ENDOCARDIAL THICKENING ASSOCIATED WITH DISEASED VALVES

BY

W. J. S. STILL

From the Royal Free Hospital

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Focal endocardial thickening is often found in relation to diseased valves and is particularly frequent on the upper part of the interventricular septum in association with aortic regurgitation. Some of the endocardial thickenings may be in the form of endocardial pockets or false valves (Fig. 1), and at times a similar type of localized thickening is found in the aortic intima just above the valve. It is now generally accepted that these lesions are the result of the abnormal jets and eddies of blood set up by the distorted valve impinging on these particular areas of the endocardium or intima (Krasso, 1929; Saphir, 1930; Ingham and Henthorne, 1938; Hellerstein, 1947).
What appears to be a related type of endocardial thickening constitutes one form of sub-aortic stenosis. This consists of a semi-circular or annular bar of endocardium situated just below an aortic valve, which is usually stenosed or otherwise diseased. Gruenwald (1947) considered this type of endocardial thickening to be the result of inflammation, but it seems likely that many of the examples of subaortic stenosis combined with aortic valve disease are due, like the focal thickenings, to abnormal blood flow (Saphir, 1953).

The pathogenesis, as distinct from the aetiology, of these thickenings has hardly been considered in earlier writings, and it was of some interest therefore to find mural deposits of fibrin in random sections of focal thickenings. To find out whether these deposits were of any significance, a more detailed study of focal thickenings was made in ten cases of aortic valve disease and in two cases of adult sub-aortic stenosis. This paper describes the results of the study and illustrates the important part played by mural deposits of fibrin in the pathogenesis of these types of thickening.

RESULTS

The focal thickenings show some variation in their histological appearance. Some are compact and hyaline in structure (Fig. 2), while others are more fibrillary and cellular (Fig. 3); and all grades between these may be found. A few, particularly some of those most obvious macroscopically, are amorphous in appearance and friable when cut. These usually contain quantities of partially organized thrombus (Fig. 4). The principal fibrillary content in all is collagen, and there is only slight elastic tissue proliferation, which occurs at the base of the thickening and round its circumference. None of the plaques show generalized elastic tissue proliferation. All show some
degree of subendocardial fibrosis: in some, this change is conspicuous (Fig. 4); in others, it is minimal in degree (Fig. 3) and the appearances suggest that the thickenings are lesions superimposed on the endocardium and that any changes in the subendocardium and adjacent myocardium are secondary events.

The presence of partially organized mural thrombus in the larger thickenings is usually not hard to find, and serial section of the more compact plaques show that mural deposits of fibrin occur on many of these also. In most, the deposits are small (Fig. 5), but may be multiple, while in others the thrombotic material is more extensive, and these plaques have usually a hyaline appearance. The smaller deposits always show evidence of active incorporation into the endocardium, while the larger thrombi often show only minimal cellular activity around them. It seems likely that the latter circumstances lead to the production of the larger, more amorphous plaques, already described.

Four of the ten hearts with focal thickenings showed also endocardial pockets or pseudo-valve formation. These too were found to vary in appearance in a similar manner to the focal thickenings. Some were well-formed structures, composed principally of collagen with a little stiffening of elastic tissue on the surface exposed to the regurgitating stream of blood (Fig. 6). Others were smaller in size, more hyaline in appearance, with a core of material that at times stained as fibrin (Fig. 7), and contained no elastic tissue. Again, others were thin cellular tags of fibrous tissue flattened against the endocardial surface so as not to appear to be separate until examined histologically.

It is supposed (Ingham and Henthorne, 1939; Hellerstion, 1947) that these endocardial pockets are formed from pre-existing collagenous thickenings which have been dissected by the force of the
regurgitating blood stream. While this may be so, it is clear from the appearance of early formations, such as that seen in Fig. 8 and some of the well formed smaller lesions, that some at least arise directly from deposited thrombotic material and that the pockets begin to form soon after deposition has occurred. It would seem likely that this is the time, when the deposited material is only partly organized and therefore malleable, that the pockets can form most easily. These pockets may attract further mural deposition after their formation (Fig. 7) and it may be that some pockets silt up in this manner and become focal thickenings, a reverse of the accepted sequence. Only four of the ten hearts showed these endocardial pockets, and their formation did not appear to depend on the degree of functional disorder of the valve or on the number of focal thickenings or on their distribution. In one heart (Fig. 1) almost all the focal thickenings were of the pocket variety.

Three of the hearts showed focal areas of aortic intimal thickening just above the aortic valve (Fig. 1). These were similar in gross appearance and position to the intimal thickenings ascribed by Krasso (1929) to the traumatic effect of abnormal jets of blood on these areas. They differ, however, in their histological structure from the endocardial lesions. They, the aortic lesions, tend to project into the lumen less, they are also more hyaline in appearance than the majority of the endocardial lesions, and in the depths of the thickening there is an area of medial destruction, well shown in sections stained for elastic tissue (Fig. 9). This destruction is confined to the centre of the lesion, although the intimal thickening is conspicuous for some distance on either side. The appearance is quite unlike that of a fibrous atheromatous plaque. No mural thrombi were found in any of the three lesions examined, but each had a layered appearance suggesting it may have been built up of successive mural deposits.

The structure of the endocardial thickening in sub-aortic stenosis is similar to that of the focal
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thickenings, although the degree of thickening is much greater. The main fibrillary content is collagen and any elastic tissue is confined to the base of the thickening, or may sometimes be present at the edges (Fig. 10). At times the elastic tissue in the base shows fragmentation, a change that is not apparent in the focal thickenings. The two annular thickenings examined varied in the amount of subendocardial and myocardial fibrosis present. In one it was conspicuous, in the other minimal in degree. Both, however, showed areas of mural thrombosis and fibrin deposition on their surface, and in the part of the thickening where these occurred, the appearance was similar to that of the larger and more amorphous of the focal thickenings (Fig. 11). In both examples there were, distal to the sub-aortic thickening, smaller areas of focal thickening, and in one case endocardial pocket formation. These were similar in structure to the other focal thickenings previously described.

DISCUSSION

Both these types of endocardial thickening are apparently the result of abnormal jets and eddies of blood set up by a diseased and distorted valve. Both show mural deposits of fibrin which are in the process of being incorporated into the endocardium, and the evidence suggests that these processes occur at an early stage in the formation of the thickening and also provide suitable circumstances for the production of pseudo-valves.

These appearances, namely mural thrombus formation, have not gone unnoticed in the past. Saphir (1930) found organizing thrombi in two out of six cases of endocardial pocket formations, but he ascribed these thrombi to an underlying acute bacterial endocarditis of the aortic valve which was present in these particular cases, and did not believe that mural thrombosis played any

Fig. 8.—Two endocardial pockets in the process of formation. The material lining the clefts or potential clefts stains as fibrin. H. and E., × 150.

Fig. 9.—An aortic lesion. Note the destruction of the media as displayed by the absence of elastic tissue. Weigert's elastica, × 130.
part in the formation of focal thickenings in general. It is clear, however, from the evidence presented here that mural deposition does not depend on bacterial infection of the endocardium for its occurrence, since none of the hearts in this series showed any inflammatory change.

These mural deposits are clearly an important factor in the thickening process, and indeed, it is not surprising that this should be so, since the continual trauma evoked by jets of blood impinging on a particular area of endocardium would seem to create suitable conditions for deposition. The conditions are similar to those that dictate where fibrinous vegetations will occur on the valve, and mural encrustation on the left atrium in acute rheumatic endocarditis (Hadfield and Garrod, 1947).

**Summary**

Focal endocardial thickening associated with diseased aortic valves and the endocardial thickening in sub-aortic stenosis were examined histologically. It was found that, in both these types of endocardial thickening, mural deposits of fibrin were present and were being incorporated into the endocardium. The importance of this process in the formation of the thickening is emphasized.

**References**
