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RHEUMATIC FEVER AND THE ARTERIES

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Cardiac lesions are no longer considered as complications of acute rheumatic fever, but are just as much a part of the disease as the affection of the joints. The frequency of the association of pericarditis, endocarditis, and myocarditis or any one of them with other lesions making up the picture of acute rheumatism is very great, and I think many will agree with Aschoff that every attack of rheumatic fever leaves its mark on the heart. It has been particularly emphasized that the myocardium is most often affected, and this for the reason, as we shall subsequently indicate, that the reactions to rheumatism occur in the neighborhood of the fine nutrient vessels of the myocardium. Inflammatory exudates occur about these fine arteries, and are replaced in the chronic stages of the disease, by fibrosis.

In general our conception of acute rheumatic fever is being modified with the progress of the pathological studies made upon it. That it belongs to the acute infections no one will deny, and many are willing to place a considerable stress upon the organism of Poynton and Paine as the causative agent. Whether it is the initial factor, or whether some other condition predisposes to the invasion of the diplococcus rheumaticus, we cannot here argue; but it is more than probable that the lesions as we find them in diverse parts of the body are the result of the action of these diplococci.

In the late stages of the disease process we not infrequently observe the association of heart, kidney, and arterial lesions making up a picture very different from that of acute rheumatic fever.

Nevertheless we are compelled to admit that all of them are either the result of the primary acute process or else that in the process of a vicious circle one lesion has followed the other. A close study of the various organs can alone determine the direct effect of this systemic disease upon each, and with this in view I have followed, in a few cases, the lesions to be observed in the arteries and more particularly the aorta during the course and different stages of rheumatism. This study presents purely the pathological side of the question. The cases studied were selected from a series of autopsies, only those being taken in which one or more previous attacks of acute rheumatic fever were established in the clinical history and in the presence of interstitial myocarditis.

In classifying the cases here examined I have divided them into three groups: (1) Acute rheumatic fever, first attack; (2) recurrent rheumatic fever, and (3) chronic rheumatism. It was interesting to find that the changes in certain arteries were analogous to the lesions found in the heart in the different stages of the disease; in fact, the resemblance of the inflammatory reaction in the aorta to that of the myocardium was very great. It may, however, at the very beginning, be pointed out that the causative agent of acute rheumatic fever has a predilection for the perivascular tissues of the smaller vessels, the arterioles, and does not appear to disturb the larger arteries directly, save by damage in the vicinity of the vasa vasorum. Up to the present I have not made a systematic study of the arterioles of all the viscera of the body. My observations have, however, indicated that the arterioles of the internal organs, except the circulatory system, are not attacked with any constancy.

The aorta shows a fairly typical lesion. This lesion is particularly to be observed in the ascending limb and in the arch, less frequently in the descending thoracic and seldom in the abdominal aorta. The distribution of the process in the aorta is similar to that of syphilis, and, as a matter of fact, to that of many bacterial infections. The main coronary arteries of the heart are inconstantly involved, while, on the other hand, the finer ramifications of this vessel are invariably affected, being a part of the myocardial disease which forms an important factor in the pathological picture of rheumatic fever. Moreover, the arterioles passing to the serous

cavities, particularly the pericardium and the joints, partake of a reaction similar to that of the nutrient arteries of the aorta and heart. In how far the vessels of the meninges and the abdominal viscera respond to the irritant present in rheumatism I am not prepared to say.

Acute Rheumatic Fever (First Attack). Of such cases I have had only three to autopsy, aged nine, sixteen, and nineteen years respectively. All of them had associated cardiac disease, two with pericarditis, all with acute interstitial myocarditis, two with fresh mitral deposits, and one with recent mitral and aortic vegetations. The youngest case had suffered choreiform attacks during his illness.

The arterial findings being similar in these cases a single description will suffice. Macroscopically the arteries were but little changed, the oldest individual alone showing superficial fatty streaks in the intima. The elasticity of the aorta was not altered and none showed the inflammatory foci to the naked eye. Microscopically, however, there was a very striking picture present in each case. Sections of the ascending and transverse portions of the aorta showed that the intima was not thickened and the lamellæ of the media appeared regularly disposed. In the media, however, the arterioles appeared more prominent than usual, and these nutrient vessels encroached beyond the outer third into the muscularis. These arterioles had an edematous perivascular infiltration in which aggregations of lymphocytes and plasma cells were constantly found. Moreover, the elastic fibers of the media in this vicinity were interrupted, often appearing as if mechanically broken. Muscle elements of the media in the neighborhood of the vasa vasorum had also, in part, disappeared, an indication of some local toxic agent surrounding the nutrient vessels.

In the adventitia the infiltration by inflammatory cells was very extensive. Lymphocytes and plasma cells were diffusely scattered through the tissue, while more densely aggregated cells were seen about some of the vessels. Polymorphonuclear leukocytes were also seen, but in relatively small numbers. Occasionally areas indicating endothelial proliferation were observed in the vicinity of the capillaries. The connective tissue was loose and rather edematous, while the capillaries were much congested. In some of the reactions

fibroblasts were apparent, but no new connective-tissue fibers were observed.

The main coronary arteries of the heart were but little affected, save at the periphery of the adventitia. The smaller arterioles, however, showed a dense infiltration about them, with a considerable change in the appearance of the heart tissue in the immediate vicinity. In places the infiltrating cells were mainly lymphocytes, while in others again leukocytes and endothelial cells appeared to make up the main type of invading cell. The heart muscle adjoining these involved vessels showed evidence of degeneration and not infrequently complete death. In the place of these heart muscle cells there remained a homogeneous and almost structureless material with occasional evidence of replacement by fibroblasts. The perivascular infiltration was very widespread and quite uniform throughout the heart muscle.

It is indicated in the above that the main reaction occurring about the arteries during the acute stage of rheumatic fever is in the outer coats. The adventitia and the media are probably simultaneously involved, at times by way of the nutrient vasa vasorum, or in the case of the smaller vessels, the arterioles, directly from the perivascular lymph stream. The reaction is of the acute non-suppurative variety, in which the lymphoid type of cell and the endothelial cells play the important part. Similar to the reaction in the heart, the tissues of the arteries suffer directly from the harmful agent of acute rheumatism, in which both muscle cells and elastic fibers in the immediate neighborhood are destroyed.

Recurrent Rheumatic Fever. Four cases of recurrent rheumatic fever were studied. Their ages were twenty-eight, thirty, thirty-six, and forty-four years respectively. In each case there was a history of one or more previous attacks, and the heart showed the presence of subacute and chronic interstitial myocarditis to a varying degree. Moreover, some form of recurrent endocarditis was present in each heart.

Sections of the aorta showed the intima to be fairly intact and with no definite areas of thickening. The arrangement of the media appeared quite normal and regular in its inner half. However, it was observed that the vasa vasorum were quite frequent in the

middle third of the media, and that these small bloodvessels were surrounded by an excessive amount of fibrous tissue, along with a cellular infiltration consisting of lymphocytes, plasma cells, and a few endothelial cells. This perivascular infiltration was quite constant, and at times the aggregation of wandering cells was quite marked. In some areas it was definitely indicated that some of the muscle cells and elastic fibers had been destroyed and their place taken by a meshwork of new connective tissue. Polymorphonuclear leukocytes were for the most part wanting.

The adventitia also showed a lymphocytic infiltration around the vasa, as well as an increase in the connective tissue close to the media. Some of the nutrient vessels showed a thickening of their walls with a narrowing of their lumina.

It is evident that in these cases of recurrent rheumatic fever certain changes have been produced about the aorta, which subsequently lead to an increase of fibrous tissue in the outer portion of the media and in the adventitia. Moreover, it would appear that with each recurrent attack of the disease a new non-suppurative inflammatory reaction occurs in the sites of the former lesion. Therefore in the recurrent types of the disease various stages of the inflammatory process may be observed in the same specimen. The former attacks are indicated in the presence of adult connective tissue, while the recent progressive condition is seen in the non-suppurative inflammatory infiltration.

Chronic Rheumatism. All of the eight cases considered in this class were such as had suffered, for a considerable time, recurrent or progressive heart disease associated with acute rheumatic fever. The majority had died of broken cardiac compensation. The most constant cardiac finding was a chronic interstitial myocarditis, while an old endocarditis involving one or other of the valves was not uncommon. In this series of cases the lesions of the aorta and of the smaller coronary arteries was quite constant, but varied in the extent of the reaction. Macroscopically the intima was more or less nodular. At times the thickening of the intima was quite extensive, while, however, it showed little evidence of degeneration or atheromatous change. There was usually a great loss in the elasticity of the entire vessel wall, and the artery felt thicker and heavier.

Sections of the aorta showed that the thickened intima consisted mainly of a hyaline looking fibrous tissue, in which numerous fine elastic fibers were seen. The media appeared compact and dense, and the muscle cells did not appear as frequent as usual. The vasa vasorum were seen commonly in the middle third of the media, and some were found in the inner third. The majority of these vessels had their direction parallel to the elastic fibers and a considerable number were surrounded by a fibrous tissue, which had replaced the muscle cells and interrupted the concentric layers of elastic fibers. A slight lymphocytic infiltration surrounded many of them, and plasma cells were also present. Polymorphonuclear leukocytes were not present. In the adventitia there was a fairly dense stroma of connective tissue built closely upon the outer border of the media, so that the thickness of the entire wall was increased. The small bloodvessels were not congested, but in their vicinity there were some scattered lymphocytes. The vasa vasorum in the adventitia had thickened walls.

The changes observed in the vicinity of the coronary arteries of the heart are those with which we are all familiar in chronic interstitial myocarditis. In fact, these very interstitial myocardial changes which have attracted our attention are the result of non-suppurative processes occurring in the neighborhood of the finer coronary arteries. Thus the pathological process about the arteries in the late stages of rheumatic fever is one of inflammatory fibrosis. This fibrosis is particularly evident in the first part of the aorta and about the smaller branches of the coronary artery of the heart.

Discussion. There appears to be a fairly definite form of arterial disease which is associated with rheumatic fever in its different stages. The arteries react to the irritant in a true inflammation and this reaction is to be observed in the adventitia and the outer portion of the media. In the acute stages the inflammatory exudate is of the non-suppurative variety in which the lymphoid cell is most prominent. The inflammation occurs particularly in the neighborhood of the smaller arteries, while the medium-sized vessels are little affected. On the other hand, the larger arteries, which are supplied in their outer coats by nutrient vessels, are damaged by the inflammatory process which travels along the vasa vasorum.

During the acute process the fixed tissues in the immediate neighborhood of the small arterioles are damaged or even destroyed, but abscesses are not formed. In the aorta the destruction of tissue is particularly noted in the loss of muscle and elastic elements. Similar degenerations are common in the heart. At times the degenerative processes are quite extensive, leading to the loss of considerable tissue of the part, and probably weakening the media. The intima of the arteries does not appear to be primarily affected. In the early stages a slight superficial fatty change is sometimes noted, while later, in the chronic stages, the intima proliferates, giving rise to a nodular endarteritis.

The repair, following the inflammatory process of the media and adventitia of the arteries, is by fibrous tissue. Thus the aorta in chronic rheumatism is disturbed by a patchy fibrosis, better spoken of as chronic productive mesaortitis. It is evident that the arteries which are involved in a chronic mesarteritis have lost much of their elasticity and may become subject to a diffuse dilatation of their lumen.

In some respects the acute stage of the mesarteritis resembles the early process of syphilis, but with this difference, that the destruction of the tissues in syphilitic mesarteritis has other qualities, in that the lymphoid infiltration about the vasa vasorum is greater, gummy necroses are often seen, and granulomatous tissue surrounds the areas of greatest reaction. The invasion of the capillaries through the media toward and into the intima is more marked in syphilis, while the nodular endarteritis is also far more decided.

In 1903 Chiari suggested the division of productive mesaortitis (as well as mesarteritis) into two groups, type "A" and type "B" respectively. His type "A" is a chronic inflammatory disease of the media secondary to an intimal process. The mesarteritis type "B" is a primary inflammatory process involving the media, which is usually of infectious origin and most commonly due to syphilis.

As I have on a previous occasion pointed out, Chiari's classification is a good one, but it must always be borne in mind that this type "B" (productive mesaortitis) must include other infectious inflammatory conditions of the media than syphilis. As has been indicated above, the lesions occurring in the arteries in rheumatic fever belong to the group of productive mesarteritis type "B."