Section of right cochlea through the region of basal and mid-coils. The scala tympani (ST) and modiolus (M) of the basal coil contain a deposit of myxoid connective tissue (MCT). There is severe reduction of spiral ganglion cells in modiolar spaces that would normally contain many. The organ of Corti (C) is atrophic in all places. There is moderate hydrops with some outward bulging of Reissner's membrane (R) (haematoxylin and eosin).

both cochlea and vestibules were severely damaged with atrophy of basilar membrane nerve fibres and spiral and vestibular ganglion cells. These changes may represent the end and vestibular structures. Such changes most frequently result from severe labyrinthine infection, usually secondary to otitis media or meningitis, but there was no clinical evidence

of infection in this patient. Hyperviscosity is unlikely to lead to such profound permanent changes affecting sensory and ganglion cells or labyrinthine structures. Haemorrhage could cause widespread labyrinthine changes but these are usually irregular. There was no evidence of haemosiderin or cholesterol granuloma at post mortem to suggest this as a cause. The most likely cause seems to be leukaemic infiltration of the labyrinthine spaces involving the perilymphatic space and basilar membrane; disappearance of leukaemic cells with treatment could be followed by extensive fibrosis and bony reaction with loss of sensory cells and their nerve supply.⁶ The cranial nerve palsies remain unexplained.

It is difficult to distinguish between deafness due to hyperviscosity or leukaemic infiltration in patients with CML. We advocate both leucopheresis and high dose chemotherapy capable of rapid cytorreduction, as conventional chemotherapy is rarely followed by recovery.⁴

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Pulmonary infarction, myocardial infarction, and acute disseminated intravascular coagulation

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Abstract

Pulmonary and myocardial damage are frequently cited as manifestations of disseminated intravascular coagulation (DIC), but rarely as causes. Three elderly cases of severe DIC due to pulmonary and myocardial infarction are reported. All three patients died. Necropsy showed extensive pulmonary emboli in each case with large pulmonary infarcts in cases 1 and 2 and a ventricular aneurysm containing thrombus in cases 2 and 3. Early diagnosis and treatment of pulmonary embolism requires a high degree of

clinical suspicion but may prevent progression to the irreversible stage of severe DIC.

Disseminated intravascular coagulation (DIC) is characterised by inappropriate activation of the coagulation system, with consumption of coagulation factors and secondary fibrinolysis.¹ It is not a single disease process, but a common pathway in a large number of primary disorders. Pulmonary and myocardial damage are frequently cited as manifestations of DIC, which we believe obscures the fact they also number among its causes.

Haematological results of the three patients confirming the diagnosis of disseminated intravascular coagulation (DIC)

	Reference range	Case 1	Case 2	Case 3
Haemoglobin	11.5–15.6 g/l	12.4	14.5	14.8
Platelets	150–400 × 10 ⁹ /l	82	41	25
PT	(controls)s	36 (15.5)	26 (14)	30 (15.5)
APPT	(controls)s	51 (45)	61 (41)	52 (37)
Serum fibrinogen	2–4 g/l	0.7	0.9	1.7
FDP-D-Dimers	< 0.25 mg/l	> 4	> 4	> 4
RCF		Yes	Yes	Yes

PT prothrombin time; APTT activated partial thromboplastin time; FDP-D-Dimers fibrinogen degradation product-D-Dimers; RCF fragmented red cells in peripheral blood.

Case reports**CASE 1**

A 78 year old woman was admitted with a one week history of breathlessness, productive cough, central chest pain, easy bruising and jaundice. Her medical history included cholecystectomy, myocardial infarction 12 months previously, and diabetes mellitus that had not been treated with insulin. On examination she was centrally cyanosed, hypotensive, and had biventricular cardiac failure, purpura, and bruising.

Haematological investigations confirmed the diagnosis of DIC (table). Biochemical investigations were as follows: plasma sodium 134 mmol/l, potassium 5.6 mmol/l, urea 21.3 mmol/l, creatinine 140 µmol/l, glucose 6.5 mmol/l, bilirubin 30 µmol/l, amylase 276 IU/l, and creatine kinase 180 IU/l. A chest radiograph showed cardiomegaly with shadowing of the middle and lower zones of the right lung. The electrocardiogram showed right bundle branch block and lateral ischaemia. She died 10 days after admission to hospital. Necropsy showed pulmonary embolism and infarction of the middle and lower lobes of the right lung.

CASE 2

A previously fit 85 year old woman presented with a two week history of breathlessness and left sided pleuritic chest pain, and a five day history of haemoptysis. Examination showed hypotension with severe cardiac failure. Two days later she developed purpura and extensive bruising around venepuncture sites. DIC was confirmed (table). The electrocardiogram showed an extensive anterior myocardial infarction and the chest radiograph confirmed left ventricular failure. A ventilation and perfusion lung scan showed a matched defect at the right lung base, not thought typical of pulmonary embolism. Twenty four hours later she was jaundiced; bilirubin 51 µmol/l, creatine kinase 113 IU/l, aspartate transaminase (AST) 2580 IU/l and alanine transaminase (ALT) 2220 IU/l. An abdominal ultrasound scan showed only features of congestive cardiac failure. She died nine days after admission. Necropsy showed bilateral pulmonary emboli with infarction of the lower lobes of both lungs. There was recent thrombosis of the anterior descending branch of the left coronary artery with an extensive infarct of the anterior wall of the left ventricle covered by mural thrombus.

CASE 3

A 75 year old woman was admitted with a one month history of increasing dyspnoea. She had no clinically important medical history. She was hypothermic (core temperature 32°C), hypotensive, and had purpura and severe biventricular cardiac failure.

The haematological results were compatible with DIC (table). Biochemical investigations: plasma sodium 135 mmol/l, potassium 5.3 mmol/l, urea 17.4 mmol/l, creatinine 203 µmol/l, bilirubin 125 µmol/l, creatine kinase 1781 IU/l, AST 221 IU/l and ALT 149 IU/l. The chest radiograph showed cardiomegaly, collapse of the lower lobe of the right lung, and consolidation of the lower lobe of the left lung. The electrocardiogram suggested an old anterior myocardial infarction. A ventilation and perfusion lung scan showed decreased perfusion at the left lung base, compatible with pulmonary embolism. Intravenous heparin was started but was discontinued the next day when melaena developed. She died three days after admission to hospital. Necropsy confirmed the presence of deep vein thrombosis and pulmonary embolism. There was a large left ventricular aneurysm due to an old infarct, which contained thrombus.

Discussion

DIC may be induced by factors released from hypoxic or infarcted tissue,¹ but myocardial infarction and pulmonary embolism or infarction have rarely been reported as causes. Sub-clinical changes in circulating clotting factors occur in pulmonary embolism and to a lesser extent in deep vein thrombosis, but do not usually fulfil the definition criteria for DIC.² These changes may be due to clotting factor consumption by the pulmonary thrombosis,³ or thromboplastin release from infarcted tissue.¹ If sufficient thromboplastin is released by a large pulmonary infarct, then the coagulation abnormality can progress from symptomless haematological change to clinical DIC. The pulmonary infarcts in cases 1 and 2 were extensive, a feature they share with previous examples of DIC attributable to pulmonary infarcts.⁴

Abnormalities in circulating clotting factors are also seen in myocardial infarctions.⁵ Myocardium contains less thromboplastic activity than lung, however,⁶ and quantitatively less tissue is infarcted, thus thromboplastin release secondary to myocardial infarction may be insufficient to trigger DIC. An alternative mechanism exists whereby myocardial infarction might lead to DIC; thrombosis within a ventricular aneurysm has been associated with DIC;⁷ both cases 2 and 3 had a large ventricular aneurysm filled with thrombus.

We believe these three cases are examples of pulmonary and myocardial infarction causing rather than complicating DIC; no other cause could be found at necropsy. Review of cases 1 and 2 after necropsy suggests that the clinical presentation was due to a combination of pulmonary embolism and infarction. In case 3 the presentation was with cardiac failure, but

consumption of clotting factors by the large intracardiac thrombus precipitated DIC.⁷

The use of heparin in DIC is controversial. Stahl *et al* reported the successful treatment of six cases of mild consumption coagulopathy (normal or near normal clotting) due to occult pulmonary embolism, with full heparinisation.⁸ In contrast, Mant and King reviewed 47 patients with severe DIC⁹: 12 patients had received heparin, in seven bleeding worsened, and in only one was any benefit seen.

Identification and treatment of the precipitating cause is essential in the management of DIC, but in this series the underlying cause of the DIC was only apparent at necropsy. Case 2 had a matched defect on the ventilation and perfusion lung scan which was not thought to represent pulmonary embolic disease. This investigation is neither sensitive nor specific for pulmonary embolism, however,¹⁰ and while mismatched defects are compatible with pulmonary embolism, pulmonary infarction may cause a matched defect. These cases highlight the need for early diagnosis and treatment of pulmonary embolism before the irreversible stage of severe DIC is reached. At this stage coagulation with heparin is unlikely to be of benefit. A high degree of clinical

suspicion is of particular importance in the elderly, in whom clinical presentation may be atypical.

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