ANNALS OF THE RHEUMATIC DISEASES

THE RHEUMATIC NODULES IN THE HEART

BY LUDWIG ASCHOFF

IN 1904 Tawara and I, working in collaboration, decided that the formation of nodules in the heart was a characteristic change in rheumatic myocarditis. This latter term we used to describe a change which was the most significant local manifestation of rheumatic fever, or of specific infective rheumatism if one prefers the term recently used by Gräff. All authorities are today required to give more exact definitions of what they mean by "rheumatism." It must be admitted that this term has been used very loosely, and that it can never mean more than a symptom or group of symptoms which may appear in a variety of conditions. In this present paper I shall confine myself to that specific infective rheumatism, to use Gräff's term, or if one prefers it, the Bouillaud-Gräff disease.

The rheumatic nodules are found characteristically in this condition, and they are located for the most part in the heart muscle or in the pericardium. They may nevertheless be discovered, likewise, in the larger blood-vessels which arise from the heart, such as the aorta and the pulmonary artery, though here they are generally found in the parts which are also covered by pericardium. Nodules have also been discovered in the tendons of the musculature, in aponeuroses, the dura mater, the walls of the blood-vessels, and even in the skin in the neighbourhood of affected joints.

The terms "cardiac" or "visceral" rheumatism are used in order to describe those forms of rheumatism in which either the heart or the organs of the body are most affected. One has even heard the term "subcutaneous" rheumatism. Gräff has provided a very adequate description of the nodules found in the subcutaneous form of this disease, and has shown that they

bear a more or less close resemblance to nodules found in those conditions in which the viscera are most affected.

In this paper I will confine myself to a description of the rheumatic nodules which occur in the heart muscle, for these may be taken as the prototype of the granulomata which occur in rheumatism in general, and are in fact specific to these conditions. These rheumatic nodules, as seen in the heart muscle, are, if at all numerous, found to have a perivascular distribution. It is not common to find them spread further in the adjacent tissues. The nodules are formed from hypertrophied cells and are roughly cylindrical in shape. When the febrile stage of rheumatism has lasted for some time, the nodules gradually become scarred. In this way the non-specific but characteristic lesions round the vessels of the myocardium reach their final development.

In recent years two distinct objections have been advanced against our old conception of these appearances. It has been suggested that in the early stages of the disease the nodules become apparent as a result of a fibrinoid degeneration of the ground substance, this being particularly easily seen when Pap's stain is used. It is suggested that the cellular increase in the nodules is essentially secondary to the first change we have described. According to Klinge, the damage which develops in rheumatism occurs in all parts of the body, and in the first place involves the firm connective tissue. He thinks that the fibrinoid degeneration which follows, and which leads to the formation of the rheumatic nodules, is itself that stage in the process which is characteristic of the formation of these lesions.

The second objection is that the nodules are in no way specific to rheumatism. Nodules may occur in the heart muscle in scarlet fever which are indistinguishable from the others. In such cases I believe that there is a mixed infection with the scarlatinal toxin. Gräff has shown, as is admitted, that rheumatic infections appear to start from the same focus as does scarlet fever—namely, from the tonsillar tissue of the mouth and throat. For this reason the simultaneous appearance of rheumatic nodules and the infiltrations of scarlet fever in the heart muscle are not surprising. Attention was, at my instigation, also directed to this point by the investigations of I. W. Magladery and F. D. Billings (Stöber).

It is a striking fact that from time to time valvular lesions

of the heart are noted when scarlet fever has subsided. These may be explained by only one hypothesis, which is that in addition to the scarlet fever there has been a rheumatic infection in the sense already mentioned. In epidemics of pure scarlet fever valvular defects do not develop.

Masugi has recently drawn attention to the occurrence of rheumatic nodules in the heart muscle side by side with miliary tubercles. In my opinion we have in these cases also a mixed infection with the rheumatic virus and the tubercle bacillus. There is nothing surprising in the fact that when acute specific infective rheumatism develops, the tubercle bacillus is activated and brought into the blood stream. After all, the majority of human beings exhibit a primary focus in the lymph nodes round the hilus of the lung, and acute rheumatism; or the Bouillaud-Gräff disease, has a particular incidence on the heart and pericardium, which are close to the hilar regions of the lungs.

It is also very interesting to note that in miliary tubercle, as in streptococcal diseases, which may occasionally follow scarlet fever or acute rheumatism, one finds enlargement of the spleen. In uncomplicated acute rheumatism there is, according to Naegeli, no splenic enlargement at all.

I have said enough to refute the second theory which was advanced. Having surveyed the world literature I am still convinced that rheumatic nodules, as seen in the heart muscle, are specific to this rheumatic disease.

We must not neglect a consideration of the theories which try to account for the cellular hypertrophy in the nodules. I am giving now some pictures of a case of acute recurrent rheumatism involving the heart, which led to the death of a child aged six years. Despite the cellular overgrowth which has caused the formation of the nodules, there is no trace of a fibrinoid degeneration of the ground substance (Figs. 1, 2, 3 and 4). I therefore think that I have brought sufficient evidence to refute the ideas expressed in the systematic drawings made by Klinge. In this case in particular the multiplication of the cells was very marked.

Klinge has emphasised that even in the presence of cellular overgrowth fibrinoid degeneration is still easily seen. It is only when scar formation has occurred and the cells have shrunk down to form the nodule that the fibres return to the normal state.

"In this primary lesion, which exhibits a swelling of the

ground substance of the connective tissue with consequent degeneration, we believe that one sees the essential and specific change which is found in all rheumatic lesions known. From this primary lesion there develops—by multiplication of the mesenchyme cells—the cellular nodules” (F. Klinge, *Der Rheumatismus Ergeb. allgem. Path.*, 1933, xxvii. 32).

In the case we ourselves have described, typical rheumatic nodules are visible only here and there. In most of these one may see multinucleated or even giant cells. The latter may even be so numerous that the nodules, as may be seen in Fig. 6, resemble tubercles to some extent.

Anyone conversant with the case will nevertheless have no doubt that it was one of true acute rheumatism, and not miliary tuberculosis. In this case I also refuse to believe that there was any mixed infection. From the position of the nodules in the perivascular tissues, from their structure and the composition of their cells, I think tubercle may definitely be excluded.

The origin of the cells in the nodules has been a matter of dispute, but most of them are thought to be fibrocytes or histiocytes. No agreement on this matter has yet been reached. The sections which I am now showing do not help to a definite conclusion, although they are stained with pyronin. The question must therefore be allowed to remain open.

Both these types of cells occur in the connective tissue of the heart, and the following sentence, as printed in our first article on this subject, still holds good: “We think that there is no conclusive evidence which would make clear whether the cells are derived from the lymphocytoid elements or from the connective tissue” (p. 41). This statement is equally true if it is applied to the tubercle.

There is one further matter which needs discussion—namely, the part played by the granulocytes, especially the eosinophils, which ought to occur in large numbers if the nodule was the expression of an allergic phenomenon. I have stated in another place that the number of leucocytes in the nodules varied very greatly. As a rule one does not find granulocytes in the nodule itself, certainly not eosinophils. Such were our findings in the case now presented. Leucocytes in any number are only seen inside the nodule and in the area around it (Fig. 5). I think one may therefore say that the number of leucocytes in the nodule varies considerably.

FIG. 1.

FIG. 2.

FIG. 1.—PERIVASCULAR NODULES FORMED OF NUMEROUS CELLS, SOME OF WHICH ARE MULTINUCLEATED.

Lymphocytes are seen in the surrounding tissues. Hæmatoxylin-eosin. ($\times 85$ times.)

FIG. 2.—CONNECTIVE TISSUE FIBRES ARE SEEN PASSING THROUGH A NODULE, BUT WITH NO DEGENERATIVE SOFTENING.

Multinucleated and giant cells are visible in that part of the nodule lying above the blood-vessel. Van Gieson's stain. ($\times 180$.)

Ludwig Aschoff.

FIG. 3.

FIG. 4.

FIG. 3.—HIGHLY CELLULAR SPINDLE-SHAPED NODULE WITH MULTINUCLEATED AND GIANT CELLS.

The fibres are thrust apart, but not damaged (or warped).
Tibor-Pap stain. ($\times 180$.)

FIG. 4.—UNALTERED FIBRES TRAVERSE A RICHLY CELLULAR NODULE.
Very numerous lymphocytes. Tibor-Pap stain. ($\times 160$.)

Ludwig Aschoff.

FIG. 6.—NODULE WITH MULTINUCLEATED GIANT CELL.
Note resemblance to a tubercle. Hematoxylin-eosin. ($\times 200$.)

FIG. 5.—MULTIPLE NODULES WITH GIANT CELLS AND LYMPHOCYTES IN THE SURROUNDING TISSUES.
Hematoxylin-eosin. ($\times 140$.)

It is possible that the proportion seen varies with the stage of development of the nodule, although in this acute and recent lesion no eosinophils can be seen. But the lymphocytes, in addition to the actual cells forming the nodule, play an important part.

The nodules are, as I have already stated, particularly rich in the characteristic cells. The cells may unite to form giant cells with two or more nuclei (Fig. 6). These do not, however, bear any marked resemblance to tuberculous giant cells. For the most part they are multinucleated structures such as may also be seen in osteoclasts. We may here again draw attention to the fact that some believe osteoclasts derive from the histiocyte cells, while others are inclined to group them with the fibrocytes.

As a result of my experiences I can state emphatically that the rheumatic nodules which appear in the myocardium are specific to the Bouillaud-Gräff disease (rheumatic fever). It is in no way essential that the formation of the richly cellular nodules should be preceded by fibrinoid degeneration of the ground substance. If the changes associated with scarlet fever or tuberculosis are seen side by side with what are certainly rheumatic nodules, then I consider the picture must necessarily be one of a mixed infection.

With these words I will conclude my remarks on the rheumatic nodules, which are cell formations specific to, and exclusively seen in, the Bouillaud-Gräff disease.

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