial cells and surrounding hepatocytes, leading to cellular detachment, hepatocyte demise, and necrotizing hepatitis.

Moreover, the toxins (alpha and beta) were released into the bloodstream, potentially accompanied by viable bacteria, thereby inducing systemic effects. These systemic consequences affected various organs. The kidneys experienced tubular necrosis, interstitial inflammation, and glomerular pathology. Similarly, the heart was influenced by toxins and/or bacterial dissemination, giving rise to epicardial inflammation and mild myocarditis. Furthermore, the spleen affected by systemic toxin dissemination, exhibited signs of edema, spleenitis, and necrosis.

Upon histopathological examination, the liver displayed various pathological lesions. The presence of mononuclear infiltration and fibrosis encircling the central vein, extending from one central vein to another, was indicative of significant hepatic alterations induced by the infection. This pattern of fibrosis and inflammation as highlighted by research of Niza MMRE, et al. [10] can be understood as a response to the presence of bacterial toxins and their effects on the surrounding tissue.

Similarly, extensive hepatocytic necrosis and inflammation were evident throughout the liver parenchyma, indicating the wide-reaching effects of the infection. The presence of necrotizing hepatocytes with intralesional endospore-forming bacilli underscored the direct impact of the bacterial infection on hepatocytes. Research by Jeong CG, et al. [11] indicate these bacilli are likely *Clostridium* endospores that had germinated within the liver's anaerobic environment, contributing to the production of toxins that led to hepatocyte death and subsequent necrosis.

Similarly, at kidney, with the potential for endospores and toxins to reach the kidneys through the bloodstream, glomeruli and tubular capillaries may have entrapped circulating endospores, fostering localized infection. The toxins, primarily alpha toxin (TcnA) and beta toxin, could have inflicted damage on endothelial cells lining blood vessels and renal tubular epithelial cells.

Consequently, the renal vasculature's integrity might have suffered due to increased vascular permeability, enabling fluid and inflammatory cells to escape into the surrounding interstitial spaces. It is consistent with the findings of Dezana E, et al. [12] which emphasizes that defects in endothelial permeability can lead to edema and an increase in interstitial pressure, which in turn induces compression and altered tissue perfusion.

Direct harm to renal tubular cells by the toxins could have led to tubular necrosis, triggering severe interstitial nephritis and fibrosis. The article "Fatal *Clostridium novyi* Type B Infection in a Sow" by Akayama N, et al. [13] highlights the presence of mild focal necrotic lesions in kidney. Notably, deposition of proteinaceous material in Bowman's capsule signified compromised filtration and kidney function. Atrophy of glomerular ducts and necrosis of Bowman's capsule walls pointed toward substantial damage to glomerular structural integrity, essential for proper filtration.

Moving to the spleen, its involvement in disseminated infection became apparent. Similar to other affected organs, endospores and toxins could have reached the spleen through the bloodstream, specifically *via* the splenic circulation. Pathogenic bacteria use the bloodstream as a highway for getting around the body, and thus have to find ways to enter and exit through the endothelium. Many bacteria approach this problem by producing toxins that can breach the endothelial barrier through diverse creative mechanisms, including directly killing endothelial cells (ECs), weakening the cytoskeleton within ECs, and breaking the junctions between ECs [14]. Endothelial cells lining spleen blood vessels may have suffered damage due to the toxins, increasing vascular permeability, causing edema, and promoting hemorrhage within the spleen. Necrosis could have further compromised the spleen's immune function, given its role as an essential immune organ. The presence of edema, splenitis, and necrosis substantiated the spleen's involvement, with hemosiderosis potentially resulting from toxin-induced hemolysis. Notably, *C. novyi* type B produces the necrotizing and hemolytic beta toxin [9], which may have contributed to the hemolysis in the spleen.

Moreover, the spleen's dysfunction could have repercussions on the dog's immune response and overall health, considering the organ's responsibility for filtering blood, eliminating damaged cells, pathogens, and other particles.

In the heart, even though the primary site of infection is likely the liver, *Clostridium* endospores' dissemination to other organs, including the heart, is conceivable *via* the bloodstream. The circulation could have carried endospores from the infected liver throughout the body, leading to localized infection upon entrapment in heart capillaries and small blood vessels. This scenario gains particular significance considering recent case study by Ma M, et al. [15], who documented a case of fatal myocarditis caused by *Clostridium novyi* type B in humans. In the heart, the toxins, notably alpha toxin (TcnA) and beta toxin, could have inflicted damage on endothelial cells lining blood vessels and cardiomyocytes.

The consequences could involve increased vascular permeability, allowing fluid leakage into the surrounding tissues, along with myocardial inflammation and necrosis. Additionally, beta toxin's hemolytic activity might have contributed to further heart tissue damage. The combined effect of toxin-induced vascular damage and myocardial inflammation could have compromised cardiac function, resulting in weakness, lethargy, and potential cardiovascular compromise.

Similarly, in the lungs, endospores and toxins could have reached the pulmonary capillaries through the bloodstream, given the circulation's connection between the heart and lungs. Upon entering the lungs, the toxins might have inflicted damage on endothelial cells lining pulmonary blood vessels, resulting in increased vascular permeability and fluid leakage into lung tissue.

Consequently, fluid accumulation in alveoli and interalveolar septa could have led to pulmonary edema, hindering normal gas exchange and causing respiratory distress [16]. Moreover, the toxins' presence in lung tissue could have triggered an inflammatory response characterized by mild mononuclear cell infiltration.

Lucas R, et al. [16] discussed the pivotal role of bacterial toxins in lung disease pathogenesis. These toxins target cellular signaling pathways, impacting alveolar fluid clearance, barrier function, and host defense mechanisms. The resulting compromise in alveolar-capillary barrier integrity may lead to conditions such as Acute Lung Injury (ALI), Acute Respiratory Syndrome (ARDS), and severe pneumonia.

Transitioning to the gross lesions observed during the post-mortem examination, various abnormalities were observed. The rupture of the spleen, a notable finding, appears to interconnect with the profound necrotizing hepatitis attributed to the presence of *Clostridium novyi* type B. *C. novyi* type B alpha toxin causes necrotizing hepatitis and extensive edema, congestion, and hemorrhage in multiple organs [17]. As the bacterial toxins and inflammatory response spread systemically, they can lead to vascular damage and compromise the integrity of blood vessels in various organs, including the spleen.

The extensive necrosis and inflammation observed in the liver and other organs could have contributed to the increased pressure within the circulatory system. The compromised blood vessels in the spleen may have been unable to withstand the pressure, leading to rupture and subsequent internal bleeding.

Additionally, the spleen itself might have been a target of bacterial toxins, further weakening its structure and making it more susceptible to rupture. The ruptured spleen could have resulted in the release of blood into the abdominal cavity (hemoperitoneum), contributing to the dog's critical condition and eventual collapse.

Similarly, the observation of a hemorrhagic hepatic lymph node suggests the involvement of the lymphatic system in the infection. The spread of bacterial toxins and inflammatory mediators might have affected the lymph nodes, leading to hemorrhage.

Likewise, the liver's enhanced reticulation with a net-like pattern suggests extensive fibrosis and scarring in the liver parenchyma. This fibrosis could be a result of the ongoing inflammation and necrosis caused by the bacterial infection. Additionally, the liver's firm texture and alternating white striations on the surface indicate areas of necrosis and fibrosis. The irregular texture is likely due to the presence of necrotic and scarred tissue.

Moving to the exploration of why the observed symptoms manifested, the sudden and pronounced lethargy displayed by the dog upon presentation can be attributed to the rapid and aggressive progression of the disease. The distinct nature of *Clostridium*-associated necrotizing hepatitis, known for its virulent course, aligns with the swift deterioration witnessed in this case. The release of potent bacterial toxins, prominently from *Clostridium novyi* type B, carries the potential to inflict severe harm upon the liver and various other organs. As the infection advances, these toxins unleash a cascade of tissue damage, culminating in cellular detachment and the seepage of fluid from compromised cells.

The liver's role as a pivotal hub for numerous metabolic processes underscores its significance in maintaining overall physiological equilibrium. The notable and swift hepatocytic necrosis and inflammation within the liver disrupt its customary functions, triggering imbalances in the body's metabolic dynamics and the liberation of detrimental byproducts into the bloodstream. This compromised liver function detrimentally affects the body's capacity to efficiently clear waste materials and toxins, instigating a series of systemic repercussions.

The cumulative effect of these disturbances culminated in the dog's pronounced lethargy and weakness, observed on the day of presentation. The scope of metabolic disturbances and electrolyte imbalances experienced by the dog could have been profound, amplified by compromised organ functions. The intricate interplay between the liver and various organ systems underscores the severity of the dog's condition.

Furthermore, the implication of other vital organs, including the kidneys, lungs, heart, and spleen, accentuates the systemic nature of the infection. The extensive dissemination of bacterial toxins or the presence of inflammatory mediators throughout the body magnifies the swift deterioration of the dog's health. This comprehensive involvement reinforces the notion that the dog's abrupt onset of symptoms stems from the rapid and widespread effects of the *Clostridium novyi* type B infection.

Despite all of these, it is essential to acknowledge the possibility of co-infections or other etiological agents. Parasitic infections were considered, but no evidence of such parasites was observed in the histopathological examination. Similarly, viral infections were ruled out based on the lack of characteristic viral inclusions or other viral pathology.

The selection of *Clostridium novyi* type B as the likely pathogenic agent in this case stems from its unique and well-documented association with necrotizing hepatitis and multi-organ involvement. While other species of *Clostridium* certainly possess pathogenic potential, each species possesses distinct attributes that determine their specific effects on the host. *Clostridium novyi* type B, however, is known for its ability to trigger rapid and extensive hepatocellular destruction, a phenomenon that aligns closely with the

observed gross and histopathological findings in the liver and other organs of the presented case. The alpha toxin produced by *Clostridium novyi* type B is a potent virulence factor that disrupts cellular integrity and plays a central role in the development of tissue necrosis. Additionally, the presence of beta toxin further contributes to hemolysis and necrotic processes.

Clostridium perfringens, for instance, is characterized by rapidly progressive gangrene of the injured tissue along with the production of foul-smelling gas [18], while *Clostridium difficile* is a well-known cause of colitis [19]. Each species has distinct toxins and modes of action, tailored to their specific ecological niches and targeted host tissues.

Similarly, *C. novyi* type A only encodes TcnA; this toxinotype causes gas gangrene in humans and animals, either as a primary agent or in combination with other pathogenic *Clostridium* spp. [20]. *C. novyi* type B encodes TcnA and beta toxin and is the etiologic agent of INH [5]. *C. novyi* type C does not encode either of the 2 typing toxins, and is thus nontoxigenic and not associated with disease [21]. *C. novyi* type D, which only produces beta toxin, is commonly known as *C. haemolyticum* and causes BH [17].

However, in this particular case, the intricate pattern of gross lesions, histopathological findings, and clinical progression align closely with the profile of *Clostridium novyi* type B-associated infections, suggesting it as the primary candidate responsible for the observed multi-organ involvement.

Among the existing literature, two notable case studies stand out due to their focus on hepatic lesions and limited organ involvement. However, these cases are distinct from the presented case of a Golden Retriever, where the infection manifested with major gross and histopathological lesions across multiple vital organs.

The first case study, which detailed the infection in an American 8-year-old spayed, female mixed breed dog, primarily highlighted hepatic lesions caused by *Clostridium novyi* type B [8]. While this study contributed valuable insights into the hepatic manifestations of the infection, its exclusive focus on the liver leaves a gap in our understanding of potential multisystem involvement.

Similarly, another case report described a German shepherd dog that presented with acute collapse after a presumed traumatic event. Subsequent exploratory laparotomy revealed a necrotic liver lesion, and histopathologic examination confirmed the presence of bacilli containing terminal endospores [22]. This case, like the previous one, concentrated solely on hepatic lesions, leaving the broader impact of the infection on other organs unexplored.

Conclusion

In contrast, the current case of the Golden Retriever presents a distinctive perspective by demonstrating multisystem involvement with major gross and histopathological lesions. Notably, the liver, spleen, kidneys, heart, and lungs all exhibited significant alterations, offering a comprehensive view of the infection's impact on multiple vital systems. This expanded organ involvement enriches our understanding of the disease's clinical spectrum and reinforces the need to consider diverse organ responses in cases of *Clostridium novyi* type B infections.

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Conflict of Interest

None.

References

1. Watanabe, Noriyuki, Kiyoko Kobayashi, Giichi Hashikita and Yoshitada Taji, et al. "Hepatic gas gangrene caused by *Clostridium novyi*." *Anaerobe* 57 (2019): 90-92.
2. Sasaki, Yoshimasa, Noriyasu Takikawa, Akemi Kojima and Mari Norimatsu, et al. "Phylogenetic positions of *Clostridium novyi* and *Clostridium haemolyticum* based on 16S rDNA sequences." *Int J Syst Evol Microbiol* 51 (2001): 901-904.
3. Smith, Louis Ds and Lillian V. Holdeman. "The pathogenic anaerobic bacteria." The Pathogenic Anaerobic Bacteria. (1969).
4. https://www.msdvetmanual.com/digestive-system/hepatic-diseases-of-small-animals/infectious-diseases-of-the-liver-in-small-animals
5. Uzal, Francisco A., and Mauricio Navarro. "Chapter 23: Infectious Necrotic Hepatitis." Clostridial Diseases of Animals. Hoboken, NJ: John Wiley & Sons, Inc (2016).
6. Navarro, Mauricio A. and Francisco A. Uzal. "Pathobiology and diagnosis of clostridial hepatitis in animals." *J Vet Diagn Invest* 32 (2020): 192-202.
7. Sasaki, Yoshimasa, Akemi Kojima, Hiroshi Aoki and Yasuaki Ogikubo, et al. "Phylogenetic analysis and PCR detection of *Clostridium chauvoei*, *Clostridium haemolyticum*, *Clostridium novyi* types A and B, and *Clostridium septicum* based on the flagellin gene." *Vet Microbiol* 86 (2002): 257-267.
8. Trusiano, Brie, S. Michelle Todd, Sarah Barrett and Michael Ciepluch, et al. "Necrotizing hepatitis caused by *Clostridium novyi* type B in a dog with no predisposing liver lesions: A case report." *BMC Vet Res* 18 (2022): 366.
9. Nyaoke, Akinyi C., Mauricio A. Navarro, Juliann Beingesser and Francisco A. Uzal. "Infectious necrotic hepatitis caused by *Clostridium novyi* type B in a horse: Case report and review of the literature." *J Vet Diagn Invest* 30 (2018): 294-299.
10. Niza, M. M. R. E., A. J. A. Ferreira, M. C. Peleteiro and C. L. Vilela. "Bacteriological study of the liver in dogs." *J Small Anim Pract* 45 (2004): 401-404.
11. Jeong, Chang-Gi, Byoung-Joo Seo, Salik Nazki and Byung Kwon Jung, et al. "Characterization of *Clostridium novyi* isolated from a sow in a sudden death case in Korea." *BMC Vet Res* 16 (2020): 1-9.
12. Dejana, Elisabetta, Elisabeth Tournier-Lasserve and Brant M. Weinstein. "The control of vascular integrity by endothelial cell junctions: Molecular basis and pathological implications." *Dev Cell* 16 (2009): 209-221.
13. Akiyama, Noriko, Tomoyuki Shibahara, Kazutada Ushiyama and Haruna Shimizu, et al. "Fatal *Clostridium novyi* type B infection in a sow." *Jpn Agric Res Q* 51 (2017): 85-89.
14. Lubkin, Ashira and Victor J. Torres. "Bacteria and endothelial cells: A toxic relationship." *Curr Opin Microbiol* 35 (2017): 58-63.
15. Ma, Marek, J. Todd Boyd, Hien T. Trinh and Jeremy W. Coombs, et al. "Fatal myocarditis due to *Clostridium novyi* type B in a previously healthy woman: Case report and literature review." *Scand J Infect Dis* 39 (2007): 77-80.
16. Lucas, Rudolf, Yalda Hadizamani, Joyce Gonzales and Boris Gorshkov, et al. "Impact of bacterial toxins in the lungs." *Toxins* 12 (2020): 223.
17. Navarro, M. A., F. Dutra, C. Briano and A. Romero, et al. "Pathology of naturally occurring bacillary hemoglobinuria in cattle." *Vet Pathol* 54 (2017): 457-466.
18. Buboltz, Jerome B., and Heather M. Murphy-Lavoie. "Gas gangrene." In StatPearls [Internet]. StatPearls Publishing (2023).
19. Fordtran, John S. "Colitis due to Clostridium difficile toxins: Underdiagnosed, highly virulent, and nosocomial." In *Proc Bayl Univ Med Cent* 19 (2006): 3-12.
20. MacLennan, John D. "The histotoxic clostridial infections of man." *Bacteriol Rev* 26 (1962): 177-274.
21. Nakamura, Shinichi, Imiko Kimura, Kiyotaka Yamakawa and Shoki Nishida. "Taxonomic relationships among *Clostridium novyi* types A and B, *Clostridium haemolyticum* and *Clostridium botulinum* type C." *Microbiology* 129 (1983): 1473-1479.
22. Vacher, N., P. Allan and N. Sullivan. "Clostridial hepatitis in a dog." *Aust Vet Pract* 36 (2006): 18-19.

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