Pathology of myocardial infarction

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Abstract

Myocardial infarction (MI) is an increasing problem, worldwide. An appreciation of its causes and morphology helps provide a basis for development of new interventions, as well as its management, and in the future prevention. Studies have shown that the myocardium does not suffer sudden and complete permanent damage, but rather that it takes time for the damage to start and to progress. It is this interval that is used to salvage myocardium, post ischaemic myocardial events, thus improving patient outcomes. This paper discusses the morphological findings at different time points and illustrates them.

Keywords ischaemic heart disease; morphology of MI; myocardial infarction

Introduction

Recent technological advances have allowed for more in depth understanding of myocardial infarction (MI). Through gross examination, electron and light microscopy, and histochemical techniques, various stages of myocardial damage have been further identified and characterized. The results of such studies have practical applications, such as confirming diagnoses, providing insight into risk factors, which increase the risk of developing MI, and providing evidence of beneficial effects of revascularization following MI. This paper will summarize current knowledge of pathological changes seen following MI.

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Definition

MI can be defined as the irreversible myocardial muscle fibre damage caused by prolonged ischaemia, resulting from a sustained imbalance of perfusion, supply and demand.[1]

Epidemiology

In the United States, the annual incidence of new MI has been estimated as 610,000 events while recurrent events account for 325,000 episodes.[2] Over 7.9 million Americans have experienced an MI, and at least 15% of those who have experienced them will die from it, resulting in over 150,000 deaths per year.[2,3] The average age at initial MI is 64.5 years for men and 70.3 for women.[3] The annual age adjusted rate for initial MI per 1000 people is 4.2 in black men, 3.9 in white men, 2.8 in black women, and 1.7 in white women.[3] From 2003 to 2005, the age adjusted hospitalization rate for an MI was 215 per 100,000 people.[3] The worldwide incidence of MI per 100,000 of population is quite variable, with rates of 30 in Japan, 39.8 in France, 65.2 in Italy, 94.9 in Canada, 106.5 in the USA and 216 in Slovakia, likely a result of both genetic and environmental factors. In the rest of the world, especially in the emerging industrialized nations, the incidence of MI has increased significantly due to changes in environmental factors, improving medical interventions leading to longer life expectancy, and also, with the decline of infectious diseases. The patient with a MI was often a middle aged, obese, cigarette smoking male, in a developed country, but today, this disease afflicts all patients, increasingly, in women, and with equal rates of mortality.

Aetiology and risk factors

Although there are many risk factors for a MI, atherosclerosis is by far the major underlying cause of ischaemic heart disease and MI. Genetic predisposition, age, male gender, cigarette smoking, obesity, lack of exercise, mental stress, and high risk diets (containing high cholesterol or saturated fats) are known risk factors.[4–6] A personal history of diabetes mellitus, hypertension, hyperlipidaemia, and elevated plasma homocysteine levels have also been reported to increase the risk.[5,6]

Pathologic findings

A good understanding of the consequences of an MI is based on a detailed understanding of the morphological features of coronary arteries and myocardium post-MI. For this, it is essential to appreciate the findings in a heart post-MI. These findings are variable as they do depend on the duration of ischaemia, interventions/revascularization strategy (thrombolytic therapy or percutaneous coronary intervention), and success of treatment. Each of these can and does impact the morphological findings.

Gross pathology: in the initial few minutes to hours, and up to 8–12 hours, there may be no definite evidence of ischaemic damage at gross and histological examination. Attempts however can be made to highlight the ischaemic zone, with the use of the tetrazolium and other stains.

Gross inspection – at 12–24 hours post-MI, the myocardium may exhibit dark mottling.[7] By 1–3 days post-MI, the myocardium usually appears mottled with a yellow-tan centre (Figure 1). By 3–7 days post-MI, the yellow-tan core becomes more easily identified and shows an increasingly evident

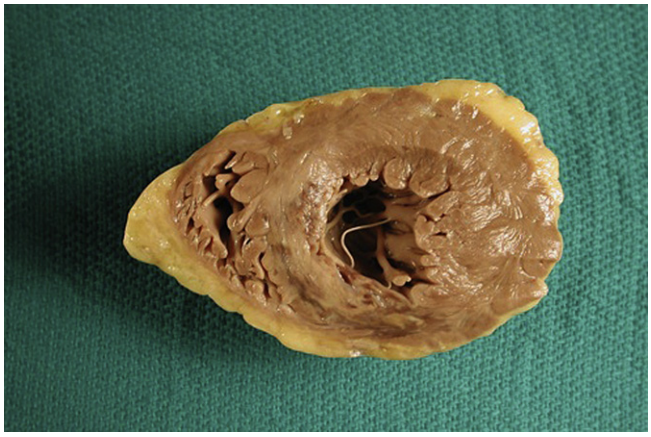

Figure 1 Gross image of a specimen in cross section with acute myocardial infarction at days 1—3. Note hyperaemic zone, and is yellow-tan in nature.

surrounding rim of a hyperaemic or darker coloured border (Figure 2), and by 7—10 days post-MI, the area of infarction appears soft and yellow-tan in colour, with depressed red-tan margins.[7] By 10—14 days post-MI, the borders become red-grey in colour, and by 3—8 weeks post-MI, a grey white scar begins to form in the junctional area and to extend inwards from the periphery towards the core of the ischaemic zone. By 6—12 weeks post-MI (Figure 3), a firm, white scar would have formed.[7—9] This area of healed transmural myocardial infarction usually appears thinner than the surrounding myocardium and shows aneurysm formation (Figure 4). After a failed revascularization, the area of infarct may appear dark red or brown in colour, due to haemorrhage into the ischaemic tissues, a change called a red or hemorrhagic infarct.[10]

Electron microscopy (EM)

EM findings are usually derived from animal studies, and the findings can be divided by organelles as discussed below:

Glycogen and the myocardial cell: at 5 minutes post-infarction, glycogen levels begin to decrease, and the spaces between

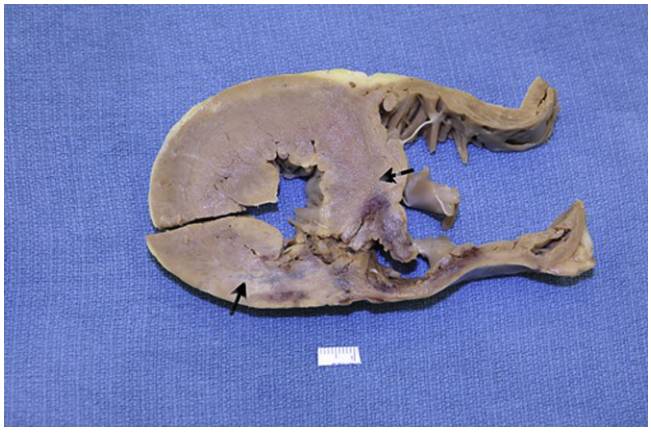

Figure 2 Gross image of a specimen in cross section with acute infero-septal myocardial infarction (demarcated in the zone between the two arrows) complicated by ventricular septal defect and free wall rupture. The area of infarct is hyperaemic and darker in colour.

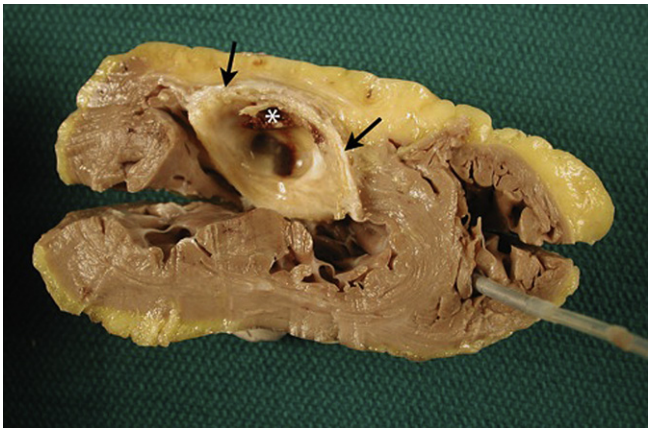

Figure 3 Gross image of an old healed transmural infarct. Endocardial fibrosis can be seen along the area of infarct (arrows). The wall itself is thinner than the neighbouring normal myocardial tissue. Mural thrombus (asterisk) can be seen in this area. A lead is seen within the right ventricle.

myofibrils starts to increase, and at 10—15 minutes post-infarct, cell separation becomes prominent.[8,11,12] At 1 hour post-infarct, increases in the spaces between the I discs are visible. At 4 hours, transverse myofibril tearing is observable, and at 5 hours, sarcolemmal rupture becomes evident.[8,11—13]

Mitochondria: early in the post-infarct period (up to 20 minutes), there are no changes detected. At 35 minutes, swelling is seen and cristae become more prominent as they begin to swell, until they rupture and disappear at 4 hours. At the 5-hour mark post-infarct, the mitochondria rupture.[8,11—13]

Endoplasmic reticulum and nucleus: At 35 minutes post-infarct, the tubules swell and Golgi apparatus becomes more apparent. At 5 minutes post-infarct, the nucleoplasm begins to clump and 2—3 hours post-infarct, drifting towards the nuclear membrane can be seen.[8,11—13]

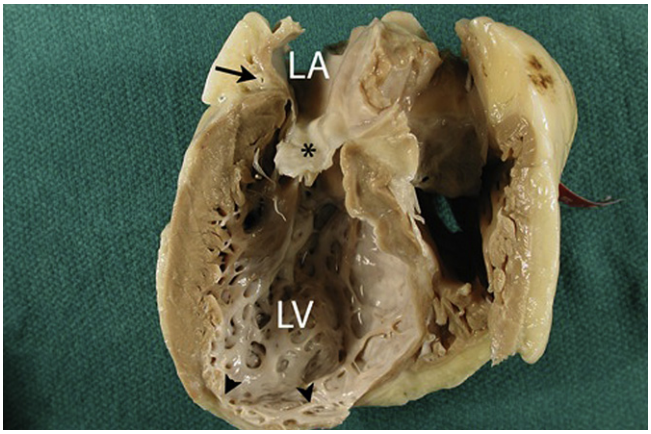

Figure 4 Gross image of a sagittal section of an old healed transmural infarct with a large aneurysm formation (arrowheads). The wall itself is grey-white, thin, fibrotic with endocardial fibrosis. The circumflex coronary artery (arrow) shows atherosclerosis, in cross section. The left atrium (LA), dilated left ventricle (LV) and anterior mitral valve leaflet (asterisk) are also seen.