Paradoxical embolism causing cerebral infarction in a young man with hereditary haemorrhagic telangiectasia

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Introduction

Paradoxical embolism is a relatively uncommon clinical condition. Only a few hundred cases have been reported in the literature.[1] Despite sophisticated technological advances, it remains an under-diagnosed clinical entity.[2] Blood clots formed either in the right side of the heart or in the venous circulation escape via an intra- or extra-cardiac right-to-left shunt into the systemic circulation. This results in an arterial embolism, hence the term paradoxical embolism. The condition can cause significant morbidity and mortality. We report a case of cerebral infarction secondary to paradoxical embolism. This is the first case to be reported in the literature with the unique and rare association of patent foramen ovale and pulmonary arteriovenous malformation with hereditary haemorrhagic telangiectasia.

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Case report

A 33-year-old engineer was admitted to our medical unit following a generalised tonic clonic seizure. There was no significant past medical history, except for mild bronchial asthma and recurrent epistaxis. He was a non-smoker and took regular exercise in the gym. His alcohol consumption was well within recommended levels. He was using salbutamol and beclomethasone inhalers and Naseptin (chlorhexidine) nasal cream. His father had late-onset epilepsy.

Physical examination revealed a rating of 10/15 on the Glasgow coma scale. Within a couple of hours of admission his conscious level improved to 15/15. He was haemodynamically stable, with a regular heart rate of 56/minute and a blood pressure of 122/87 mmHg. He had a few telangiectasiae on his lips. A faint bruit was heard in his left lower chest. He had complete right hemiparesis with non-fluent dysphasia. Four hours following admission he became breathless and developed central cyanosis. An arterial oxygen saturation was (PaO_2) was 6.4 kPa.

A computerised tomographic scan of his brain showed a non-haemorrhagic infarct in the left parietal lobe. Routine blood tests, namely full blood count, urea and electrolytes, liver function tests, glucose, calcium and cholesterol, were all normal. Thrombophilia and vasculitis screening were normal. Autoantibody tests were within normal limits. The electrocardiogram showed sinus bradycardia. Chest X-ray was suggestive of a possible soft tissue shadow behind the left heart border. Doppler sonography of the leg veins ruled out deep vein thrombosis. A ventilation:perfusion scan revealed a mismatch in the left lower lung suggestive of a pul-

Figure 1. **a**: CT scan of the thorax with contrast, showing a large (4 cm x 3.5 cm) left basal arteriovenous malformation (AVM) resembling a bunch of grapes behind the heart. **b**: A three-dimensional CT scan of the thorax shows the AVM vividly

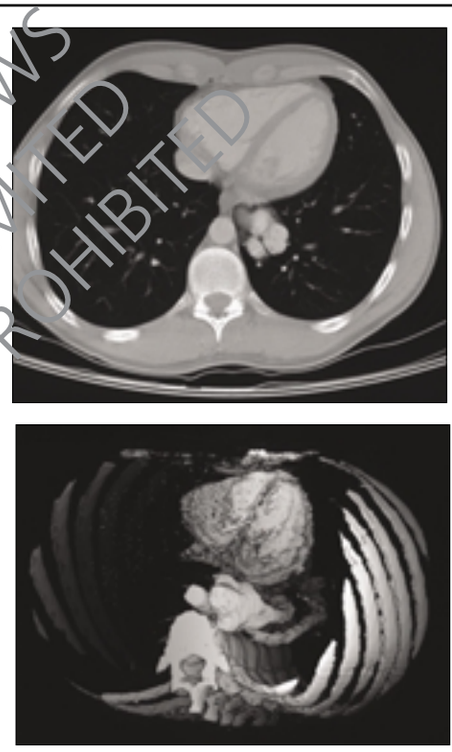

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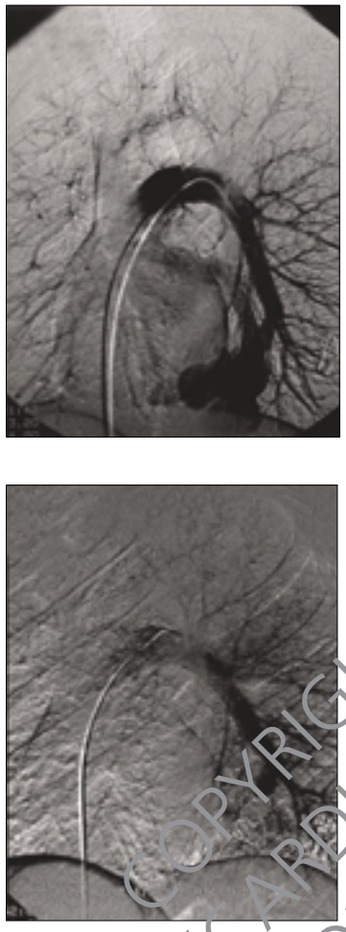
Figure 2. **a**: Pulmonary angiogram, showing a large left basal arteriovenous malformation (AVM). **b**: After coil embolisation, the AVM has disappeared



monary embolism. Transthoracic echocardiography and carotid Doppler studies were normal.

A provisional diagnosis of paradoxical embolism was made. The concomitant ischaemic stroke and pulmonary embolism in the presence of a bruit and a soft tissue mass in the chest X-ray indicated the diagnosis. The patient was anticoagulated with warfarin. A diagnosis of hereditary haemorrhagic telangiectasia was made on the basis of his recurrent nosebleeds and the telangiectatic lesions.[3] Although there was no relevant family history, he was referred to a geneticist for further assessment.

Following discharge from hospital the patient's neurological deficits resolved completely. However, he continued to suffer from recurrent attacks of breathlessness with cyanotic episodes. He was treated with oxygen at home. Subsequent investigations revealed a significant drop of PaO_2 from 91% (supine posture) to 84% (erect posture). An exercise pulse oximetry revealed a similar drop from 83% to 76%, thus indicating a significant right-to-left shunt.

A computerised tomographic (CT) scan of the thorax revealed a pulmonary arteriovenous malformation (PAVM) at the left lung base (figure 1). A pulmonary angiogram confirmed the diagnosis (figure 2). Contrast echocardiography and transoesophageal echocardiography showed a patent foramen ovale. He was referred to an interventional radiologist and underwent successful percutaneous coil embolisation of the pulmonary arteriovenous malformation. His arterial blood gas studies reverted to normal. He had no further episodes of breathlessness, cyanosis, and no further embolic episodes. He could once again perform regular exercise in the gym.

Discussion

Paradoxical embolism is a well-known clinical entity. The diagnosis is based on evidence of a thrombus in the venous system or the right heart; a right-to-left shunt, usually in the form of a patent foramen ovale or pulmonary arteriovenous malformation, and systemic embolisation.

In our case, though there was no evidence of deep vein thrombosis: a ventilation perfusion scan confirmed a pulmonary embolism. A CT scan revealed an ischaemic cerebral infarct. A CT scan of the thorax and a pulmonary angiogram confirmed a PAVM. Transoesophageal echocardiography revealed a patent foramen ovale. Simultaneous pulmonary embolism and cerebral infarction in a young patient with a concomitant PAVM is extremely rare. So far only two previous cases have been reported.[4]

Pulmonary arteriovenous malformations are usually multiple. Eighty per cent of PAVMs are associated with hereditary haemorrhagic telangiectasia (HHT). Conversely, the prevalence of PAVM is 24–33% among HHT patients.[5,6] The usual clinical presentation of PAVMs is exertional dyspnoea and hypoxia.[7] In our patient, in spite of clinical evidence of telangiectasia and recurrent epistaxis, only one PAVM was identified. The patent foramen ovale is once again a rare association. A combination of these findings has not been reported previously.

The complications of PAVM are chronic hypoxia and paradoxical embolism. Paradoxical embolism can affect any organ system of the body, especially the brain, peripheral circulation, gut, kidneys or heart. Two major series of patients with HHT studied at the Hammersmith Hospital and at Johns Hopkins showed cerebral abscess in 20%, stroke on 18% and transient ischaemic attack in 37% of cases.[4]

Treatment options for PAVMs are surgical resection or angiographic embolisation with fibrin-coated steel coil or balloon occlusion.[8] The first surgical resection was performed in 1942.[4] Presently, angiographic occlusion is the treatment of choice.[7,8] After a short period of anticoagulation therapy our patient underwent a successful coil embolisation.

The patent foramen ovale (PFO) in our case report was probably a rare association. Published series indicate unexplained ischaemic strokes in 3–4% per year of patients with PFO. Long-term anticoagulation for prevention of paradoxical embolism seems to be of questionable benefit.[9] Surgical closure of PFO appears to be the treatment of choice for secondary prevention of paradoxical

Key messages

- In paradoxical embolism, a thrombus forms in the right heart or venous system and passes through a right-to-left shunt into the systemic circulation
- This patient had paradoxical embolism causing cerebral infarction; hereditary haemorrhagic telangiectasia, a pulmonary arteriovenous malformation and a patent foramen ovale
- All young stroke patients should undergo a battery of investigations, such as TOE and a thrombophilia screen, to identify treatable causes
- Treatment options for pulmonary arteriovenous malformations are surgical resection or angiographic embolisation

embolism.[10] Percutaneous or transcatheter closure of PFO is a promising alternative technique. However, further technical improvements and studies are necessary to identify those patients most likely to benefit from this procedure.[11,12]

Hyperhomocysteinaemia is an established risk factor for deep vein thrombosis.[13] Moderate hyperhomocysteinaemia is associated with an increased risk of both arterial and venous thrombotic disease.[14] Homocysteine assay is currently available at specialist research settings only, and for organisational reasons our patient did not have his homocysteinie level measured.

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