In conclusion, SSPE is a rare progressive brain disease due to a mutated measles virus. The diagnosis is easily overlooked because of an insidious or bizarre presentation together with normal neuroimaging. The variable natural history, where spontaneous remissions may occur, creates major problems for small therapeutic trials. However, given its catastrophic course in the young, adequate evaluation of the various treatment options in a controlled prospective international study is long overdue.

Final diagnosis

Subacute sclerosing panencephalitis.

Keywords: subacute sclerosing panencephalitis, interferon-alpha, isoprinosine

We are grateful to Dr CS McKinstry, Consultant Neuroradiologist.

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Mental dullness after thrombolytic therapy

KS Woo, HCK Chan, WS Poon

A 68-year-old hypertensive man was admitted to the coronary care unit with acute inferior myocardial infarction presenting with sudden severe gripping central chest pain for two hours and ST elevation at inferior leads of electrocardiogram. Recombinant tissue plasminogen activator (rtPA) 100 mg (10 mg bolus, 50 mg infusion in one hour and then 40 mg infusion over two hours) was given intravenously, followed by intravenous heparin (4000 units bolus then 800 units/h) and isosorbide dinitrate. Morphine and oral aspirin were also given. The patient responded well. His chest pain subsided soon after admission. There was early peaking of the creatine phosphokinase 14 hours after onset of chest pain. However, he started to appear mentally dull 20 hours after receiving the rtPA. His conscious state deteriorated rapidly over the next two hours.

Questions

- 1 What is the most probable cause of his mental dullness?
- 2 What further investigation would you undertake to confirm this?

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Answers

QUESTION 1

Stroke, cardiac arrhythmia and low output state (pump failure or cardiac tamponade) are possibilities. However, the close temporal association with thrombolytic therapy suggests a high possibility of haemorrhagic stroke.

QUESTION 2

Computed tomography (CT) scan of the brain (figure), which revealed an extensive intraventricular haemorrhage (more on right side) without hydrocephalus.

Discussion

Acute myocardial infarction is a common problem with a high morbidity and mortality. Thrombolytic therapy has revolutionised its treatment by reducing mortality and preserving left ventricular function.^{1,2} Although it is generally safe and cost-effective, patients re-

ceiving thrombolytic therapy are at risk of developing adverse effects including major bleeding, intracranial haemorrhage, hypotension, allergy, stroke, cholesterol crystal embolisation, splenic rupture and aortic dissection.³ Of these, intracranial haemorrhage is the most ominous complication.

The incidence of intracerebral haemorrhagic complications varies from 0.08 to 0.72%.^{2,3} Among the four widely available thrombolytic agents, namely recombinant tissue plasminogen activator (rtPA), anistreplase, streptokinase and urokinase, rtPA is clinically the most potent but carries a higher rate (0.72%) of this complication. Hypertension, older age, female gender, low body weight, fibrinogen depletion and a prolonged bleeding time are risk factors that would increase the incidence of intracranial bleeding.⁴ The decision to use thrombolytic therapy should be determined by the overall benefit-risk ratio in the individual patient.

The exact underlying pathogenesis of intracranial bleeding is not known. Severe amyloid angiopathy has been postulated to be a cause for or a contributing factor in fibrinolysis-associated intracranial haemorrhage.⁴ There is no relationship between the degree of lytic state (degradation of fibrinogen and other coagulation protein) and the incidence of bleeding complications. The specific underlying reason that predisposes patients treated with rtPA to increase intracerebral bleeding is unknown. More lysis of intracranial physiological haemostatic thrombi is a possible explanation.

A high level of alertness is needed for this complication after thrombolytic therapy. After a full neurological examination for neurological deficit, CT brain scan is mandatory for early detection. Magnetic resonance imaging or cerebral angiography is indicated, especially in younger patients, to identify underlying lesions such as arteriovenous malformation or berry aneurysm which are amenable to surgical intervention.

As soon as this bleeding complication is suspected or confirmed, a full coagulation screen should be carried out and adjunctive anticoagulant (heparin, hirudin or aspirin) should be withheld. Significant coagulopathy in blood should be corrected. Decompression therapy using intravenous mannitol or glycerin infusion should be started. Use of anti-fibrinolytic drugs (tranexamic acid intravenously 24 g daily for three days) has also been advocated.⁵ Should this fail, with a complication such as recurrent haemorrhage or hydrocephalus, surgical intervention should be considered.

Intracranial haemorrhage complicating thrombolytic therapy carries a high mortality of over 70% in the acute state. The prognosis of intraventricular bleeding in patients with underlying pathology is better than those without underlying disease. The survival rate in patients without underlying disease is only 8%.⁶ In the survivors, approximately one-half are left with important disability at hospital discharge.

Figure CT scan of brain on day 2 after admission

Contraindications and precautions for thrombolytic therapy

Contraindications:

- haemorrhagic stroke (ever)
- embolic or thrombotic stroke within 6 months
- brain surgery or head trauma within 6 months
- uncontrolled hypertension (blood pressure >200/110 mmHg)
- aortic dissection
- active internal bleeding within 2 weeks
- major surgery, trauma or organ biopsy within 2 weeks
- known bleeding disorder
- diabetic retinopathy (relative)
- pregnancy or first week post-partum
- active pancreatitis

Precautions:

- recent puncture of noncompressible vessel (within a week)
- active peptic ulceration
- active cavitating pulmonary tuberculosis
- infective endocarditis
- advanced liver disease
- anticoagulant therapy
- fresh intracardiac thrombi
- menstruation (relative)

Final diagnosis

Intracerebral haemorrhage complicating thrombolytic therapy for acute myocardial infarction.

Keywords: acute myocardial infarction, thrombolytic therapy, intracerebral haemorrhage

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Ectopic acromegaly

JK Platts, DF Child, P Meadows, JN Harvey

A 53-year-old woman presented to her general practitioner in November 1992 asking to be considered for hormone replacement therapy. She had noticed excessive sweating and tiredness but had no other symptoms. Her general practitioner noticed features suggestive of acromegaly.

In 1988 she had developed cough and haemoptysis and was investigated elsewhere. The chest X-ray at that time showed a right hilar mass. Thirteen years earlier she had had pneumonia. The mass was found to be present on X-rays taken then and had changed little over the intervening period. It had been felt to be benign with no further investigation necessary. In 1990 she presented with a nodular goitre which she felt to be unsightly. She was euthyroid. Surgery was offered but declined and no further action was taken. She was a life-long non-smoker on no medication.

Examination in 1992 revealed acromegalic facial features and enlargement of the hands and feet. She was normotensive and had a large multi-nodular goitre. Photographs taken nine years previously appeared normal. She was an anxious woman who at times declined investigation or treatment.

In a 75 g oral glucose tolerance test the plasma glucose was 5.6 mmol.l⁻¹ fasting and 7.3 mmol.l⁻¹ after 2 h; growth hormone (GH) was 68.5 mU.l⁻¹ fasting and did not suppress. After 200 µg intravenous thyroid-releasing hormone, serum GH increased from 67.4 to >150 mU.l⁻¹ at 20 min. Thyroid function, prolactin and a short synacthen test were normal. Luteinising hormone and follicle-stimulating hormone concentrations were at normal post-menopausal levels. The chest X-ray revealed a 9 cm diameter mass contiguous with the right hilum (figure 1). Computed tomography (CT) scan of the pituitary region was normal.

Figure 1 Chest X-ray showing right hilar mass

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Questions

- 1 What is the most likely diagnosis?
- 2 What further investigations might be helpful?
- 3 What line of management should be pursued?