

Streptokinase in acute aortic dissection

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The benefits of treatment with thrombolytic agents in acute coronary thrombosis are well established.¹⁻¹⁰ For optimal effect these agents must be given early in the course of the event before irreversible ischaemic necrosis occurs.¹⁵ Accurate diagnosis in patients with chest pain is therefore essential. We describe four cases of acute aortic dissection in which streptokinase was mistakenly given.

Case reports

CASE 1

A 50 year old man presented to a district general hospital with acute severe chest pain radiating to the interscapular region. The house officer who admitted him noted a normal electrocardiogram and mistakenly considered an x ray film of the chest to be normal. Acute myocardial infarction was diagnosed and treatment with intravenous streptokinase started. An acute hypotensive episode occurred early the next morning, when a chest x ray film showed an obvious widened mediastinum.

The patient was transferred to this centre, where initial treatment consisted of control of blood pressure as defects in coagulation precluded catheterisation or operation. Despite the use of vitamin K, fresh frozen plasma, and platelets three days were required to restore clotting variables to values at which an operation could be considered. Figure 1 shows the progress of mediastinal widening during this period. Angiography confirmed an ascending aortic dissection with aortic reflux. At operation, unusually, no blood clots were found between layers of the dissection. A woven double velour tube graft was used to replace the ascending aorta, with resuspension of the aortic valve. Aprotinin (2 million kallikrein inactivating units) was given during bypass of the cardiopulmonary system. Altogether 1900 ml fluid was lost through chest drains in the postoperative period. He made an uneventful recovery and was well six months later.

CASE 2

A man aged 64 presented to a district general hospital with sudden collapse and severe central chest

pain. His systolic blood pressure on admission was 60 mm Hg, and an electrocardiogram showed ST segment elevation in leads V1 and V2 only. An x ray film of his chest was described as showing an "odd" right hilum. The house officer diagnosed acute myocardial infarction from these findings, and streptokinase was given intravenously. The patient remained hypotensive despite an infusion of dobutamine.

Four hours later he suffered a small haematemesis and bleeding from the urethra. An electrocardiogram was normal. The original diagnosis was deemed incorrect, and fresh frozen plasma and vitamin K were given. The probability of acute aortic dissection was considered by a consultant 12 hours after admission; computed tomography confirmed this diagnosis, and the patient was transferred to this centre.

Aortography showed acute dissection of the ascending aorta with normal coronary arteries. The fibrinogen titre was 1/64 (normal 1/512) with an international normalised ratio of 1.3. An operation was performed immediately to replace the ascending aorta with a woven double velour Dacron tube graft. Aprotinin (2 million kallikrein inactivating units) was given during bypass of the cardiopulmonary system. Seven units of whole blood, six units of platelets, and four units of fresh frozen plasma were required in the operating theatre before bleeding after the bypass was brought under control. Apart from some early pulmonary dysfunction the patient made an excellent recovery and was discharged 12 days after operation.

CASE 3

A 66 year old man with a history of gastrointestinal bleeding and dyspepsia presented to a district general hospital with sudden severe central chest pain, sweating, and nausea. Although an electrocardiogram was normal, the houseman diagnosed myocardial infarction and prescribed streptokinase intravenously. A chest x ray film obtained on admission showed an abnormally widened mediastinum (fig 2). Subsequent electrocardiograms and cardiac enzyme activities did not support the diagnosis of myocardial infarction. Five days later the patient complained of upper gastrointestinal symptoms and endoscopy of the upper gastrointestinal tract showed superficial gastric erosions and a small hiatus hernia. The next day he collapsed with further chest pain and was profoundly hypotensive. After resuscitation an x ray film showed a left sided pleural effusion, and a ruptured oesophagus was diagnosed. This was not confirmed by an x ray film after the patient had swallowed a contrast medium (Omnipaque). The next morning 750 ml blood was drained from the left side of his chest. A diagnosis of pulmonary embolus was considered, and he was transferred to this centre.

Aortic dissection was diagnosed from his history and the first chest x ray film. This was confirmed by angiography, which showed an extensive dissection of the transverse and descending thoracic aorta. The ascending aorta was normal. In view of the patient's

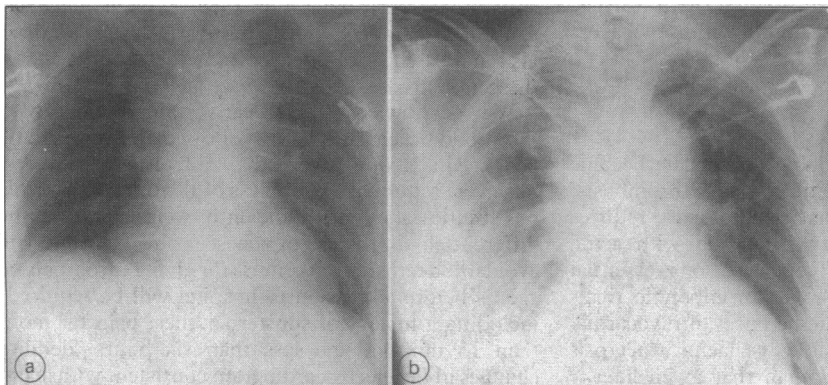
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FIG 1—x Ray film of chest (case 1) showing progress of mediastinal widening between (a) presentation and (b) time of operation



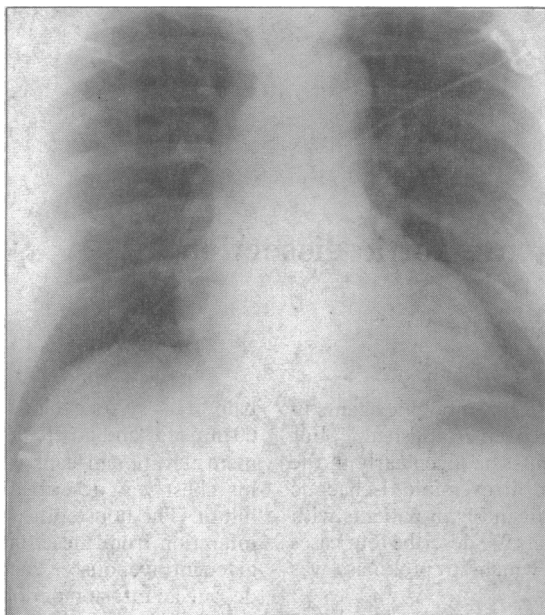


FIG 2—x Ray film of chest (case 3) at presentation showing abnormally widened mediastinum

age and the site and extent of the dissection he was treated with captopril and nifedipine to control his hypertension. Later the regimen was changed to atenolol and frusemide. He made good progress until he died suddenly 20 days after his first presentation. A postmortem examination confirmed the cause of death as ruptured aortic dissection.

CASE 4

A 66 year old man was admitted to this hospital with acute severe central chest pain radiating to both arms associated with dyspnoea. Although known to have been hypertensive in the past he was not taking antihypertensive drugs. He had a heart rate of 56 beats/minute, blood pressure of 80/60 mm Hg, palpable peripheral pulses, and a clear chest. An electrocardiogram showed first degree heart block with T wave inversion in leads III and aVF. Acute inferior myocardial infarction was diagnosed and treatment started with streptokinase (infused intravenously at a dose of 1.5 million units). Immediately after streptokinase was given he became restless and haematuria was noted, together with weakness of the left arm and leg. Blood pressure was lower on the left side, and the possibility of acute aortic dissection was considered.

Two dimensional echocardiography showed a dilated aortic root with an ascending aortic tear. A false lumen was clearly shown by abdominal ultrasound scanning. Clotting variables were very abnormal, as occurs after administration of streptokinase. Action was taken to correct the coagulation defects with a view to carrying out an operation. Control of blood pressure, however, was poor, and soon afterwards he suffered a cardiac arrest with electromechanical dissociation from which he could not be resuscitated. Postmortem examination showed a ruptured aortic dissection with cardiac tamponade. No blood clot was found within the layers of the dissected aorta.

Discussion

In the past 10 years thrombolytic drugs have become the first line treatment for acute coronary thrombosis. Recent trials have shown that streptokinase reduces the morbidity and mortality associated with acute myocardial infarction.¹⁻¹⁰ Early intervention is essential for maximal effect. Predictably, thrombolytic treatment within four hours after the onset of myocardial infarction, before irreversible ischaemic necrosis occurs, is of greater benefit than that given later.¹¹

Unfortunately, in the United Kingdom around 60% of patients admitted to coronary care units arrive too late for maximal benefit.¹¹ It has therefore been suggested that streptokinase might be given before admission to hospital to reduce delays in intervention.¹² The Seattle myocardial infarction, triage, and intervention (MITI) trial and the European myocardial infarction project are currently assessing the ratio of efficacy to risk of thrombolytic treatment given before admission to hospital compared with that given in hospital.^{13,14} If treatment before admission is to be accepted, however, accurate diagnosis of the cause of the chest pain is essential. A district general hospital recently reported a 10% incidence (five of 51 cases) of inappropriate administration of streptokinase.¹⁵ In three patients the hospital concluded retrospectively that there was no evidence of myocardial infarction.

The true incidence of acute aortic dissection is difficult to determine as some cases are diagnosed as acute myocardial infarction. Thoracic aortic dissection has been estimated to occur two to three times more frequently than rupture of an abdominal aneurysm, at a rate of five to 10 per million people per year.¹⁶ Four fifths of patients die within 14 days of onset of the dissection, rupture being the commonest cause of death. Thrombolytic agents are likely to extend the dissection and adversely affect the outcome.

Streptokinase binds to both circulating plasminogen and plasminogen bound to clots. Systemic activation of components of the haemostatic system therefore occurs, with consumption of plasminogen, low fibrinogen concentrations, and high concentrations of degradation products of fibrinogen; these high concentrations in turn inhibit aggregation of platelets.¹⁷ Thus haemostatic mechanisms are severely affected. Carrying out operations soon after administration of streptokinase is potentially hazardous owing to excessive loss of blood.¹⁸ The serine protease inhibitor aprotinin (Trasylol; Bayer) reduces loss of blood associated with procedures requiring bypass of the cardiopulmonary system.^{19,20} It may act as a specific antidote to streptokinase,²¹ though it would need to be given early to inhibit the fibrinolytic effect.

Several clinical features help to differentiate between aortic dissection and acute myocardial infarction. Unlike myocardial infarction, the pain associated with a dissection is sudden and severe in onset; it is tearing in quality, radiates to the back, and may spread down to the abdomen. A history of hypertension is common. An aortic regurgitant murmur due to prolapse of the aortic valve is often present, and missing and varying pulses support the diagnosis. Further confirmation requires investigations in hospital, such as x ray examination and computed tomography or aortography.

In the cases described here an accurate diagnosis was not made in the early stages despite investigation in hospital. In retrospect, aortic dissection should have been considered on the basis of the chest x ray appearance in all four cases. One patient otherwise suitable for early operation died through the delay caused by deranged clotting. Probably streptokinase also increased the extent of the descending aortic dissection in case 4.

We acknowledge that early intervention with thrombolytic agents is likely to be of major therapeutic benefit in acute myocardial infarction. It does, however, require an awareness of the other diagnostic possibilities and staff sufficiently well trained in the differential diagnosis of chest pain to eliminate avoidable deaths. Strict criteria for giving thrombolytic agents before admission to hospital will be required, including a history of substernal chest pain for more than 15 minutes and less than six hours, definite changes in the electrocardiogram consistent with acute

myocardial infarction, no disorders precluding the use of thrombolytic agents, and no appreciable hypertension or difference in blood pressure between the left and right arms.¹³ The cases described here emphasise this point. The protease inhibitor aprotinin, used as an antidote to streptokinase, may be beneficial when given intraoperatively to reduce blood loss if an operation is required soon after streptokinase has been given.

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