CASE REPORT

Ischaemic stroke secondary to paradoxical emboli through an arteriovenous malformation of the lung in a patient with known breast cancer

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SUMMARY

We presented an unusual case of a young woman who suffered an ischaemic stroke while receiving chemotherapy postsurgery for breast cancer. No cause was identified at that time and a year later an incidental pulmonary arteriovenous malformation (PAVM) was diagnosed during an MR review of her breasts. This was confirmed on the CT and she subsequently underwent successful endovascular embolisation. Ischaemic stroke as a presenting symptom of an undiagnosed PAVM or hereditary haemorrhagic telangiectasia is rare. PAVM is a clinically important and treatable cause of ischaemic stroke and should therefore be considered in young patients with ischaemic stroke, with or without concurrent venous thrombotic risk factors. As far as we are aware, this is the first reported incidental finding of PAVM on MR of the breast.

BACKGROUND

Pulmonary arteriovenous malformations (PAVM) are rare pulmonary vascular anomalies that are usually asymptomatic despite their association with a right to left shunt. They are strongly associated with hereditary haemorrhagic telangiectasia (HHT) and as such have been described in the literature as a possible cause of stroke in young and otherwise healthy patients.^{1–5} There are just a few cases in the literature of PAVM presenting with stroke in the absence of clinically suspected HHT.^{3–6} These case reports remind us of the need for both thorough cardiological and radiological investigation, particularly in the young adult.

CASE PRESENTATION

A 49-year-old woman underwent a left-sided wide local excision and axillary node dissection for a multifocal grade 3 invasive ductal carcinoma. None of the eight axillary lymph nodes examined were involved, and the tumour was oestrogen receptor positive and human epidermal growth factor receptor 2 negative. She started a course of adjuvant chemotherapy planned to be four cycles of epirubicin—followed by four cycles cyclophosphamide, methotrexate and 5-fluorouracil. Treatment was administered through a right subclavian Groshong line, owing to problems with peripheral venous access.

Following five cycles of chemotherapy she presented with the sudden onset right arm and leg weakness, sensory loss, with a significant expressive dysphasia. She underwent MRI of the brain and an

ischaemic left basal ganglia infarct was demonstrated (figure 1). She had no history of hypertension, ischaemic heart disease, diabetes or hyperlipidaemia and had no relevant family history. She was an ex-smoker. Thrombophilia screen (proteins C and S, antithrombin, activated protein C resistance assay, factor V Leiden, prothrombin and lupus anticoagulant), antinuclear and anticardiolipin antibodies, 12-lead ECG, 24 h Holter monitoring, carotid Doppler and echocardiogram were normal. Leg vein ultrasound was also normal. Her cholesterol was 4.1 and triglycerides 0.7. She was managed on a specialist stroke unit by two consultant stroke physicians and a neurologist. The cause of her stroke remained unclear, although was thought to be related to venous thromboembolism secondary to recent surgery and adjuvant chemotherapy. She started aspirin, dipyridamole and simvastatin, and made a full neurological recovery. She completed her breast cancer therapy with adjuvant

Figure 1 MR axial fluid-attenuated inversion recovery sequence image of the brain demonstrating an abnormal area of high signal consistent with an anterior left middle cerebral artery territorial infarct. (Unfortunately diffusion-weighted image/apparent-diffusion coefficient sequences were not performed at this time. Follow-up MR studies confirmed size reduction in keeping with an infarct).

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Figure 2 MR axial fat suppressed postcontrast image of the breast demonstrating prominent enhancing serpiginous vessels within the middle lobe of the right lung (arrow).

radiotherapy to the breast, 1 year of adjuvant trastuzumab and adjuvant endocrine therapy in the form of anastrozole.

Clinical review 1 year later, however, revealed thickening around the scar which raised concern of possible recurrence. Initial mammogram and ultrasound imaging demonstrated probable scarring only, and so she underwent further evaluation with contrast-enhanced MRI (figure 2). This demonstrated no evidence of recurrence but an additional finding of prominent serpiginous vessels within the middle lobe of the right lung. Arteriovenous malformation was suspected and confirmed on subsequent spiral contrast-enhanced CT (CECT) of the chest (figure 3). This raised the possibility that she had developed a deep vein or line associated venous clot while on chemotherapy, and suffered a cerebral vascular accident as a result of a paradoxical embolism. This was thought to be the cause of her previous embolic episode and she was referred for investigation and treatment of the pulmonary lesion (figure 4).

DIFFERENTIAL DIAGNOSIS

The table below lists some of the specific diseases associated with stroke in young adults, along with their contributory diagnostic features (descending order of frequency).¹

Cervical arterial dissection	Minor head or cervical trauma, headache or neck pain, local signs such as Horner's syndrome or cranial nerve palsy
Atherosclerotic large-vessel disease	Multiple vascular risk factors, stroke preceded by transient ischaemic attacks
Small-vessel disease	Hypertension, diabetes, lacunar syndrome, (infections, vasculitis and Fabry's disease can also cause lacunar infarcts). Capsular warning syndrome
Patent foramen ovale (PFO)	Direct or indirect sign of paradoxical embolus (stroke following Valsalva manoeuvre or with venous thrombosis risk factors such as prolonged immobilisation). Atrial septal aneurysm. Transoesophageal echocardiography (TOE) with contrast is recommended
Other cardioembolic diseases	Clinical history and examination, illicit drug use (amphetamines) and atrial fibrillation, cortical stroke, haemorrhagic transformation, multiple infarcts in different arterial territories
Pulmonary arteriovenous malformation	Right-to-left shunt, no patent foramen ovale, family history of HHT. TOE with contrast and contrast-enhanced CT are recommended
CADASIL syndrome (subcortical disease)	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy. Headaches, transient ischaemic attacks and absent cardiovascular risk factors. Lacunar syndrome and subcortical dementia

Figure 3 CT pulmonary angiogram, lung-windowed image of the chest demonstrating a large right pulmonary arteriovenous malformation (PAVM) in the medial segment of the middle lobe. Moderate-sized PAVMs were also seen within the lateral segment of the middle lobe and the anterior segment of the right upper lobe.

TREATMENT

The patient underwent successful endovascular embolisation of her PAVM (figure 4). No extra-PAVM were found.

OUTCOME AND FOLLOW-UP

The patient had no recurrence of her breast cancer and suffered no further ischaemic episodes. Specialist clinical and genetic review found no evidence to support a diagnosis of HHT.

DISCUSSION

The case highlights the importance of considering PAVM with paradoxical embolism in the list of differential causes of ischaemic stroke. Surgery and chemotherapy are risk factors for venous (as opposed to arterial) thromboembolic disease, as is the presence of a central venous line. The resected early breast cancer itself did not constitute either an increased venous or arterial thromboembolic risk.

We recommend that young patients (<55 years) with ischaemic stroke are screened for PAVM with a plain chest film and an arterial blood gas, in addition to routine stroke investigations (including CT/MRI of the brain, carotid Doppler, echocardiogram, blood screen), even in the context of concurrent risk factors. Population-study results suggest that there may be an overestimation of the involvement of PFO in cryptogenic stroke.⁶ Recurrent episodes or the presence of venous

Figure 4 Contrast-enhanced CT (CECT) of the chest demonstrating postembolisation appearances of the lateral segment, middle lobe right pulmonary arteriovenous malformation with an amplatzer plug.

thrombosis risk factors should therefore raise concern of paradoxical embolism secondary to PAVM or PFO and be investigated with CECT of the thorax as well as bubble-contrast TOE.

MRI is increasingly used in the investigation of the symptomatic breast and is particularly used in the assessment of the post-operative breast. This trend can be expected to be accompanied by an increase in the number of incidental pathologies detected outside the margin of the breast. As far as we are aware, this is the first reported incidental finding of PAVM on MRI of the breast.

Two similar case reports in the literature of stroke secondary to PAVM in the absence of HHT:

1. *Stroke after prolonged air travel with an undiagnosed pulmonary arteriovenous malformation.*³ Case of a 44-year-old woman who presented with a stroke 5 days after an air flight. Paradoxical embolism was suspected because of the recent air travel. Bubble-contrast transthoracic echocardiography demonstrated an extracardiac shunt and PAVM was detected on contrast-enhanced CT.

Learning points

- Pulmonary arteriovenous malformations (PAVM) is an important and treatable cause of stroke in young adults and should be considered in the context of other causes of right-to-left shunt.
- Initial investigation with chest radiograph and arterial blood gas is suggested in all young adults (<55 years) who presented with stroke.
- Contrast-enhanced CT and bubble-contrast transoesophageal echocardiography are the investigations of choice when ischaemic episodes are recurrent or PAVM is suspected.

2. *Pulmonary arteriovenous malformation: a rare, treatable cause of stroke in young adults.*⁶ Case of a 36-year-old man who presented with a stroke. Bubble-contrast transoesophageal echocardiography was suggestive of a transpulmonary shunt and contrast-enhanced CT detected PAVM. No particular venous thrombosis risk factors were identified.

In both of these cases and in the case we described, there was no family history of early stroke or known thrombophilia. Haematology, coagulation screen, ECG, 24 h Holter monitoring and carotid Doppler were also normal. Our case differs in that PAVM was discovered incidentally, and this serves as a valuable reminder of the need for a robust specialist imaging pathway for young patients with stroke.

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Competing interests None.

Patient consent Obtained.

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