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PRETELANGIECTASIS OF THE BOVINE LIVER AND CAPILLARISATION OF SINUSOIDS. IMMUNOLABELING AND ELECTRON MICROSCOPY

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The pathogenesis of telangiectasis (TA), the most common liver lesion in the bovine (9), remains a matter of debate since the various hypotheses are not confirmed.

We focused on immunohistochemical and ultrastructural alterations of the sinusoidal barrier in pretelangiectatic lesions to suggest a possible pathogenetic mechanism of TA.

Material and methods

45 livers of young adult cattle with early TA and 6 control livers were fixed after slaughter in Carson's formalin and phosphate-buffered glutaraldehyde. Serial paraffin sections were stained with HE, PTAH, PAS, Gomori's for reticulin. Immunoperoxidase technique for detection of type IV collagen, laminin and fibronectin (BMCs = basement membrane components) was performed. Samples were also treated for transmission electron microscopy (TEM).

Results

Both in early sinusoidal dilatation (ESD) and in telangiectatic cavities, the perisinusoidal reticulum framework appeared thicker and tortuous (perisinusoidal fibrosis). In ESD small tracts of hepatocytic plates were disorganized by focal dilatation of Disse's spaces, endothelial disruption and hepatocyte atrophy. Immunostaining revealed, in ESD and TA, an abnormal deposition of BMCs in the form of a markedly thick linear pattern in the perisinusoidal space (fig. 1). This contrasted with the very thin subendothelial layer formed by BMCs.

TEM confirmed the sinusoidal barrier abnormality: the formation of a thick basement membrane-like lining and the increased deposition of collagen fibres in the perisinusoidal space (fig. 2). The ESD was also focally lined by double cytoplasmic extensions of endothelial cells.

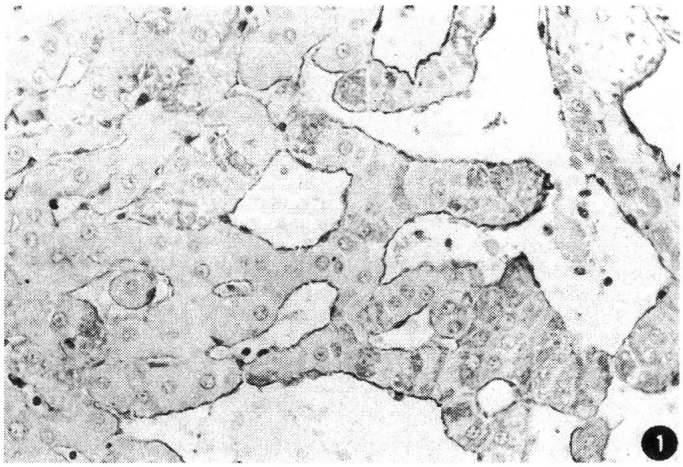

Fig. 1: PAP. Type IV collagen.

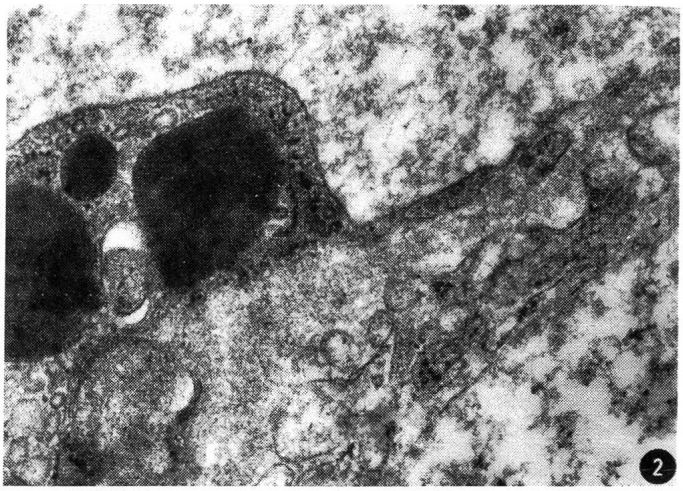

Fig. 2: TEM. 20000 X.

Discussion

Our results indicate that ESD, or pretelangiectasis, shows constant and prominent changes, i.e. the formation of an abnormal basement membrane (capillarisation of sinusoids) and perisinusoidal fibrosis. None of the previously emphasized alterations in pretelangiectasis are evident, i.e. necrosis, hepatitis, thromboembolism or accumulation in the Disse's space of glycogen extruded from hepatocytes (1, 4, 5, 6, 7). In contrast to the findings of Dimitrovic et al. (3), we find an early thickening of the reticulin framework. The observations suggest close mircoscopic similarities between bovine liver TA and human peliosis hepatis. Moreover, the most favored pathogenetic hypothesis for peliosis, i.e. a direct toxic or infectious lesion of the sinusoidal barrier (8, 10), seems also to be applicable to bovine TA. It is noteworthy that certain toxic agents involved in the production of peliosis are also considered responsible for the capillarisation of sinusoids and perisinusoidal fibrosis (10). These alterations are likely to render the exchange of oxygen and substrates between blood and hepatocytes more difficult, leading to hepatocyte atrophy and eventually to a disruption of the sinusoid (2). On the other hand, stimulation of fibroplasia is accelerated in the liver by low oxygen tension and by a rise of sinusoidal pressure caused by an increase of BMCs in the perisinusoidal region (2).

We do not hypothesize on the primary cause of TA, but our research reinforces the concept of direct injury to the sinusoidal barrier. The consequent circumscribed capillarisation of sinusoids may be the trigger which initiates the vicious circle of alterations leading to TA (table 1).

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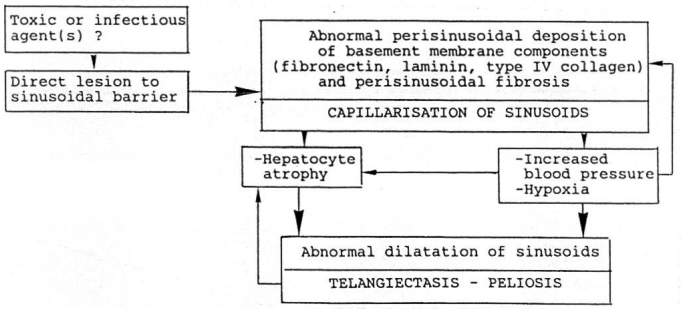

Table 1: Suggested pathogenesis of telangiectasis.

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TUMOR REGISTRY DATA BASE: ADVANTAGES USING A SYSTEMATIZED NOMENCLATURE

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In the development of new chemical or pharmaceutical products, long-term studies with laboratory rodents are required for the risk assessment of these substances. In order to evaluate and interpret the results of those studies by comparing the incidence and degree of pathological alterations in treatment groups with those in control groups, a fundamental knowledge of the frequency and type of spontaneously occurring lesions (in particular tumours) is necessary, because these lesions vary between different animal species and strains. The analysis of experimental data can decisively be improved by using a large pool of historical control data.

Scientists from a number of chemical and pharmaceutical companies and from research institutes have established a joint project to set up a computerized data base for the collection and evaluation of histopathological data from control rats of various strains. This REGISTRY data base is located at the Fraunhofer Institute of Toxicology and Aerosol Research in Hannover.

Besides data describing the maintenance and environmental conditions of particular studies, histopathological diagnoses of tumours and relevant pre-neoplastic lesions from rats used in carcinogenicity and toxicity studies are stored in the data base.

Significance of a systematized nomenclature

If historical data from control animals is to be used to improve the evaluation of study results, one major requirement must be taken into account:

Histopathological data which are not based on a systematized nomenclature cannot be used for any reliable statistical analysis.

One reason is that different names are often used in literature for lesions of the same histological type. On the other hand, however, the criteria which lead to a specific diagnosis are sometimes ambiguously defined in various textbooks or publications. In particular, if data are collected from different studies which are carried out at different laboratories and are evaluated by different pathologists, it is of significant importance to agree on a standardized nomenclature system. Needless to say, that a consistent nomenclature must also be used in any single experiment when summary tables of diagnostic findings are to be produced.

Another requirement for a pathology data base is the use of a generalized structure of a diagnosis.

The registry nomenclature and the structure of diagnoses

A diagnosis for the *registry* data base consists of many individual items which are all stored as separate entities in the system. The following information lists the main parts of a diagnosis:

the localization of the lesion
the name of the lesion
the biological behavior (e.g. malignancy) of the lesion
one or more modifiers
information about the multiplicity of a tumor.

The first step in starting the *registry* data base project was to standardize the usable names of organs and lesions and to build a hierarchical and highly uniform structure (Mohr et al., 1990). All terms are stored in the lexicon part of the data base and the data acquisition program controls their correct utilization.

The topography consists of 13 organ systems which are subclassified into organs and subtopographies. Lesions are divided into two categories: The first are specific to a distinct organ according to their site of origin and histogenesis and consequently can be used for diagnoses only for that particular organ. The second class of proliferative lesions are the so-called «generally used preferred terms» which can occur potentially in all organs, because they originate from connective tissue or other tissues distributed throughout the body.

Optionally, a diagnosis can be extended with one or more modifiers for a more precise subclassification e.g. to define a specific growth pattern of a lesion or to subdivide a finding into various cell types.

Information about the biological behaviour is necessary in order to classify a tumour as benign, malignant, metastasizing, invading, etc. or as a metastasis. Special rules are defined for using these terms in placing a finding.

A possible multiplicity of a tumour of the same type and histogenesis is another important type of information to be stored in the data base.