Zeitschrift: Schweizer Archiv für Tierheilkunde SAT : die Fachzeitschrift für Tierärztinnen und Tierärzte = Archives Suisses de Médecine Vétérinaire ASMV : la revue professionnelle des vétérinaires

Herausgeber: Gesellschaft Schweizer Tierärztinnen und Tierärzte

Band: 132 (1990)

Heft: 8

Artikel: Systemic siderosis after prophylactic parenteral iron administration to Munich : mini-pigs with special reference to the kidneys

Autor: Rinke, M.

DOI: https://doi.org/10.5169/seals-593697

plasms were excluded, these patients had microscopic evidence of a subacute encephalitis.[5,8] SIV also causes a subacute meningoencephalomyelitis which is characterized by randomly distributed, perivascular collections of macrophages, glial cells, and multinucleated giant (syncytial) cells throughout the neuraxis.[9,10] During early stages of SIV-CNS infection, leptomeningeal lesions predominated; in more advanced stages the lesions were mainly parenchymal. Both early and advanced lesions in HIV-CNS infection were parenchymal with minimal involvement of the leptomeninges. Numerous investigators have demonstrated the presence of HIV and SIV proteins and genome in syncytial and other mononuclear cells.[11,12] Infected cells have been immunophenotyped to a monocytic lineage and the presence of virions in monocytes has been demonstrated by electron mircoscopy,[8-12] although neuroglia and endothelium have also been incriminated. In our material, SIV proteins were localized in cells of monocytic lineage only.[13] It appears from these data that both HIV and SIV cross the blood-brain barrier in a «trojan horse» fashion via infected mononuclear cells and replicate mainly within macrophages and syncytial cells infiltrating the brain parenchyma.

Vacuolar myelopathy is a thoracic spinal cord syndrome seen in adult late stage HIV-CNS disease and characterized by loss of myelin and spongy degeneration.[6] It was not demonstrated in our animals, although it has been reported in one monkey.[14] Gross cerebrocortical atrophy occurred in 30% of HIV-infected brains, but none in SIV-infected brains. Vascular calcification was seen in pediatric HIV-CNS, only.

Some features of SIV-CNS infection, notably direct lentivirus-induced lesions, resemble more closely pediatric than adult HIV-CNS encephalitis.[10] Both viruses cause CNS lesions, and the extent and severity of these lesions increase with duration of infection. The differences between adult HIV and SIV-induced CNS disease may be due, among other factors, to the fact that in an experimental setting there is no intervention to slow down or halt the progression of disease. Consequently, the lifespan of a SIV-infected monkey is by design shortened as compared to the lifespan of a HIV-infected person. In addition, considerably fewer monkeys have died of SIV infection than people infected with HIV. Despite these caveats, however, there are significant differences in HIV- and SIV-CNS pathological expression and, therefore, as the AIDS pandemic continues to take its toll, there is an urgent need to develop SIV strains with enhanced ability to cause chronic CNS clinical and pathological disease (supported in part by Grants RROO165 and AFIP/WRAIR U941).

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Institute for Toxicology / Pharma, Bayer AG, Wuppertal, GFR

SYSTEMIC SIDEROSIS AFTER PROPHYLACTIC PARENTERAL IRON ADMINISTRATION TO MUNICH MINI-PIGS WITH SPECIAL REFERENCE TO THE KIDNEYS

M. Rinke

When speaking of iron in connection with pigs, the first idea to arise spontaneously concerns iron deficiency anemia in suckling piglets. Perhaps one also remembers the violent myotoxic alterations after intramuscular injection of ionic iron, as it was sometimes given in former days. This report however, concerns systemic iron overload, occurring after the preventive administration of a common iron dextran compound (Myofer, Hoechst, 1 ml) usually given to mini-pigs at the breeding station during the first days of life.

Material and methods

The mini-pigs used at BAYER belong to the Troll® strain of the Munich breeding-line of miniature swine (MSM). The following results derive from histopathological investigations of 96 animals of both sexes, ageing between 5 and 12 months, and are not related to the application of test compounds. The animals were housed two to a pen, given tap water (free choice), and fed a commercially prepared, standardized diet for mini-pigs (Altromin 8023). At the end of the study they were killed by exsanguination in deep hexobarbital-Na-anesthesia (Evipan®, Bayer) and necropsied immediately. Organs were fixed in Bouin's fluid and embedded in paraplast. Sections about 5 µm thick were stained with H & E and by the Prussian-blue reaction. Sections of the kidneys were additionally stained by PAS and the Turnbull-blue reaction, as well as the Azan method. To exclude the presence of melanin, sections were bleached with 10% hydrogen peroxide over 72 hours.

Results

The histopathological investigation revealed an accumulation of pigmented cells in a few organs. First, numerous brownish pigment deposits were observed in the livers of 94/96 animals, chiefly in the interstitial tissue at the lobular periphery, in blood-vessel walls and

– above all – in MPS, mainly in Kupffer cells. Subsequent Prussian-blue staining revealed that not only the localizations mentioned showed higher stainability, but also the cytoplasm of the hepatocytes themselves, and that the pigment represented iron. Massive deposits of iron-positive cells were also found in the sinuses of the lymph nodes. The pigment deposits were not confined to inguinal or popliteal lymph nodes (which would be understandable, being the direct places of resorption after intramuscular injection), but, in some cases affected lymph nodes throughout the body. Further deposits of pigment were found in the spleens, the skeletal muscles of the hind legs, in the perineural connective tissue – especially of the sciatic nerve(s), within reticulocytes of the bone marrow, and sometimes in endothelial cells of adrenocortical sinuses. However, the central findings were pigment deposits in the kidneys of again 94 out of 96 animals. Interestingly enough, the pigment was located mainly intraglomerularly, and only isolated deposits could be detected in mesangial cells at the glomerular vascular pole. The Prussian-blue reaction turned out to be positive, identifying the pigment as trivalent iron. The glomeruli concerned were located mainly in the inner or cortical region, while in the outer glomeruli only a light yellow pigment could be detected. The Turnbull-blue reaction showed this to be protein-bound or bivalent iron. Furthermore focal sclerotic glomeruli were observed, mainly located in the juxtamedullary zone, which contained iron pigment as well. As a further consequence of glomerular ischemia due to vascular occlusion, a periglomerular fibrosis could be shown in some cases.

Discussion

Well-known examples of excessive iron storage in man are thalassemia and especially idiopathic hemochromatosis. The latter disease usually results in a cirrhotic transformation of the liver, of which the pathogenesis is still unclear. Massive iron deposits in the liver and kidneys of animals are familiar after chronic hemorrhaging, in equine infectious anemia, and due to copper or cobalt deficiency in swine and goats. In the kidneys, siderin was located mainly in the epithelial cells of proximal tubules or Henle's loops. Iron deposits were not observed intraglomerularly, either in the diseases mentioned or in experimental studies, which attempted to simulate idiopathic hemochromatosis by means of chronic parenteral iron administration to rats and dogs. With respect to intraglomerular iron-(pigment-)storage in man and animals, the literature search found only two references (1, 2). Both give accounts of iron overload with subsequent glomerulosclerotic changes in pigs, and this pathological alteration seems to be specific to this species.

A possible explanation of the glomerular sclerosis is, we think, the age of the glomeruli. At the time of iron injection, some of the glomeruli have not matured (3, 4) and therefore the endothelium of the immature glomerulus, which is mostly unfenestrated, offers a barrier to the ferritin passage (5). The ontogenetically older glomeruli of the juxtamedullary region, which were more often sclerotic, perhaps received a higher iron concentration, and their mesangial cells, capable of phagocytosis, may have filtered out molecules, which were too large to pass through the endothelial pores. This large mass of deposits may possibly lead to the subsequent glomerulosclerosis. On the other hand, it is also conceivable, that the transferrin's iron-binding capacity is exhausted. Some observations indicate that the administered iron is not mobilized. Certainly there is no need for its mobilization because of the high iron supply of commercial feeds. For these reasons, and that because mini-pigs grow more slowly than farm swine, we think that for animals of this strain one additional iron injection, containing 50 mg available iron, should be enough to prevent iron deficiency anemia and to avoid kidney disturbances.

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Institute of Pathology and Toxicology, Byk Gulden Pharmaceuticals, Hamburg, FRG

EXOCYTOSIS OF ENTEROCHROMAFFIN-LIKE (ECL) CELLS IN RAT FUNDIC MUCOSA AFTER POTENT ACID INHIBITION

I. Rohr, K. Tuch

Enterochromaffin-like (ECL) cells of the rat gestric fundus display a high degree of degranulation and a marked increase of exocytosis after short-time treatment with B831-78, a potent H^+, K^{+-} -ATPase inhibitor. (1).

The present paper describes the mode of granula release of rat fundic ECL cells.

Material and methods

4 female rats (Sprague-Dawley) were used for elctron microscopic investigation of the fundic ECL cells. 2 animals were treated with 50 mg B831-78 per kg body weight daily for two days and 2 animals served as controls receiving vehicle only.

24 hours after the last dosing the rats were anesthesized with ether and the stomachs perfused via the abdominal aorta with glutaraldehyde 5%. Specimens from the fundic mucosa were embedded in Epon and ultrathin sections were stained with uranyl acetate and lead citrate.

Results

After 2 administrations of B831-78 the ECL cells showed a massive granule depletion and an increased number of exocytic figures. Lysosomal structures occurred more frequently in ECL cells of treated animals. The density of the typical vesicular type granules was markedly reduced and a major part of the granules was empty. The exocytotic figures opened mainly towards chief cells, occasio-