

CONSIDERATION ON SOME HISTOMORPHOLOGICAL CHANGES IN EXPERIMENTAL ARTHRITIS IN RATS

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The pathogenesis of rheumatic arthritis is still obscure. A great variety of methods for experimental reproduction of arthritis have been used and changes in the joints of animals obtained, simulating those in humans with past rheumatic affections. Thus, for instance, Beletzkaya (1961), Kemileva (1963) and Keitel (cited by Sborovski, 1968) induced typical arthritis in rats after injecting β hemolytic streptococcus. Kiprova (1955) similarly obtained arthritis in dogs upon two-fold injection of β hemolytic streptococcus. Kemileva and co-workers (1963, 1964) inoculated rats with β hemolytic streptococcus in combination with homogenate of rat's heart tissue. The changes produced in the joints are explained as allergic. Struganova (1956) and Zuza (1964) reproduced allergic arthritis in sensitized rabbits by means of injecting horse serum in the knee joints. Of the methods employed hitherto, the mostly pronounced articular and myocardial changes were produced in animals injected with hemolytic streptococcus.

We undertook the task to study in dynamics the influence of the number of infections on the development of histomorphological changes in the articulations of animals, undergoing intravenous injection with β hemolytic streptococcus.

Material and Method

The investigations were conducted on 90 albino rats, aged 3 months and weighing from 150 to 200 g. The animals were distributed in 5 experimental groups with 10 rats each. The remaining 40 animals, divided in 4 groups of 10 were used for control purposes. All the animals were kept on ordinary nutritive regime. Experimental polyarthritis was induced by means of intravenous injection of β hemolytic streptococcus, group A. The streptococcus culture was injected at weekly intervals, at dose 0.2 cc, 1000 million suspension, in the tail vein; once in the animals of group one, twice in the animals of group two, three times in those of group three and so on. The control animals were injected in the identical manner, but a single time only (at the beginning of the experiment). Three days after the last injection, the animals under investigation and the controls of the respective group were killed by means of severing one of the carotid arteries. Only the first group was without controls since they were injected a single time and duplicated the controls. Material for histological investigation of arthritic manifestations was prelevated from all major joints of the limbs. Such

a material comprised: skin and subcutis, paraarticular muscle and tendons, articular sheaths and joint surfaces. Following fixation in 10% neutral formalin and processing according to the paraffin method, the sections were stained with hemalaun-eosin, with pyrofuchsin after van Gieson, after Weigert — for fibrin, toluidine blue — for demonstrating acid mucopolysaccharides and PAS reaction — for mucoproteid complexes.

Results

In three of 10 animals injected a single time (30%), histomorphological and histochemical changes were observed, giving sufficient reason to assume arthritis development. The blood vessels in the subcutis were dilated and

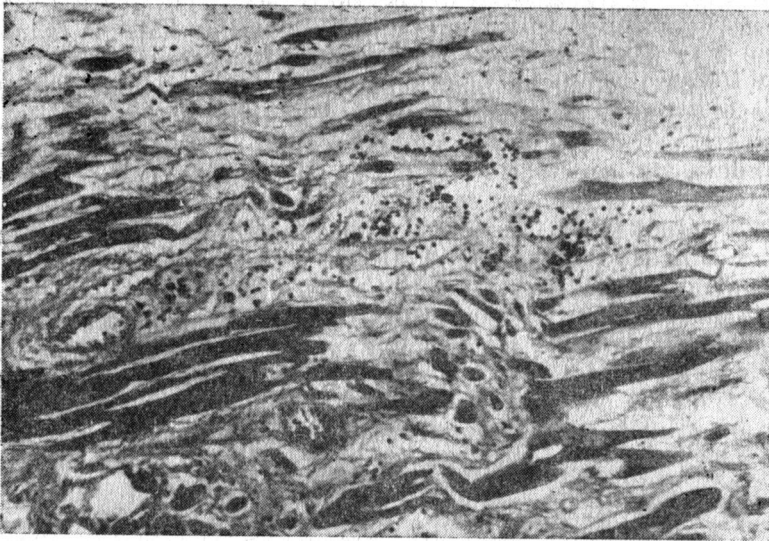


Fig. 1. Striated musculature, connective tissue with blood vessels and infiltration by isolated plasmatic cells and eosinophilic leukocytes

hyperemized with slightly pronounced edema in their surroundings, rich in PAS-positive substances and acid mucopolysaccharides. The interstitium of the striated musculature was similarly edematous, with slightly turgid perivascular collagenous tissue. Also limited infiltrates of lymphoid elements, eosinophilic leukocytes and plasmatic cells were found (Fig. 1).

The synovial membrane of the joints revealed no morphological changes whatsoever.

Arthritic changes were established also in three of the animals undergoing two-fold injection (30%). They were manifested with clearcut edema, disorganization and fibrinoid turgescence of the connective tissue in all the layers of the articular sheaths, presenting yellowish tinge of the collagen upon staining with pyrofuchsin. Focal perivascular infiltrates of histiocytes, lymphocytes, plasmatic and eosinophilic cells were found in the subcutis, muscles and tendons (Fig. 2).

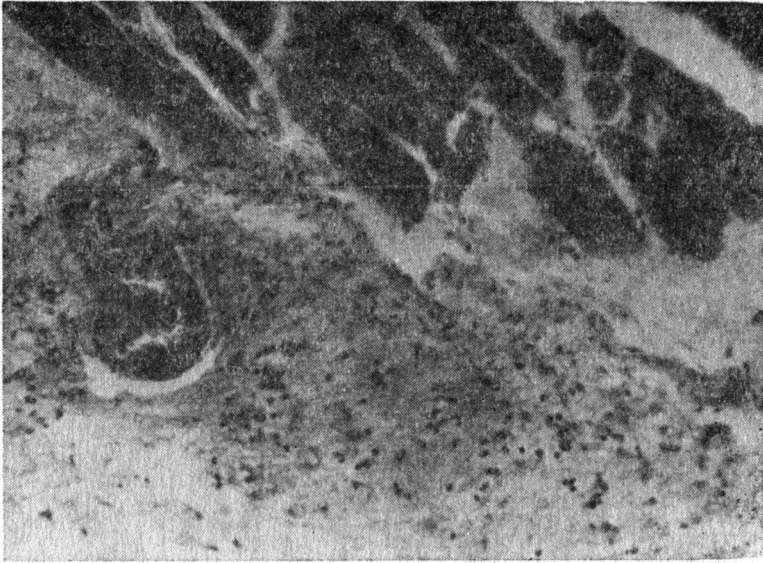


Fig. 2. Striated musculature and blood vessel with perivascular infiltration by lymphocytes, plasmatic cells, eosinophilic leukocytes and histiocytes

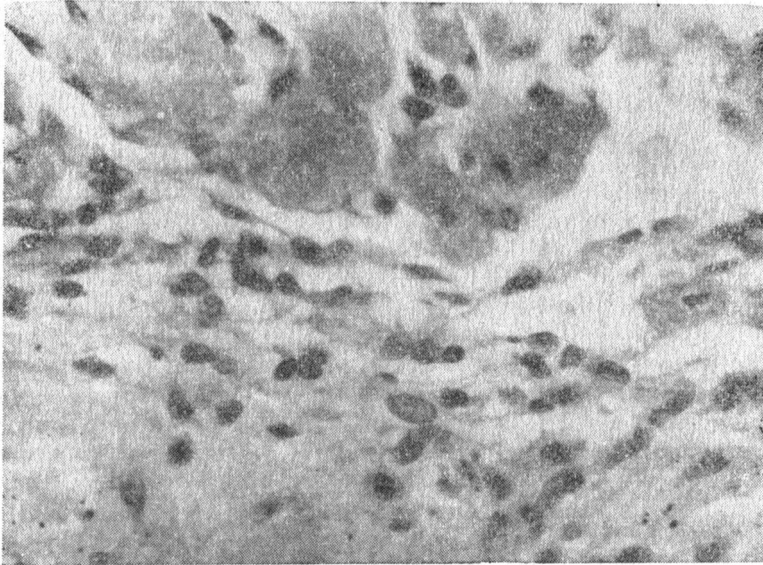


Fig. 3. Disorganization of collagen tissue, round-cellular infiltration and proliferation of fibroblasts with basophilic protoplasm

The investigation of the control animals, subjected to single-time injection, did not show morphological changes.

After three-fold injection in 5 animals (50%) well pronounced inflammatory changes of alterative-exudative character were established: edema and deep disorganization of the collagen tissue, copious round cellular

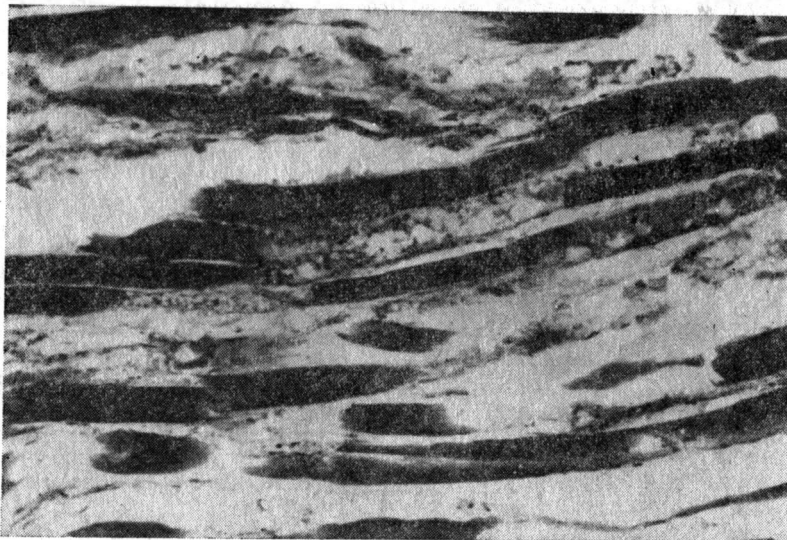


Fig. 4. Interstitial inflammatory process in the striated musculature

elements represented by plasmatic, histiocytic and lymphoid cells. Within the focal cellular ammassments proliferation was noted of fibroblasts with basophilic cytoplasm (Fig. 3). Particularly severe were the interstitial inflammatory changes in the muscles, manifested by focal and diffuse infiltrates, edema of the interstitium and dystrophic changes in the myofibers. The perimysium was edematous, infiltrated with round cells wherein eosinophilic leukocytes prevailed. No succulent cells were observed. Histomorphological changes in the joints were neither discovered in the control-group.

Pathological changes in the joints were established in three of the animals undergoing four-fold injection (30%). By character and severity they exhibited no essential differences from the changes described in the preceding group. The inflammatory process in the interstitium of the striated musculature was clearly outlined (Fig. 4). Abundant, focal round-cellular infiltrates, perivasally, were disclosed in one animal only of the control group.

Of the total number of animals injected 5 times, histomorphological changes of the joints were detected in five. The subcutaneous connective tissue was strongly turgescient, with abundant (diffuse and focal) round-cellular infiltrates. Unlike the first groups, here the leukocytes prevailed (Fig. 5). The changes in the muscles reveal the character of a non-specific septic interstitial myositis. In two of the animals, periosteal manifestations were present — the periosteum was thickened, loose with copious infiltrates

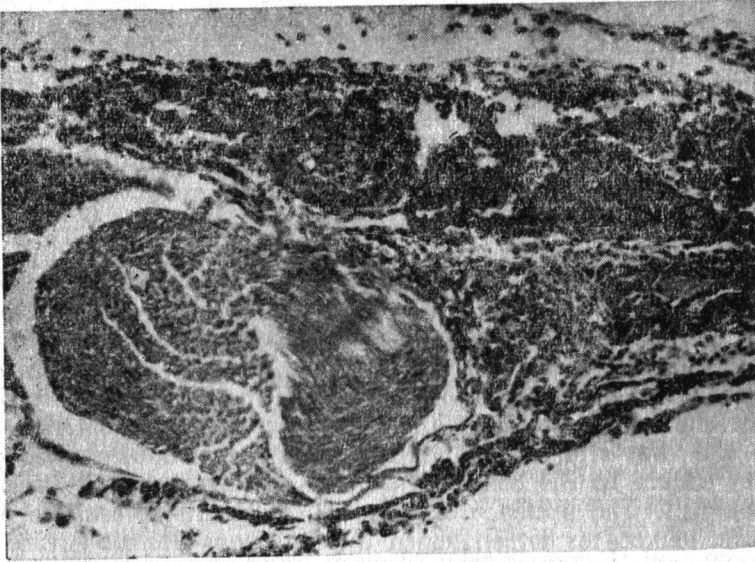


Fig. 5. Subcutaneous connective tissue with copious leukocytic and round-cellular infiltrates

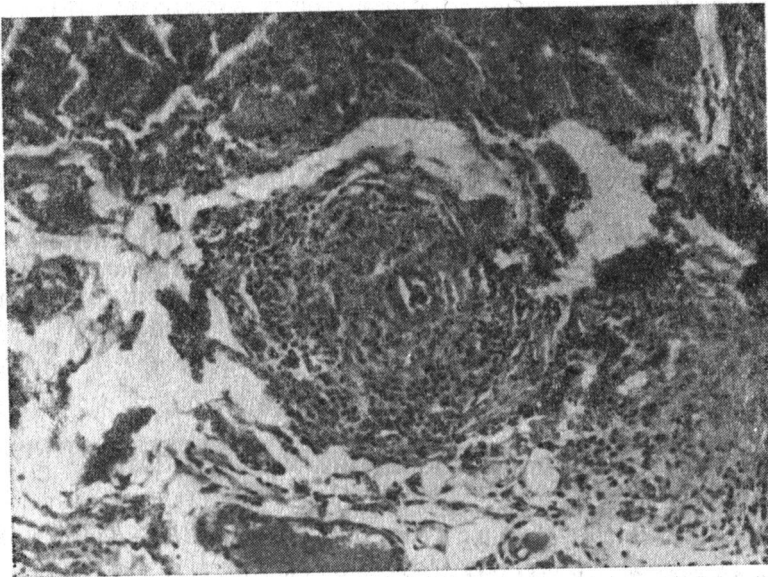


Fig. 6. Collagen tissue and tiny arterial vessel with panarthritic changes

of segmented nuclear leukocytes. In some of the blood vessels panarthritic and periarthritic manifestations were present (Fig. 6).

In one of the control animals, scanty, diffuse, round-cellular infiltrates were found, whereas in the joints of the remainder no changes were established.

Discussion

Upon single-time or several-fold injection of β hemolytic streptococcus in albino rats, at weekly intervals, arthritic changes were established in 30—50% of the experimental animals. In comparison with the myocardial changes (Velikov and Markov) observed, subject to a separate report, this percentage is much lower, but anyway, in line with the clinical evidence (the rheumatic myocarditis is more frequent in arthritis).

After the first and second contamination, development was observed of mucoid edema in the connective tissue and slight round-cellular infiltration as well. The presence of lymphoid elements, plasmatic cells and eosinophilic leukocytes demonstrated the infectious-allergic nature of these changes. Our data comply with those of Shehter (1963) and Gritzman (1964) in humans. Along with increasing the number of contaminations, the picture develops of non-specific septic interstitial myositis, periarthrititis and periostitis. These facts are in support of the statement that an essential role for the development of arthritis is played by the immunoallergic condition of the organism. The role attributed to infection might be assumed as secondary. Otherwise, an increase of the incidence of affected animals following each consecutive injection of infective material should have been anticipated.

The morphological changes in the region of the joints do not reveal the specific granulomatous nature, characteristic of the experimentally induced myocarditis, except for the mucoid edema and fibrinoid turgor — phenomena accepted as characteristic of all allergic reactions. In the arthritis picture produced by us, the paraarticular soft tissues are mainly and most severely involved. The articular sheaths and surfaces disclose insignificant changes.

In conclusion, it might be stated that in several-fold injection of albino rats with β hemolytic streptococcus, group A, the arthritic manifestations exhibit a specific allergic character in two-fold contaminations, whilst in three- and more-fold injections — a septic character.

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ОТНОСИТЕЛЬНО НЕКОТОРЫХ ГИСТОМОРФОЛОГИЧЕСКИХ ИЗМЕНЕНИЙ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ АРТРИТЕ У КРЫС

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РЕЗЮМЕ

При экспериментально воспроизведенном артрите у белых крыс путем неоднократного введения β -гемолитического стрептококка, авторы наблюдали после первых двух инъекций гистологические изменения аллергического характера — отек и дезорганизацию соединительной ткани в мягких суставных оболочках и мезенхиматозную реакцию — лимфоидные, гистиоцитные и плазматические клетки.

После третьей и последующих инъекций развивается септический периартрит. Возникшие артритные явления локализуются преимущественно в мягких тканях вокруг суставов. Синовиальные оболочки и суставные поверхности поражаются в незначительной степени.