Clinical and pathological features of viral haemorrhagic disease of rabbits and the European brown hare syndrome

P.S. MARCATO *, C. BENAZZI *, G. VECCHI **, M. GALEOTTI *, L. DELLA SALDA *, G. SARLI * and P. LUCIDI *

Summary: The authors review the clinical, macro- and microscopical features, and pathogenesis of viral haemorrhagic disease (VHD) of rabbits and the European brown hare syndrome (EBHS). The two diseases share similar clinical and pathological manifestations involving an acute syndrome, sometimes accompanied by nervous and respiratory symptoms and epistaxis, and in all cases by severe hepatic damage and multifocal haemorrhages leading to fatal shock. The hepatic lesions (necrosis and inflammation) result from direct cytolitic and indirect microthrombotic effects of the causal agent. Endothelial lesions and a primary or secondary defect of coagulation factors are possible causes of the haemorrhagic syndrome. Typical lesions consist of necrotic hepatitis and congestion, haemorrhaging and oedema of the lungs and trachea. The histological and ultrastructural alterations of the liver are similar to those found in certain cases of acute fatal hepatitis in man. The high correlation between histologically typical hepatic findings and immunohistochemistry and immunoelectron microscopy is of diagnostic value. Both microscopic lesions and pathogenesis favour the unifying definition of “infectious necrotic hepatitis of Leporids” for the two disease entities.


INTRODUCTION

The first detailed report on the pathology of a new disease of rabbits, which the authors have called “rabbit infectious necrotic hepatitis” (RINH), was published in September 1988 (27).

This acute and fatal disease, which has spread since 1986 throughout Western Europe, shared pathological features with “viral haemorrhagic disease” (VHD) of
rabbits described in the People's Republic of China since early 1984 (45). Moreover, the disease was transmitted experimentally to healthy rabbits by inoculating fresh organ extract from affected rabbits (27). In late 1988, the authors also studied the pathological changes of hares which had died of a disease very similar both to RINH-VHD and to the European brown hare syndrome (EBHS) (28), first recognised in Sweden (22) and then in Italy (23, 26, 35), Germany (16) and France (25). Using solid phase immune electron microscopy (SPIEM) with protein A on liver homogenates of rabbits which had died of RINH-VHD, virus particles of approximately 30 nm, resembling those found in hares affected with EBHS (23, 41), were detected (12, 28). In addition, by means of the PAP (peroxidase anti-peroxidase) method and an antiserum from convalescent rabbits, PAP-positive antigens were found in the liver, kidneys and lungs of diseased hares (28). It was concluded that close morphological and antigenic correlations exist between the viral agents of the two diseases (RINH-VHD and EBHS), as also suggested later by others (14, 26, 41; J.-P. Morisse et al., 1989, unpublished findings). A further common feature of the two diseases is the central pathogenetic role of hepatic damage, microscopically quite similar to fatal viral hepatitis in humans, particularly non-A non-B hepatitis. Hence, the name "infectious necrotic hepatitis" was proposed for the disease in rabbits (27). Other workers have subsequently confirmed the assumption of the authors regarding pathogenesis not only in the disease in rabbits but also in the disease in hares (3, 22). The causative agent of RINH-VHD is now classified as a member of the Caliciviridae family (8, 32).

This paper is devoted to the clinical and pathological aspects of both viral haemorrhagic disease of rabbits and the European brown hare syndrome. Data from the literature and from our research is summarised, including some new histopathological observations on serologically positive hares.

**CLINICAL ASPECTS**

The spectrum of clinical responses of the disease of rabbits (RINH-VHD) is presented below (6, 18, 45).

The peracute form affects highly susceptible rabbits which have not previously been infected, especially bucks and does of all breeds. The animals die suddenly without any clinical sign. Haematuria and/or vaginal haemorrhage and foamy discharge from the nostrils are occasionally noted (45).

The acute form is highly prevalent in epidemic areas, affecting adults or young rabbits over the age of two months.

The subacute form occurs with attenuated symptoms in the later stages of an epidemic. Most animals survive and become resistant to reinfection.

The chronic form is considered rare and symptomless and the subclinical form is only hypothesised in suckling rabbits.

The clinical manifestations of RINH-VHD have been described mainly in the acute infection, as the peracute form is usually symptomless and the subacute form exhibits similar but milder signs.
The incubation period is 1-2 days (33, 36, 40, 43, 44), or a maximum of 3 days, and death may take place 12-48 hours after sudden onset of various inconstant signs (1, 2, 3, 4, 5, 6, 7, 10, 11, 14, 15, 17, 19, 21, 24, 27, 30, 31, 33, 36, 38, 40, 42, 43, 44, 45), such as anorexia, pyrexia, apathy, dullness, prostration, side recumbency, severe nervous signs (convulsions, contractions, ataxia, posterior paralysis, "pedalage", opisthotonos), groans and cries before death, respiratory signs (dyspnoea, epistaxis or mucohaemorrhagic nasal discharge), ocular signs (lacrimation, haemorrhaging), cyanosis of mucous membranes, ears and eyelids.

Animals which recover from the acute form sometimes exhibit severe icteric discolouration of the mucous membranes followed by death a few weeks later (20). Shortly before death, the animals show relaxation of the anus (10), abdominal dilatation with constipation or diarrhoea (45) and faecal or mucous material soiling the perianal area (10, 37). In rare cases, does may abort dead foetuses (10).

A severe decrease in the proportion of lymphocytes is usually revealed by haematological tests (45).

In the disease of hares (EBHS), most affected animals are found dead. In some cases animals are captured moribund or, in rare instances, are found to be affected by such symptoms as blindness, loss of balance, opisthotonos, inability to move, cramps and prostration (22). The course of EBHS is usually very short. In some cases, however, a protracted course has been suggested by occasional post-mortem findings of chronic hepatitis (28).

Epidemics of EBHS are restricted to areas of intensive agriculture where the population of European brown hares is dense (22).

**PATHOLOGICAL ASPECTS**

**Gross lesions**

In the naturally occurring disease of rabbits (RINH-VHD), the nose is often soiled by bloody discharge. The most severe lesions found at necropsy are in the liver, trachea and lungs; these are accompanied by poor blood coagulation, petechial haemorrhages in almost all organs, and sometimes splenomegaly and jaundice. Icteric discolouration is immediately evident in the pinnae of the ears and subcutis. Catarrhal gastritis with mucosal erosions, hyperplastic enlargement of mesenteric lymph nodes and dull pale discolouration of the kidneys are also detected occasionally. Hyperaemic dark reddening of the tracheal mucosa, which contains abundant frothy fluid, along with lung congestion and oedema with multifocal haemorrhages up to one cm or more in diameter (Fig. 1), are constant respiratory changes. Although the trachea and lungs are the organs most severely affected from a macroscopic point of view (27, 45), microscopic hepatic lesions are, in fact, of greater diagnostic significance. The liver, which is also affected, is of reduced consistency, pale yellow or greyish, with a marked lobular pattern, or sometimes a finely granular surface (Fig. 2).

The authors have recently observed that, in pregnant does, necropsy may reveal foetuses with multi-organic focal haemorrhages.
FIG. 1

Trachea and lung in a case of viral haemorrhagic disease (VHD)

Congestion and haemorrhage may be seen in the mucosa of the trachea and in lung parenchyma.

FIG. 2

Hepatic lesions in VHD in a rabbit

Disseminated necrotic hepatitis
Experimentally infected rabbits show pathological changes quite similar to those seen in natural cases; these changes, however, are consistently icteric (27).

In the disease of hares (EBHS), the respiratory organs and liver are also the most severely affected and show lesions similar to those observed in the disease of rabbits (25, 28). Moreover, in some cases, the liver shows congestion and haemorrhaging (16, 41), appearing diffusely red and turgid or exhibiting pinpoint central reddening of the lobules. Icteric discolouration, congestive splenomegaly and acute nephrosis are also constant features. The urine in the bladder is often tinged with blood (16). Internal organs are sometimes reported to be congested but not haemorrhagic, and gross liver lesions are reported to be inconspicuous both in the natural and experimental disease (41). A catarrhal to necrotising conjunctivitis, associated with opacity and occasional ulceration of the cornea (41), seems to explain the blindness noted by some authors (16).

**Microscopic lesions**

A comparative presentation of histological lesions in 70 rabbits and hares is reported in Table I. This Table differs slightly from the one previously published (28).

**TABLE I**

*Summary of histological lesions*

(53 rabbits and 17 hares)

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Rabbits (%)</th>
<th>Hares (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necrotic hepatitis</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Hepatocyte calcification</td>
<td>8</td>
<td>65</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td><strong>Spleen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follicular karyorrhexis</td>
<td>86</td>
<td>73</td>
</tr>
<tr>
<td>Red pulp hyaline necrosis</td>
<td>54</td>
<td>27</td>
</tr>
<tr>
<td><strong>Lungs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperaemia + haemorrhage</td>
<td>89</td>
<td>89</td>
</tr>
<tr>
<td>Oedema</td>
<td>44</td>
<td>6</td>
</tr>
<tr>
<td>BALT karyorrhexis</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td><strong>Trachea</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperaemia</td>
<td>81</td>
<td>71</td>
</tr>
<tr>
<td>Oedema</td>
<td>22</td>
<td>14</td>
</tr>
<tr>
<td>Leukocyte infiltration</td>
<td>43</td>
<td>29</td>
</tr>
<tr>
<td>Calcification of tracheal cartilage</td>
<td>41</td>
<td>71</td>
</tr>
<tr>
<td><strong>Kidney</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tubulonephrosis</td>
<td>64</td>
<td>75</td>
</tr>
<tr>
<td>Glomerular microthrombi</td>
<td>73</td>
<td>6</td>
</tr>
<tr>
<td>Tubulonephrosis + necrosis</td>
<td>23</td>
<td>31</td>
</tr>
<tr>
<td>Hyperaemia + haemorrhage</td>
<td>75</td>
<td>87</td>
</tr>
<tr>
<td>Epithelial calcification</td>
<td>6</td>
<td>31</td>
</tr>
<tr>
<td><strong>SNC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intramyelinic oedema</td>
<td>71</td>
<td>67</td>
</tr>
<tr>
<td>Microthrombi</td>
<td>26</td>
<td>–</td>
</tr>
</tbody>
</table>
In rabbits, the liver is always the most severely affected organ, showing multifocal necrosis and early leukocytic exudation (acute necrotic hepatitis) (Figs. 3 and 4). Small, scattered intralobular foci of haemorrhage are present. A variable degree of anisomorphism is observed in hepatocytes. Necrosis appears in disseminated foci in which single or groups of hepatocytes show acidophilic shrinkage (subcutaneous acidophilic degeneration, occasionally with formation of Councilman bodies) or lysis of their cytoplasms. The foci may sometimes become confluent, thus forming extensive local areas, mainly at the periphery of the lobules. Inside small necrotic foci, intrasinusoidal microthrombi are sometimes present (Fig. 5). Other hepatocytic lesions are hydropic rarefaction and cytoplasmic swelling, microvascular steatosis, apoptosis, bile pigment and/or iron pigment deposition. Single hepatocytes occasionally show megalocytosis, binucleation and dystrophic granular calcification. Inflammatory infiltrate is mild to moderate and consists of lymphocytes in portal spaces and sinusoids, and granulocytes in sinusoids, the latter being present only in foci of necrosis. A moderate periportal fibrosis is an infrequent finding. Tracheal and pulmonary lesions (Figs. 6 and 7) are mainly of the hyperaemic-oedematous type, often associated with haemorrhage and sometimes with microthrombi in alveolar capillaries. In regard to other organs and tissues, special consideration must be paid to karyorrhexis of lymphoid tissue (BALT, GALT, spleen, thymus, lymph nodes), leading to depletion and lymphopenia (45), and to microthrombosis, which is very frequent in the glomerular capillaries (Fig. 8) though less common in other organs, such as the central nervous system.

FIG. 3

Histological lesions from VHD in a rabbit liver

Focal necrosis of hepatocytes and infiltration of mononuclear cells. HE
**FIG. 4**

**VHD in a rabbit liver**

Focal necrosis of hepatocytes and leukocyte infiltration. Anisomorphism of hepatocytes. The darkest hepatocytes are necrotic. Semi-thin section. Toluidine blue.

**FIG. 5**

**VHD in a rabbit liver**

Regressive lesions and slight mononuclear infiltrate. Leukocytes and microthrombi (arrow) within the sinusoids. Semi-thin section. Toluidine blue.
FIG. 6
VHD in a rabbit trachea
Congestion of blood vessels, oedema and slight cellular inflammatory infiltrate in the lamina propria-submucosa. HE

FIG. 7
Lung of a foetus from a rabbit doe which died of VHD
Extensive parenchymal haemorrhage. HE
In addition to the lesions listed in Table I and described in detail in previous work by the authors (27, 28), some authors report membranous glomerulonephritis, non-suppurative encephalomyelitis (with occasional acidophilic inclusions in the cytoplasm of neurons and glial cells in the brain and spinal cord), gastritis, adrenocortical necrosis, endometrial congestion and haemorrhaging, degeneration of the pancreatic acinar epithelial and islet cells, focal necrosis in the mucosa of the gall bladder, and inflammatory cells and serous exudate filling pulmonary airways and alveoli (45).

In hares, as well, the organ showing the most severe lesions is the liver (Table I). However, the hepatic damage differs from that in the rabbit by a sometimes less marked early exudation (mononuclear cells), and especially by a more extensive granular calcification in periportal and midlobular hepatocytes (Figs. 9 and 10). On the basis of chemical analysis, some authors have calculated that the calcium content of these livers can reach twenty times that of normal hares (16). In addition, haemorrhagic and sinusoidal congestion are usually more pronounced than in rabbit livers. Intrahepatocytic deposition of iron pigment is more extensive. Moreover, the percentage of chronic cases of liver disease is tripled in hares (Fig. 11). A further difference between the two species is the rare occurrence of microthrombosis in hares, perhaps due to a more advanced autolysis and consequent dissolution of fibrinous microthrombi. Not only in the rabbits, but also in 27% of the hares, a peculiar
regressive lesion of the red pulp of the spleen is evident; this is characterised by marked cellular depletion and hyaline-like change in sinuses and cords. Hyaline-like material shows yellow primary fluorescence (slides stained with haematoxylin-eosin: HE), is phosphotungstic acid haematoxylin (PTAH) negative for fibrin, periodic acid Schiff (PAS) and Alcian blue negative, while it stains light blue with Masson’s trichrome and appears finely granular with interspersed myelin figures with transmission electron microscopy (TEM) (27). Nephrosis is frequently present, with medullary nephrocalcinosis in some cases.

Other workers have described changes indicating a low activity of B-cell areas in lymph nodes (16) and bile duct proliferation, without fibrosis, in most of the livers (41). A correlation between virological and histopathological studies has recently been published (26): the concentration of virus particles in liver homogenates was found to be significantly high both in livers with necrosis and in livers with milder degenerative changes of a vacuolar type.

**Ultrastructural studies**

Ultrastructurally (TEM), the liver in RINH-VHD reveals severe degenerative and necrotic lesions of hepatocytes: accumulation of lipofuscin granules, myelin bodies
FIG. 10

**EBHS in a hare liver**

Hepatocytes with granular dystrophic calcification in a focus of hepatitis. Alizarin Red

FIG. 11

**EBHS in a hare liver**

Heavy cellular inflammatory infiltration in a case of hepatitis in transition to chronicity. HE
and ferritin, numerous lysosomes and large lipid droplets, glycogen depletion, fragmented cytoplasmic membranes, vesicular dilatation and degranulation of endoplasmic reticulum, large vacuoles filled with granular osmophilic material, tubular structures of 25-27 nm with double membrane and rod shape or C shape (attaching curved membranes) (Fig. 12), mitochondrial alterations (swelling, calcium or, rarely, granular depositions with paracrystalline array), nuclear alterations (annular fibrillary structures or ring bodies, increased deposition of interchromatinic granules, pyknosis and membrane disruption).

**FIG. 12**

VHD in a rabbit liver (hepatocyte)

Intracytoplasmatic tubular structures formed by two membranes and electron-dense material filling the space between them. These formations derive from the fusion of agranular membranes of adjacent ergastoplasmatic cisternae and have been described in human natural and experimental non-A non-B hepatitis.

TEM (20,000 ×)
In many hepatocytes, aggregates of roundish intranuclear particles can be seen. Some of these measure 17 nm in diameter, others 22-27 nm (Fig. 13). Particles like these have also been observed in hepatocytes of chimpanzees experimentally infected with the agent of human non-A non-B hepatitis (9). The above-mentioned intracytoplasmic tubular structures, formed by two membranes, are derived from the fusion of agranular membranes of adjacent ergastoplasmic cisternae and have also been described in human non-A non-B hepatitis (9, 13, 34).

FIG. 13
VHD in a rabbit liver (hepatocyte)
Aggregates of roundish intranuclear particles, some of which have a diameter of 17 nm, others of 25 nm. Particles like these have also been observed in hepatocytes of chimpanzees experimentally infected with the agent of non-A non-B human hepatitis.
TEM (40,000 ×)
In rare cases, virus-like particles of 25-30 nm in diameter, arrayed in a paracrystalline pattern, can be seen in the cytoplasm of both hepatocytes (Fig. 14) and endothelial cells of the rabbit (28) and in hepatocytes of the hare (41).

To detect the agent responsible for the disease in rabbits from liver homogenates, the authors have employed solid phase immune-electron microscopy (SPIEM) with protein A, a method not previously used on organ homogenates in veterinary medicine (12, 28). Virus particles of about 30 nm have been found (Fig. 15). SPIEM has been
compared with the standard negative stain for electron microscopy (EM) and another immunoelectron microscopy method (direct IEM) and appears to be the most efficient and specific technique, with a sensitivity comparable to ELISA and radioimmunoassay. The aforementioned virus particles, few of which present spikes, are similar to those detected in the disease in hares (23, 41).

**FIG. 15**

VHD in tissue homogenate from a rabbit liver

Viral particles of about 30 nm, presenting spikes.
These particles are similar to those previously found in hares by other authors. SPIEM

**Immunohistological studies**

Immunohistological studies on the disease in rabbits (with biotinylated rabbit anti-RINH-VHD obtained from a healthy rabbit which had been raised on a farm where the disease was present) have revealed both intranuclear and intracytoplasmic antigen-positive staining in hepatocytes of infected rabbits (39). In some animals, positive staining of macrophages in the lungs, spleen and lymph nodes was also observed (39).

The authors, by using the PAP method with an antiserum from convalescent rabbits, have demonstrated PAP-positive antigens in the liver, kidneys and lungs of diseased hares. The antigen-positive cells correspond to hepatocytes and endothelial
cells in the liver (Fig. 16) and endothelial cells in the kidneys and lungs (28). Using both rabbit polyclonal antiserum and mouse monoclonal antibodies against RINH-VHD virus, a specific staining of viral antigens in hepatocytes, as well as in mononuclear cells in the spleen and lymph nodes of diseased hares, was subsequently obtained by others (26).

FIG. 16

**EBHS in a hare liver**

Hepatocyte with antigen positive cytoplasm (arrows) in a focus of inflammation. PAP method using an antiserum from convalescent rabbits

**HISTOLOGICAL RESEARCH ON APPARENTLY HEALTHY BUT SEROLOGICALLY POSITIVE HARES**

Forty-nine apparently healthy hares were captured last year in Bologna province and then euthanised. ELISA testing of blood samples revealed the presence of antibodies against EBHS (positive haemagglutinating titre $\geq 1:80$), but no viral particles were detectable in organs by means of negative staining EM and ELISA.

Histological research was routinely performed (HE) on tissue sections from liver, spleen and trachea specimens fixed in buffered formalin and embedded in paraffin.
Hepatic vacuolar degeneration in 20 hares, and milder hepatosis (cloudy swelling) in 12 others, was evident. Some hepatocytes showed vesiculation of their nuclei with chromatin margination. Hepatitis, in the form of small scattered foci of mononuclear cells, was present in 17 hares.

Tracheitis was found in 25 hares; this was characterised by infiltration of mononuclear cells in 22 cases and of granulocytes in the remaining 3 cases. Of the 20 hares in which the spleen was examined histologically, 17 showed hyperplasia of splenic follicles.

Serological examinations revealed that all the animals tested had had contact with the agent of EBHS and had developed antibody. This contact, although not fatal, would be responsible for the histological lesions in almost half of the animals. Hepatitis was focal and milder than that observed in the hares mentioned by the authors in their previous report (28). There was a high incidence of hepatic vacuolar degeneration (20/49), very similar to that registered by other workers (26) in serologically positive hares (15/30). There was an even higher incidence of tracheitis, which was also more severe than that observed in the dead animals previously reported by the authors (28). This might suggest that the respiratory system is a portal of entry for the agent which, in the studies conducted by the authors, might have had its pathogenic power reduced by the cellular inflammatory reaction of the upper respiratory tract. Such a different response is also suggested by the reactive hyperplasia of spleen lymphoid tissue observed in 17 of 20 animals.

**PATHOGENESIS**

The main route of infection in the disease of rabbits seems to be oral, followed by the conjunctival and respiratory routes and skin trauma (45). Both in the rabbit and hare diseases, the survival of the virus is influenced by environmental temperature. Epidemics occur most frequently at the beginning of the cold season (22, 45).

Lesions are likely to be caused by viraemia; sudden death is suggested to be a consequence of multiple organ failure resulting from lung edema and haemorrhage, adrenocortical necrosis, circulatory disorders of kidneys and hepatic necrosis (45). The presence of numerous fibrin thrombi in the microvasculature of many organs together with the demonstration of a reduction in platelet numbers, as well as prolonged prothrombin and thrombin times (45), supports the hypothesis of an exhaustion of procoagulant factors (consumption coagulopathy) leading to poor blood coagulation and multifocal haemorrhages. Disseminated intravascular coagulation (DIC) may result from systemic endothelial damage caused by viraemia, but it could also be a consequence of massive hepatic necrosis. In fact, the latter might lead to activation of extrinsic factors and failure of clearance of activated procoagulant factors which would be exhausted later on as DIC ensues (27).

In summary, a primary or secondary defect of coagulation factors and endothelial lesions are possible causes of the haemorrhagic syndrome. According to the hypothesis of the authors (Fig. 17), necrotic and inflammatory damage to the liver is central to the pathogenesis of the disease. Prominent virus-induced hepatic damage is supported by the demonstration that the concentration of the virus is highest in the
liver (45). As antigen-antibody reaction is known to effectively provoke microthrombosis and subsequent hepatic necrosis (29), virus-induced immunocomplexes have also been hypothesised in the pathogenesis of hepatic damage. Comparison among immunohistochemistry, immunoelectron microscopy, haemagglutination (HA) and histology reveals that a strong correlation exists between these methods in regard to the hepatic lesions of RINH-VHD (27, 39). Histological lesions in the liver may also be used to classify an animal as EBHS-positive, since a high correlation can be demonstrated among the immunohistochemistry, immunoelectron microscopy and histology of the hepatic lesions in hares, as well (26, 28, 41).

FIG. 17
Pathogenetic hypothesis concerning necrotic hepatitis of the rabbit and hare

Direct and indirect actions of the causal agent converge in the liver, provoking cell damage

In both the rabbit and hare diseases, the ultrastructural alterations may suggest that hepatocyte necrosis is a direct effect of virus replication and that endothelial injury, also directly virus-induced, may contribute to the rapid course of the disease by initiating DIC and/or haemorrhages, all leading to fatal shock. In a few cases, especially in hares (28), the hepatic lesions can undergo chronic evolution.

Although the virus-like particles observed by electron microscopy in the livers of experimentally infected hares are reported to be morphologically similar to those observed in rabbits exposed to RINH-VHD virus (41), it has not yet been demonstrated
that the two viruses are identical. However, at least a close antigenic correlation between the two agents (or the two supposed biotypes of the virus) can be shown from the immunohistological research so far published.

In conclusion, the pathological changes and the pathogenetic mechanism outlined recently by most authors still support the unifying definition, proposed by the present authors, of “infectious necrotic hepatitis of Leporids” for the two disease entities (28).

ACKNOWLEDGMENTS

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Resumen: Los autores examinan las características clínicas, las lesiones macro y microscópicas así como la patogenia de la enfermedad hemorrágica viral del conejo (VHD) y del síndrome de la liebre parda europea (EBHS). Estas dos enfermedades se presentan como un síndrome agudo con manifestaciones clínicas y patológicas similares, ocasionalmente acompañado de síntomas nerviosos y respiratorios con epistaxis, y siempre de lesiones hepáticas graves y hemorragias multifocales que conducen a un choque mortal. Las lesiones hepáticas (necrosis e inflamaciones) son debidas a los efectos citolíticos directos del agente causal y a las microtrombosis que éste provoca indirectamente. Las lesiones endoteliales así como un defecto primario o secundario de los factores de coagulación pueden ser las causas del síndrome hemorrágico. Las lesiones típicas consisten en una hepatitis necrótica con congestión, hemorragia y edema en los pulmones y traquea. Las alteraciones histológicas del hígado, así como las que son visibles por microscopía electrónica, son similares a aquellas observadas en ciertos casos de hepatitis agudas mortales en el hombre. El alto grado de correlación entre las observaciones histológicamente típicas de las hepatitis y las de la inmunohistoquímica así como de la inmunoelectromicroscopía tiene un gran valor para el diagnóstico. Tanto las lesiones microscópicas como la patogenia favorecen que se adopte una denominación común para las dos enfermedades: «hepatitis infecciosa necrótica de los Lepóridos».


REFERENCES


