Acute myeloid leukaemia as a cause of acute ischaemic heart disease

P.L. van Haelst, B. Schot, E.S. Hoendermis, M.P. van den Berg

Ischaemic heart disease is almost invariably the result of atherosclerotic degeneration of the coronary arteries. However, other causes of ischaemic heart disease should always be considered. Here we describe two patients with a classic presentation of ischaemic heart disease resulting from acute leukaemia. The pathophysiological mechanisms of acute leukaemia leading to ischaemic heart disease are discussed. (*Neth Heart J* 2006;14:62-5.)

Keywords: myocardial ischaemia, acute myeloid leukaemia, left ventricular function

Ischaemic heart disease is almost invariably the result of atherosclerotic degeneration of the coronary arteries.[1] However, other causes of ischaemic heart disease should always be considered. We describe two patients with a classic presentation of ischaemic heart disease resulting from acute leukaemia.

Case 1

A 54-year-old man was admitted because of a rescue percutaneous transluminal coronary angioplasty. Earlier that day he had received thrombolysis in another hospital because of an acute myocardial infarction (MI).

During the last two days he had experienced retrosternal pain radiating to the shoulder region and both arms. The pain was not related to exercise. The patient did not suffer from dyspnoea, nor did he have any other specific symptoms, but in the last few weeks he had been suffering from fatigue.

On the day of admission the pain had worsened and it was accompanied by severe perspiration. Oral administration of nitroglycerine did not improve his condition. The patient was not on any other medication. Smoking was the only cardiovascular risk factor.

Physical examination revealed an ill, clammy patient. The blood pressure was initially 150/90 mmHg, but fell to 100/50 mmHg when the pain aggravated. There was a regular pulse and central venous pressure was not elevated. Auscultation of the precordium revealed normal heart sounds without any murmurs. Later a gallop rhythm was heard. Initially, examination of the lungs was normal, but later the patient was found to have rales. Examination of the abdomen was without abnormalities except for abdominal obesity.

Laboratory investigations showed elevated troponin I levels, with a mild thrombopenia; the leucocyte count was 8.6×10^9/l with 2% blasts in the differentiation (table 1).

The electrocardiogram on admission showed only minor abnormalities, but after the chest pain intensified, ST-segment elevation and a QS pattern were seen in the precordial leads and lead I and aVL, with reciprocal ST-segment depression in leads II, III, aVF (figures 1A and 1B.).

An acute anteroseptal myocardial infarction was diagnosed and thrombolysis was started. No signs of reperfusion were seen and patient was referred to our hospital for a rescue PTCA. In the cath lab single-vessel disease was diagnosed and a stent was placed in the proximal left anterior descending coronary artery (LAD). The patient was then sent back to the referring hospital until he was readmitted to our coronary care unit a few days later due to progressive heart failure, despite maximal therapy including inotropics. Moreover, his leucocyte count had progressed to 88.1×10^9/l and an acute leukaemia was considered. The diagnosis of acute myeloid leukaemia was confirmed immunophenotypically by the haematologist.

P.L. van Haelst
E.S. Hoendermis
M.P. van den Berg
Department of Cardiology, University Medical Centre, Groningen, the Netherlands
B. Schot
Department of Haematology, University Medical Centre, Groningen, the Netherlands

Correspondence to: P.L. van Haelst
Department of Cardiology, University Medical Centre,
PO Box 30001, 9700 RB Groningen, the Netherlands
E-mail: p.l.van.haelst@thorax.azg.nl

Table 1. Laboratory tests during admission in patient 1.

	Day 1	6 Hours	Day 2	Day 5
Leucocyte count (×10⁹)	8.3	n.a.	14.9	88.1
Thrombocyte count (×10⁹)	97	n.a.	87	22
LDH	309	308	1502	1415
CK	132	207	6411	n.a.
CK-MB	9	21	657	n.a.
Troponin I	2.6	3.4	n.a.	n.a.

n.a= not available, LDH=lactate dehydrogenase, CK (MB)=creatine phosphokinase (myocardial fraction).

However, due to a deteriorated left ventricular function (LVEF 25%), only palliative options were available. Within a few days the patient's condition worsened and eventually he died due to cardiogenic shock, seven days after his first presentation.

Pathological examination revealed necrosis of the entire left ventricle, with bleeding in the anterior wall and septum. There was an older (10 to 14 days) myocardial infarction present in the lateral wall next to fresh myocardial infarction throughout the complete left ventricle. Massive disseminated intravascular coagulation with microthrombi was present in the microcirculation, LAD and stent, aorta and lungs. Importantly, no signs of coronary atherosclerosis were found. The bone marrow was leukaemic with proliferation of a myeloid clone, compatible with acute myeloid leukaemia.

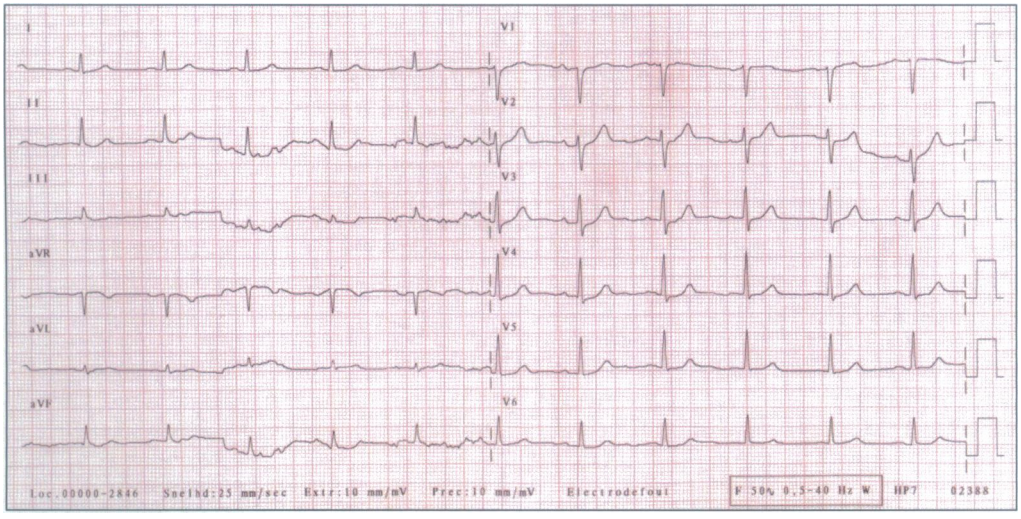

Figure 1A. The ECG on admission (case 1).

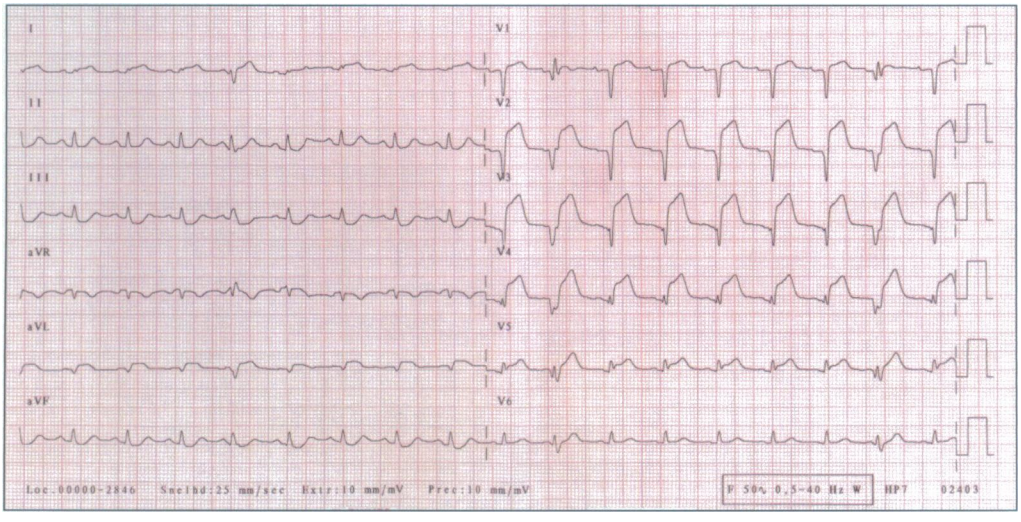

Figure 1B. The ECG after the chest pain intensified (case 1).

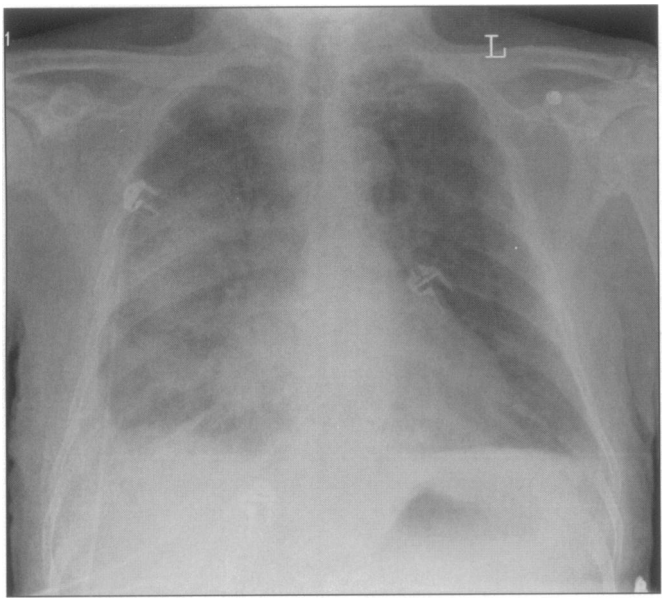

Figure 2. X-ray of patient 2, showing pronounced venous redistribution and pleural fluid compatible with pulmonary oedema.

Case 2

An 89-year-old man, who had been treated with oral nitrates because of chronic stable angina, presented with acute dyspnoea that occurred after a brief episode of chest pain. A few days before, his general practitioner had prescribed him antibiotics because of an upper respiratory tract infection. He had not been feeling well in the last few weeks. There was no history of night sweats, bleeding or weight loss.

On admission an extremely dyspnoeic man was seen with a respiratory frequency of 25/minute. Blood pressure was 180/100 mmHg, the pulse rate was 100 beats/min and the central venous pressure was elevated. On chest auscultation there were rales in all fields. Heart sounds were hard to interpret because of the pulmonary sounds. The extremities were cold but peripheral pulsations were intact. The ECG showed a sinus tachycardia, with a left axis, known Q waves were present in leads II, II and aVF and new downsloping ST depression was seen in leads V_2 to V_6. A chest X-ray was suggestive of vascular congestion with redistribution of blood to the upper lung fields, whereas an infiltrate in the right middle lobe could not be excluded (figure 2).

A clinical diagnosis of acute ischaemic congestive heart failure was made and immediate treatment was started with oxygen and intravenous nitrates and diuretics. Soon afterwards, the patient's condition ameliorated. The laboratory tests showed a leucocyte count of 160×10^9/l with 58% blasts in the differentiation (table 2). It was concluded that the patient was suffering from acute congestive heart failure due to leucostasis and a nontransmural myocardial infarction. Treatment was started with steroids, hydroxyurea and allopurinol. The patient responded favourably to this treatment and eventually he was discharged. Palliative treatment with 6-mercaptopurine was started.

Discussion

Ischaemic heart disease is almost invariably the result of atherosclerotic vascular occlusion.[1] In about 3% of all patients a normal epicardial anatomy is seen. In these cases other causes can be identified, such as spasm of a coronary artery as, for instance, in Prinzmetal angina or substance abuse such as cocaine. Other causes of nonatherosclerotic myocardial infarction are aberrant anatomy of the coronary arteries, inherited or acquired coagulation disorders, embolisation and collagen tissue disorders such as systemic vasculitis.[2]

Here, we present two patients who presented with acute ischaemic heart disease due to acute myeloid leukaemia. Several mechanisms have been suggested for the occurrence of cardiovascular disease during acute leukaemia:[3]

- Leukaemic thrombi or leucostasis can occur in major arteries;
- Leukaemic infiltration into the myocardium or pericardium;
- Disorders of coagulation secondary to leukaemia may cause emboli due to a hypercoaguable state or haemorrhage;
- Antileukaemic therapies may have cardiovascular side effects.

Table 2. Laboratory tests during admission of patient 2.

	Day 1	6 Hours	Day 2	Day 5
Leucocyte count ($\times10^9$)	160	n.a.	118	2.8
Thrombocyte count ($\times10^9$)	97	n.a.	88	20
LDH	1842	308	3171	n.a.
CK	70	207	149	n.a.
CK-MB	5	6	6	n.a.
Troponin I	1.7	9.7	11.2	n.a.

n.a= not available, LDH=lactate dehydrogenase, CK (MB)=creatine phosphokinase (myocardial fraction).

Table 3. Disorders of coagulation in acute leukaemias.

Disorder	Basis
Thrombocytopenia	Disturbance of development (infiltration of bone marrow)
	Increased breakdown (hypersplenism)
	Disseminated intravascular coagulation (DIC)
DIC	Tissue factor activity of leukaemic cells activates the extrinsic coagulation system and causes increased consumption of fibrinolysis factors and their inhibitors
	Disturbance of microcirculation
	Microangiopathic haemolysis
Hyperfibrinolysis	Activators of plasminogen
	DIC
	Disturbance of the microcirculation
	Microangiopathic haemolysis
	Direct splitting of fibrinogen through elastases and cathepsin from leukaemic blast cells
Deficiency of coagulation factors	Immunological diseases
	Antibodies against factor II, V, VIII, IX, XII, XIII
	Lupus anticoagulant
	Hepatic disease from leukaemic infiltration or drugs toxicity
	DIC

Adapted from reference 3.

The first patient suffered from an acute anterior wall infarction due to a thrombus in the proximal LAD without any sign of atherosclerosis. Leukaemic thrombi have been described as a cause of acute MI in patients with leukaemia; however, these are associated with high leucocyte counts. Thus, it is more likely that the thrombus was the result of a coagulation disorder secondary to the leukaemia. This was confirmed by the finding of diffuse thrombi throughout the heart on autopsy. An overview of the coagulation disorders in acute leukaemias is shown in table 3.

The second patient most probably suffered from the complications of leucostasis in the myocardium and pulmonary veins. This phenomenon is almost exclusively found in acute myeloid leukaemia, where large myeloblasts tend to adhere, usually when cell counts are above 100×10^9/l. Intravenous fluid loading, prednisolone, radiotherapy and a fast reduction of the volume of blasts by cytotoxic treatment may be useful in this situation. Also, leucapheresis can improve outcome in hyperleucocytosis.[4]

The antileukaemic therapies containing anthracyclines are notorious for their toxic adverse effects on cardiac function. The use of anthracyclines in patients with impaired heart function should be restricted. In order to control side effects, intensive chemotherapy is supported by aggressive fluid infusion. Since both patients had a severely decreased left ventricular function, treatment for leukaemia could not be initiated. Only patients with a good performance state are able to undergo intensive treatment such as high-dose chemotherapy or stem cell transplantation in order to reach remission. Patients who cannot cope with an adequate fluid load or who are not fit enough to overcome infectious complications during aplasia will not be offered these treatments. Therefore, leukaemia patients presenting with ischaemic heart disease have an extremely poor prognosis.

Conclusion

These cases illustrate that a nonatherosclerotic cause of coronary heart disease should always be considered. Both patients suffered from acute myeloid leukaemia, a disease in which complete remission can be achieved. However, treatment for acute leukaemia has important cardiovascular side effects and the treatment itself requires an adequate cardiac performance. Thus, the initial presentation of the disease prohibited further therapy in these patients. Rapid diagnosis and treatment for both the cardiovascular and the haematological disease are warranted in these patients. ■

Reference

1 Libby P. Molecular bases of the acute coronary syndromes. *Circulation* 1995;**91**:2844-50.

2 Da Costa A, Isaaz K, Faure E, Mourot S, Cerisier A, Lamaud M. Clinical characteristics, aetiological factors and long-term prognosis of myocardial infarction with an absolutely normal coronary angiogram; a 3-year follow-up study of 91 patients. *Eur Heart J* 2001;**22**:1459-65.

3 Jachmann-Jahn U, Cornely OA, Laufs U, Hopp HW, Meuthen I, Krakau M, et al. Acute anterior myocardial infarction as first manifestation of acute myeloid leukemia. *Ann Hematol* 2001; **80**:677-81.

4 Thiebaut A, Thomas X, Belhabri A, Anglaret B, Archimbaud E. Impact of pre-induction therapy leukapheresis on treatment outcome in adult acute myelogenous leukemia presenting with hyperleukocytosis. *Ann Hematol* 2000;79:501-6.