Acute myocardial infarction in young adults: causes and management

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The case report in this review illustrates an acute myocardial infarction in a young adult probably due to arterial thrombosis that can be attributed to a hypercoagulable state resulting from the nephrotic syndrome. Although rare, acute myocardial infarction should be considered in young adults presenting with chest pain. A detailed clinical history may help to identify the aetiology, and guide subsequent management, but diagnostic coronary angiography is essential. Careful risk factor modification and treatment of the underlying cause should reduce the incidence of recurrent cardiac events.

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Acute myocardial infarction is rare in teenagers and young adults. The pathophysiology of their infarcts is varied but not usually due to atherosclerotic plaque rupture except for those with genetically predetermined or familial hyperlipidaemias. Appropriate treatment has to be adapted from adult management protocols, as there are no controlled trials to guide early treatment of myocardial infarction in this age group.

CASE REPORT

A 16 year old boy presented to the emergency room with a 30 minute history of severe central, crushing chest pain, radiating down his left arm and associated with sweating, nausea, and breathlessness. He had never previously experienced chest pain at rest or on exertion. At the age of 5 he had meningiococcal septicaemia and meningitis from which he recovered without any long term sequelae. He was diagnosed as having nephrotic syndrome secondary to membranoproliferative glomerulonephritis at the age of 8 years and was started on immunosuppressive therapy (azathioprine and prednisolone). He had stopped taking his prednisolone a week before presentation. He was also taking enalapril and nifedipine for secondary hypertension. He was a non-smoker and did not have a family history of ischaemic heart disease.

At presentation, he was pale and sweaty with a tachycardia of 110 beats/min. His blood pressure was raised at 190/110 mm Hg. There was no peripheral oedema and all peripheral pulses were present. His heart sounds were normal and there were no signs of heart failure. A 12 lead electrocardiogram (ECG) showed ST segment changes of an acute inferior myocardial infarction. His serum creatine kinase peaked at 2500

U/l. Total cholesterol concentration was raised at 7.7 mmol/l. Urea and creatinine were normal but his serum albumin was low (19 g/l), with a total protein of 42 g/l and globulins of 23 g/l. He had a marked proteinuria on dipstick testing throughout his hospital stay. There was a transient leucocytosis of 25×10^9/l, which returned to normal within three days, and a persistent moderate thrombocytosis of 740×10^9/l. Antithrombin III, and protein C and S activity were within the normal range. The C3 component of compliment was low 0.23 g/l (0.70–1.70) as was his IgG 5.21 g/l (6.13–15.5). The rest of his serum immunoglobulins were normal with no evidence of a paraprotein band on electrophoresis. Other immunological indices including antinuclear antibody, antineutrophil cytoplasmic antibody, and antiglomerular basement membrane antibody were negative.

His raised blood pressure was controlled with intravenous atenolol and nitrates. Thrombolysis was instituted with recombinant tissue plasminogen activator followed by intravenous heparin. Post-thombolysis ECG recordings showed complete resolution of his ST segment elevation and new Q-waves in the inferior leads. Echocardiography revealed moderate concentric left ventricular hypertrophy with a hypokinetic inferior wall. Before discharge he underwent a submaximal exercise tolerance test that was negative and his subsequent hospital stay was uneventful. At the time of discharge he was taking atenolol, aspirin, azathioprine, and prednisolone. Coronary angiography was carried out two weeks after discharge and showed normal appearances of his coronary arteries. He has since remained well and asymptomatic.

CAUSES AND MANAGEMENT OF MYOCARDIAL INFARCTION IN YOUNG ADULTS

Myocardial infarction in young adults can be broadly divided into two groups, those with angiographically normal coronary arteries and those with coronary artery disease of varying aetiology. There is significant overlap in pathophysiology between these two groups.

Angiographically "normal" coronary arteries

The pathophysiology of myocardial infarction in the presence of "normal" coronary arteries

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Abbreviations: ECG, electrocardiogram; PTCA, percutaneous transluminal coronary angioplasty

remains unclear but can be explained on the basis of coronary artery thrombosis, embolisation, spasm, or a combination of these processes. Coronary thrombosis can be seen in hypercoagulable states such as in the nephrotic syndrome, antiphospholipid syndrome, and protein S and factor XII deficiencies.[1–4] Coronary embolisation is rare but has been reported with endocarditis usually affecting the aortic valve.[5] Coronary artery spasm causing myocardial infarction is recognised with both the recreational and therapeutic use of cocaine.[6 7] Coronary artery spasm has also been reported as the likely mechanism of infarction associated with alcohol binges and amphetamine use.[8–10]

Hypercoagulable states
Nephrotic syndrome
Proteinuria associated with the nephrotic syndrome results in the loss of low molecular weight proteins, which in turn alters the concentration and activity of coagulation factors. Thus factors IX, XI, and XII are decreased due to urinary excretion.[11] As the liver tries to compensate for the hypoalbuminaemic state, there is an increased synthesis of factors II, VII, VIII, X, XIII, and fibrinogen resulting in raised blood levels.[11–13]

Antithrombin III is a coagulation inhibitor that has a direct correlation with serum albumin in the nephrotic syndrome. Significant reductions in antithrombin III are observed with plasma albumin concentration below 20 g/l.[14] Protein C is a vitamin K dependent coagulation inhibitor that acts on coagulation factors V and VIII while protein S is a cofactor of activated protein C. Neither of these factors has been clearly implicated in arterial thrombosis in the nephrotic syndrome.[11]

The fibrinolytic system is also affected, with decreased concentrations of plasminogen and raised levels of plasminogen activator.[15 16] There is evidence of decreased fibrinolytic activity with hypertriglyceridaemia, which often occurs in the nephrotic syndrome.[17]

The extent of alterations in the levels of all the proteins mentioned above correlate with the degree of hypoalbuminaemia. A serum albumin of less than 25 g/l is a significant risk factor for combined arterial and venous thrombosis in the nephrotic syndrome.[18] Other factors that contribute to the hypercoagulable state are a thrombocytosis and increased platelet aggregation and adhesiveness. Platelet hyperaggregability correlates with serum cholesterol concentrations.[19 20]

Many of these abnormalities were evident in our patient and may have caused coronary thrombosis without atherosclerotic plaque rupture.

Antiphospholipid syndrome (Hughes' syndrome)
Arterial and venous thrombosis is a prominent feature of this syndrome together with antiphospholipid antibodies and miscarriages of pregnancy.[21] Antiphospholipid antibodies are associated with autoimmune diseases such as systemic lupus erythematosus, but when they occur in isolation, this is known as primary antiphospholipid syndrome. The main antiphospholipid antibodies implicated in thrombosis and atherosclerosis are the anticardiolipin antibody, the lupus anticoagulant, and IgG antibodies against plasma phospholipid-bindidng proteins such as β_2-glycoprotein I and prothombin.[22 23]

Cardiac complications include myocardial infarctions and a high prevalence of valvular abnormalities of varying severity.[24–26] It is postulated that the valvular damage is secondary to repeated thrombosis on normal valves that heal by scarring and valve distortion. There is an association between the presence of antiphospholipid antibodies in patients with intermittent claudication and young adults who survive a myocardial infarction.[3 27] The mechanism for thrombosis in this syndrome is complex and not well understood. A mild thrombocytopenia is a common finding in antiphospholipid antibody syndrome, though this does not seem to correlate with thrombosis.[28] However, there is in vitro evidence that the anticardiolipin antibody increases platelet adhesiveness.[29] It is possible that the antiphospholipid antibodies predisposes to premature atherosclerosis compounding the risk for infarction with this syndrome.[27 30 31]

Coronary artery spasm
Cocaine—Coronary artery spasm is probably the predominant mechanism for myocardial infarction with the use of cocaine. Cocaine has been associated with angina, myocardial infarction, tachyarrhythmias and bradyarrhythmias, sudden cardiac death and myocardial contraction bands, which probably act as a substrate for arrhythmias.[6 32] The cardiac effects of cocaine are mediated via four main pathways[33 34]: (1) increased myocardial oxygen demand due to an acute rise in systemic blood pressure and heart rate; (2) coronary vasoconstriction caused by its α_1-adrenergic properties and calcium dependent direct vasoconstriction; (3) endothelial dysfunction which predisposes to vasoconstriction and thrombosis; and (4) promotion of arteriosclerosis.[35 36]

Coronary embolisation
Endocarditis—Embolisation of septic vegetations from the aortic and mitral valves causing myocardial infarction has been reported.[37] Left sided infective endocarditis is common in intravenous drug abusers and usually affects morphologically abnormal valves.[38] Vegetations may be non-septic as seen in the antiphospholipid antibody syndrome and systemic lupus endocarditis. Such vegetations resolve with anticoagulation.[5] Thrombotic microembolisation causing myocardial infarction has been reported with bacteraemia in the absence of endocarditis.[39]

Myocardial bridging
This is a congenital anomaly in which a coronary artery is embedded within a tunnel of the subepicardial myocardium or has a band of myocardium overlying it. This can impede blood flow during systole that can persist during diastole resulting in myocardial ischaemia, which has been associated with myocardial infarction. Traditionally treatment involved surgical splitting of the band but there are now reports of successful treatment by stent implantation.[40]

Angiographically "abnormal" coronary arteries
The definition of normality is arbitrary, as we know that angiographically normal looking coronary arteries can have significant atherosclerotic plaque burden when assessed using intracoronary ultrasound.

Accelerated atherosclerosis
The prevalence of advanced coronary atheroma in young adults is not well established. In an autopsy study of 760 victims of accidents suicides or homicides aged 15–34 years, advanced coronary atheroma were seen in 2% of males aged 15–19 years (none in women). In the 30–34 age group, 20% of men and 8% of women had advanced coronary atheroma.[41]

Mutations in the gene encoding the low density lipoprotein receptor produces familial hypercholesterolaemia, an autosomal dominant disorder clinically characterised by high serum cholesterol (low density lipoprotein fraction) concentrations, xanthomas, and premature atherosclerosis.[42] Various other lipid fractions and hyperhomocysteinaemia are implicated in premature atherosclerosis and myocardial infarction.[43 44] Other risk factors include smoking, hypertension, insulin resistance, obesity, and a family history of premature cardiovascular events.[45]

Spontaneous dissections
Spontaneous coronary artery dissection is a rare cause of myocardial infarction. It is a condition with greater prevalence in young women, particularly in the peripartum or early postpartum period. It also has been described in association with

atherosclerotic plaque and in an idiopathic group of patients. The left anterior descending artery is often involved, but there are reports of multiple vessel involvement. The pathophysiological characteristics remain unclear. Unlike atherosclerotic intimal dissection, the dissection plane lies within the media or between the media and adventitia. Often the diagnosis is made at autopsy. Treatment options range from conservative management, bypass surgery, or angioplasty and stenting.[46]

Aneurysms, ectasia, and anomalous origin of coronary arteries

Coronary artery aneurysms are congenital or acquired secondary to Kawasaki's disease in childhood.[47] They have been linked to myocardial infarction in young adults, though the mechanism is not understood.[48] Anomalous origins of either left or right coronary arteries have been associated with myocardial infarction and are related to acute angulation and compression of the artery at its origin or along its course.[49][50]

Management

Due to the wide range of aetiologies diagnostic coronary angiography should be performed in all cases to establish the cause of infarction and guide therapy.

Thrombolysis

Successful thrombolysis in hypercoagulable states has been reported in the literature.[51] In spasm induced myocardial infarction such as with cocaine, thrombolysis should be given if there is not a prompt resolution in symptoms and ST segment changes after giving adequate doses of vasodilators (nitrates and calcium channel blockers).

Angioplasty

There are also reports of successful percutaneous transluminal coronary angioplasty (PTCA) with or without coronary artery stenting in the antiphospholipid syndrome.[52] In those patients with myocardial infarction secondary to accelerated premature atherosclerosis, early intervention with primary angioplasty has an improved outcome over thrombolysis.[53] PTCA and stenting should be considered in spontaneous coronary artery dissection and myocardial bridging.[40][46]

Antiplatelet drugs and anticoagulation

Aspirin is recommended in most cases. Anticoagulation should be considered in the nephrotic syndrome if serum albumin is less than 20 g/l.[11] In Hughes' syndrome long term anticoagulation is needed following an infarct and the international normalised ratio should be kept above 3.

β-Blockers

These drugs are best avoided in cocaine or amphetamine induced spasm leading to myocardial infarction as there is a potential risk of unopposed α_1-adrenergic action with worsening coronary spasm.

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