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Introduction

Introduction

Ischaemic heart disease resulting from degenerative disease of the coronary arteries is by far the most common single cause of death and it continues to rise steadily each year. Coronary artery disease is sometimes called `The Captain of the Men of death' and is by far the most frequent cause of sudden and unexpected deaths which constitute a significant portion of the autopsies that are conducted by Forensic Pathologists in our country. Though these deaths are natural, they carry medicolegal importance because these deaths occur in persons who have been apparently healthy, without any diagnosed disease that can be attributed to the cause of death or, the period of illness before the supervening of death is so short that the disease cannot be diagnosed so early. The circumstances of these deaths carry immense medicolegal importance and hence warrant detailed autopsies to establish the actual cause of death and rule out any foul play. Moreover a Medico-legal expert may have to appear in civil proceedings for compensation of claims and should readily admit the likelihood of precipitation of death by work stress, indeed by any exertion. If collapse during a period of exertion is followed by sudden death a few hours later it is likely that autopsy will reveal atherosclerotic narrowing of a coronary artery, often complicated with occlusion by a thrombus.

Though the cause of death, in such cases, as that being myocardial ischemia following atherosclerosis in usually accepted as confirmed by the discovery of severe coronary artery disease, in many instances further confirmation of some acute terminal episode in the natural history of the disease is essential either on purely academic grounds of for some more cogent reasons if justice is to be done to those involved in litigation. For instance many deaths are labeled as "coronary artery disease" even after postmortem examination, when in fact death is possibly due to some other cause. This most frequently occurs in older patients where some degree of coronary stenosis is almost universal. In these cases, where the true cause of death is relatively occult, the tangible evidence of severe coronary atheroma is naturally accepted as the cause of death. Though these cases may be relatively few compared with the large mass of true coronary artery disease, they certainly occur and in any event on a scientific basis are inspired guesswork.

Another group numerically much smaller but medico-legally more important, are those cases in which some unnatural event, such as a road accident, is suspected to have been precipitated by acute myocardial ischaemia. There have been cases in such accidents, where the drivers were shown to have severe coronary atheroma at postmortem and in which, the circumstances

suggested that they may have collapsed while driving. In such cases any technique where an early infract can be demonstrated would be of assistance in reconstructing the circumstances of the accident and this could be of vital importance from the point of view of insurance, compensation or even criminal responsibility. So, too, industrial accidents such as falls may be attributed to myocardial ischaemia without appreciation of the implications by the dependents.

The likelihood of identifying an early infarct depends on the mechanism of the terminal cardiac failure. Where death is due to sudden ventricular fibrillation unassociated with any new obstructive lesion in the coronary vessels, death may supervene far too rapidly for any detectable changes to occur in the myocardium.

This state of affairs is very common and is seen in cases with generalized coronary stenosis, especially where there is associated hypertension and consequently a large ventricular mass requiring adequate supply. Interference with the conducting system and conditions where there is widespread fibrosis from previous coronary occlusions, frequently lead to sudden immediate death with little hope of even the earliest stages of infarction being detectable by means. Excluding these, many other coronary lesions lead to ischaemic damage in the myocardium distal to the occlusion.

Though an infarct can occur without any apparent acute alteration in the nature or severity of the coronary lesion, frequent precipitating causes are ruptured atheromatous plaques, subintimal haemorrhage and the presence of thrombosis. The latter condition though most universally regarded by clinicians as the sole cause of myocardial infarction, is in fact relatively infrequent.

Whatever the causative factor inducing damage in the myocardium, the sequence of events is relatively uniform. There is a latent phase where no naked eye changes are visible at postmortem examination, even in a body which is fairly fresh, with no postmortem changes to obscure the findings. For a period of 10 to 18 hours or some times even longer, traditionally no unequivocal changes can be seen. In the absence of any postmortem change and with considerable experience, a hint of early infarction may sometimes be gained at around 8 hours, but this is exceptional and unreliable, the earliest abnormality that is seen is a loss of luster of the cut surface of the muscle.

The following features are characteristic of infarction in sections stained by haematoxylin and eosin. Eosinophilia, swelling of Muscle-fibers, granularity of cytoplasm, blurring of cell membranes, corrugation of dead muscle fibers, increase in interstitial cells, which occurs at about 18 hours.

The significance of these changes is difficult to interpret due to uncertainty about the time of onset. There seems to be evidence that the pathological changes may antedate the clinical sings and symptoms by several hours. As both technical faults and post-mortem autolysis can produce the appearance of granularity of the cytoplasm it cannot be regarded as a reliable sign of an infarct about 2 hours old. Increased eosinophilia can be seen at 4-6 hours but even in the most favorable circumstances a firm diagnosis of infarction less than 6 hours old cannot be made from sections stained with Haematoxyline and eosin.

The first substantive diagnosis may be obtained in the 8 to 12 hour range, though again this limit may be considerably extended. At the lower end of this time limit the changes are too vague to be reliable, sometimes the experienced observer may strongly suspect infarction, but the changes are so slight and subject to postmortem autolysis that they are unreliable. Apart from this unreliability, the histological methods are long-drawn by the fact that they take a long time for their preparation, fixation and processing, as a result of which it may be difficult to apply these methods in routine postmortem work, where the report is expected immediately after conclusion of the postmortem

examination. Moreover the actual site of the infarction may be missed while taking sections from the heart musculature for histological examination in the absence of gross localizing techniques.

The realization of the need for establishing the diagnosis of myocardial infarction in the initial 8 hours, where definite evidence of infarction is lacking, has propelled a number of studies on the histochemical, electron microscopic and fluorescent microscopic changes. However majority of them have been performed on experimental animals, these being sacrificed at fixed intervals after either mechanical ligation of the coronaries or following injection of necrosis producing drugs. Fixation or freezing of the tissues was performed immediately on sacrifice, thus postmortem changes being virtually eliminated, as a result of which the animal results cannot be transferred with confidence to the human material where postmortem autolysis may be all important in distorting the reactions.

Numerous investigations have been carried out on the enzyme chemistry of normal and infarcted myocardium. The basic premise behind most such enzyme reactions is related to the clinical tests for myocardial infarction. The well established serum glutamicoxaloacetic (SGOT) and pyruvic (SGPT) transaminase tests used in clinical diagnosis depend upon the leaking out of the myocardial enzyme, due to cellular break down in the infarcted area with consequent liberation into the circulating blood. Thus an increase in the blood level should be accompanied by a decrease in the infarcted area. Efforts have been made to estimate SGOT and SGPT in the cadaver blood as a diagnostic index of myocardial necrosis but the techniques are difficult and results are uncertain, the histochemical approach appears more rewarding. Many different enzyme systems have been used but the most reliable are the oxidative enzymes such as dehydrogenases, monoaminexidases, 5 nucleotidase, acid and alkali phospharases, the esteraes, AT Pase, glutaminase, cytocharome oxidase and L-hydroxybutyric dehydrogenase. Whatever system is used, the end result is a diminution or absence of deposition of the dye in the infarct, due to failure of the enzyme to act upon either endogenous or added substrates.

Since coronary heart disease is such a large determinant of morbidity and mortality, it is important to have a knowledge of the structural pathology of the affected coronaries, for example where the arterial stenosis most frequently occurs how much of the artery is likely to affected how often several arteries are involved the severity of stenosis of the affected arteries and development and progression of the disease as an age related phenomenon.

It is a generally held belief that the original lumen must be reduced to 20% or less before the ischemia in the distribution zone is sufficient to cause myocardial necrosis. However undoubted infarction is experienced in autopsies numerous times in the absence of 80% stenosis. Sometimes an infarct exists with virtually normal coronary arteries. A more common situation is the findings of complete thrombosis of a major vessel with no sign of infarction. In this case either an effective collateral circulation provided an alternative blood or the victim died before signs of infarction had time to develop. Also many times significant stenosis of coronary arteries is encountered in deaths due to some other natural disease, and due to unnatural causes like accidental trauma, poisoning. In these cases the query always arises whether myocardial ischemia might have contributed to death.

With these considerations it was thought worthwhile to study the myocardial ischemic changes, by gross histochemical staining methods which were chosen because they can detect early ischemic changes. The histochemical method for studying the enzyme reaction in the myocardium, to

differentiate between the healthy myocardium and the infarcted myocardium is by far the most sensitive method for diagnosing early myocardial ischemia, is comparatively simple as compared to other methods used and can be performed with a minimum of apparatus in the postmortem room.

A brief account of the anatomy and pathology of coronary artery disease is given below.

The anterior descending branch (anterior inter ventricular) which courses down from the interventricular septum to the apex, and the circumflex branch (left coronary artery) which follows the left atrioventricular sulcus to reach the back of the heart. The right coronary artery arises from the right coronary sinus of the aorta, passes behind the pulmonary trunk, and follows the right atrioventricular sulcus without giving off any major branch near its origin. At the right border of the heart a small marginal vessel is given off and the main part of the vessel continues to the back of the heart where it becomes the posterior descending (posterior interventricular).

Developmental anomalies of the proximal part of both coronary arteries do occur but are quite rare. However, there is considerable variation in the arrangement of the vessels on the posterior aspect of the heart. The territories of the left circumflex and right coronary arteries are very variable, and one vessel may take over almost the whole of the function of the other. This is of importance in determining the site and extent of infarction when one of the vessels is occluded.

The localization of atheromatous stenosis and occlusion varies greatly in different parts of the system. In various published analyses the ranges for the frequency of the sites of fatal stenosis with or without thrombosis are : the anterior inter ventricular coronary 45-64 per cent, right main coronary 24-46 per cent, left circumflex coronary artery 3-20 per cent and the left main coronary 0-10 per cent. Those most frequently affected site is the first part of the anterior interventricular artery. The incidence at this site is often said to exceed the combined incidence in all other parts of the coronary system.

Atheroma may be very localized and extreme stenosis may occur in few millimeters of the vessel, the adjacent segments being almost normal. This is particularly true of disease in the anterior interventricular artery where the affected part is almost always within 2 cm of its origin.

Next in frequency is the proximal part of the right coronary artery followed by the first part of the circumflex branch of the left vessel. Though the incidence of atheroma in the left circumflex is allegedly less than in the right main trunk the frequency of severe stenosis-as opposed to the mere presence of atheroma – was greater in the circumflex.

The short main trunk of the left coronary artery is the fourth most affected in decreasing order of frequency, this usually being combined with disease in the anterior descending artery. The right marginal artery and the posterior descending vessel (posterior interventricular) appear to be almost immune from severe atheroma, and posterior myocardial infarcts are usually the result of occlusion of either the right main trunk or of the circumflex vessel.

Severe atheroma is confined to the extramyocardial part of the course of coronary arteries i.e. that part which lies either on the surface of the epicardium or within epicardial fat. The lesions are absent or slight in the more distal parts of the vessels once they have once they have dipped into the muscle mass.

Types of Occlusion

1. Simple Atheroma: This may be concentric, when a central pin-hole will eventually from, or crescentric, with the lumen usually at the side of the vessel. Calcification is common, especially in older subjects, though even a grossly calcified 'pipe-stem vessel need not necessarily be severely stenosed.
2. Ulcerative Atheroma: The endothelium over atheromatous plaques frequently breaks down and exposes an ulcerated surface which is conducive to thrombus formation. The surface layer of any atheromatous plaque may become party or wholly detached, project into the lumen and cause obstruction.
3. Subintimal Haemorrhage: Tiny vessels in the wall of a coronary artery may rupture, causing sudden haemorrhage. The hematoma thus formed may force the plaque inwards, to further narrow or even occlude the lumen of the vessel.
4. Coronary Thrombosis: This may occur as already stated, on a stenosing plaque of atheroma, the endothelium of which is damaged. This precipitates mural thrombosis, which grows until it approaches the opposite wall. Often the site of thrombosis is already very much narrowed by the atheroma and only a 'pin-hole' or 'slit' remains.

Myocardial Infarction will occur in the myocardium distal to a complete occlusion of a coronary artery in the absence of an adequate collateral circulation, which can be of the following types:

Subendocardial infarction: This involves the layers of muscle adjacent to the lumen of the ventricle and does not extend to the outer surfaces of the heart. Microscopically, the layer of cells immediately beneath the endocardium is often found to the spared, due to intra-cardiac blood percolating through the lining. In spite of this, mural thrombosis is very commonly found over the inner surface of such infarcts. Intramural infarcts are less common, and are usually found as satellite areas to a more extensive infarct.

Transmural or full-thickness infarcts: These are usually of large extent and can give rise to both mural thrombi and pericarditis. The most common sites are the lower part of the interventricular septum the apex and lateral wall and posterior wall of the left ventricle. Purely subepicardial infarcts probably do not occur. Papillary muscle infarction: Infarcts of the papillary muscles in the left ventricle are quite common, especially of the posterior muscles, which seem very susceptible to ischaemia even in the absence of severe stenosis of the circumflex vessel. Rupture of one of the muscles is occasionally seen, with consequent deformity of the chordae tendineae and mitral valve cusps, and sudden death.

Gross Appearances

It is generally impossible to detect myocardial infarction by naked-eye examination within the first 8 hours after coronary occlusion and in many cases little or no change is apparent for up to 18 hours. The actual duration of the interval since occlusion is usually uncertain, and often bears no relation to the clinical symptoms. The following features are of help in recognizing the earliest states of infarction:

Edema and swelling of the infarcted area occurs early, and, on cutting the ventricle at post-mortem the affected muscle has a more coarsely fibrillar appearance than the normal. The bundles of

muscle seem separated and to have an opaque sheen, sometimes described as ‘grayish’ commonly this occurs in two planes, resulting in a granular appearance.

Color: The first alteration in color, which may be seen at about 8-9 hours, is more of a physical change in the cut surface than an actual alteration in hue. In fact, the infarcted muscle at this stage may be paler than normal, and have the opaque grayish sheen described above. The next stage in color change is a brownish-purple darkening, which progresses through a definite reddish blush until the muscle becomes necrotic and then yellow at 24-48 hours after occlusion. An alternative stage sometimes occurs after 24 hours called the ‘tigroid’ appearance, where there are alternate indistinct bands of red and pale areas. The fully developed infarct is yellowish, with a reddish marginal zone of hyperemia; this eventually becomes gelatinous and finally fibrous.

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