

MICROCIRCULATORY AND MORPHOLOGICAL MYOCARDIAL CHANGES IN CHRONIC ANAEMIA

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Chronic iron-deficiency anaemia (IDA) affects mainly the active population and represents a serious socio-medical problem of increasing health and economic importance. The author studies on 70 white female rats of Wistar breed the correlation between the morphological and microcirculatory myocardial changes and the degree of IDA as well as their reversibility after iron deficiency correction. Routine histological methods have been used to reveal the alterations in the myocardial histology and microcirculatory bed. The main results obtained show that there is a correlation between the severity of IDA and the expressiveness of the histomorphological myocardial alterations. The latter occur already with the moderate degree of IDA and aggravate with the severe degree of IDA. The anaemic hypoxia attacks most significantly the subendocardial layer of the left ventricle which fails to compensate the unfavourable effect of the pathogenetic factor. The disturbances in the microcirculatory bed determine the appearance of a perivascular oedema and fuchsino-philic necroses being the most substantial histological feature of the myocardial lesion. The incomplete reversibility of the morphological changes in the severe degree of IDA does not coincide with the normalized haemoglobin parameters after the correcting iron-replacement therapy.

Key words: Iron-deficiency anaemia, subendocardial cardiomyocytes, microcirculation, histopathology, iron replacement therapy, rats

Iron deficiency states and anaemias belong to the most common deficiency diseases of the XX century. The distribution of chronic iron-deficiency anaemia (IDA) is of global nature. The disease affects mainly the active population. That is why it represents a serious socio-medical problem

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of increasing health and economic importance. First, P. Irvine (1877) reported data about the changes in the cardiovascular system related with the IDA. Until that time the term "anemic heart" remained unclear, insufficiently comprehensively examined and rather contradictory. There was no usage of modern methods of investigation (1,5). The contemporary science poses, however, several significant questions to be solved like the following: When do

functional and morphological alterations in the cardiovascular system appear with IDA and when do they disappear after treatment? Which is the histomorphological substrate of the changes in the cardiomyocytes and haemomicrocirculatory bed of the ventricular myocardium (6,9), etc.

The objective of this communication was to study the correlation between the morphological and microcirculatory myocardial changes and the degree of IDA as well as their reversibility after iron deficiency correction.

MATERIAL AND METHODS

The experiment was carried out on 70 white female rats of Wistar breed aged one month and with mean body mass of $67,33 \pm 1.8$ g. Iron deficiency was achieved by application of an iron-deficient diet to 60 rats for 45 days. The rest 10 animals were used as controls. Author's own modification of the original iron-deficient diet of Rossi et al. (8) was applied. It ensured an optimal ratio between basic nutrients and met the energy requirements of the animals under study. The changes of haemoglobin content, erythrocyte count, and haematocrit were dynamically followed-up. According to the degree of IDA, the animals were divided into the following groups: with a severe, with a moderate, and with a slight degree of the disease. Histological material from

the myocardium was examined on cryostat sections. It was fixed in neutral formaline and in Rego's fixator and then processed after the paraffin method to small blocks. The examinations aimed at detecting the neutral fats (after Sudan III and Oilred), glycogen (with PAS-reaction under amylase control), etc. Haematoxylin-eosin stainings were done. Stainings after Rego for mitochondria and after Lee for fuchsophilic necroses were performed, too. A total of 30 experimental rats were parenterally treated with Ferrum Hausman in a dose of 1 mg/kg b. m. until normalization of the haemoglobin parameters. Then myocardial specimens were studied by the same methods in order to reveal the degree of reversibility of IDA-induced alterations.

RESULTS AND DISCUSSION

Light-microscopically, the morphological myocardial picture did not evidently differ between the rats with a slight degree of IDA and that in the controls.

In the moderate degree of IDA, however, under haematoxylin/eosin staining it could be established that there were differences in the intensity and appearance of spotted more pale-pinkly stained small fields. The striatedness of the cardiomyocytes was preserved although the anisotropic discs were enlarged and the sarcoplasmic optic density was reduced. The

striatedness was marked by the grober granularity and remoteness of granules as well as by the small-sized vacuoles formed among them. Vacuolization was most outlined in the subendocardial layer. A small-droplet fatty dystrophy was established on sections stained for neutral fats.

Mitochondrial alterations were related to their increased amount and size. In the subendocardial areas their quantity was rather diminished down to an extent of complete absence. Thus the cardiomyocytic sarcoplasm appeared optically empty. The glycogen granules were also reduced in number and volume in these regions. Black-stained structureless parts of large-spotted fields with irregular outlines stained flame-redly after Lee were detected.

In the severe degree of IDA the morphological myocardial changes were more pronounced. They presented with a severe vacuolar and fatty dystrophy in the subendocardial zones as well as with a strongly expressed reduction of the glycogen granules. The black-stained structureless regions in the shape of large-spotted fields with irregular contours were larger in surface and greater in number. This fact confirmed the statement that they were fuchsinophilic necroses. They conflated in the subendocardial areas. An oedema in the intercellular and pericapillary spaces in these zones as an expression of IDA-induced reactive and dystrophic alterations in the microcirculatory bed

of the left ventricle was established, too.

After the iron-replacement treatment the pathological changes in the moderate degree of IDA disappeared and the normal peculiarities of the cardiomyocytes were restored. In the severe degree of IDA, however, the significant structural disturbances persisted and the reversibility was protracted and incomplete. A small-droplet fatty dystrophy remained and the mitochondrial swelling did not disappear in 46,66 per cent of the animals. The fuchsinophilic necroses decreased but did not completely fade away in 20 per cent of the cases.

Our results supplement to a certain extent the recently accumulating data (2-4,7) about the microcirculation under normal and pathological conditions and could contribute to the better understanding of the intimate mechanisms of myocardial lesions induced by the chronic iron deficiency.

CONCLUSIONS

1. There is a direct correlation between the severity of IDA and the expressiveness of the histomorphological myocardial alterations. The latter occur already with the moderate degree of IDA and aggravate with the severe degree of IDA.

2. The anaemic hypoxia attacks most significantly the subendocardial layer of the left ventricle which fails to compensate the unfavourable effect of

the pathogenetic factor. The disturbances in the microcirculatory bed determine the appearance of a perivascular oedema and fuchsinophilic necroses being the most substantial histological feature of the myocardial lesion.

3. The incomplete reversibility of the morphological changes in the severe degree of IDA does not coincide with the normalization of the haemoglobin parameters after correcting iron-replacement therapy.

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Микроциркулаторни и морфологични миокардни промени при хронична анемия

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Резюме: Хроничната желязо-дефицитна анемия (ЖДА) засяга главно активното население и представлява сериозен медико-социален проблем с нарастващо здравно и икономическо значение. Върху 70 бели женски плъха от породата Wistar авторът изследва корелационната зависимост между морфологичните и микроциркулаторни изменения в миокарда и степента на ЖДА, както и обратимостта им след коригиране на желязната недоимък. За разкриване на измененията в хистологията и микроциркулаторното русло на миокарда са използвани рутинни хистологични методи. Основните получени резултати показват, че има корелация между тежестта на ЖДА и изразеността на хистоморфологичните промени в миокарда. Последните се появяват още при умерената степен на ЖДА и се задълбочават при тежката степен. Анемичната хипоксия засяга най-значимо субендокардния слой на лявата камера.