A rare cause of paradoxical embolism

Pulmonary arteriovenous malformations

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Summary

We report the case of a 54-year-old patient with a splenic infarction of unknown origin, recurrent transient focal neurological episodes and multiple subacute cerebral ischaemic lesions on magnetic resonance imaging. During stroke work-up we performed transoesophageal bubble-contrast echocardiography, which revealed a pronounced noncardiac right-to-left shunt. Subsequent pulmonary computed tomography (CT) revealed three pulmonary arteriovenous malformations (PAVMs). Paradoxical cerebral and splenic embolism caused by a right-to-left shunt due to PAVMs was diagnosed. The patient met the Curaçao criteria for hereditary haemorrhagic telangiectasia (HHT), the diagnosis was confirmed by genetic testing (*ACVRL1* mutation, HHT type 2). Because of symptomatic PAVM, pulmonary angiography was performed followed by catheter-directed placement of three vascular plugs into the feeding artery of each PAVM. The follow-up pulmonary CT 3 months after the intervention showed occlusion of the feeding arteries with all three vascular plugs in place. PAVMs are rare, and 80–90% are associated with HHT. Complications of PAVM include paradoxical embolism, brain abscess, haemoptysis and hypoxaemia. Symptomatic patients and patients with a feeding artery diameter of ≥2–3 mm should be referred for catheter embolisation. Pulmonary CT is the gold standard for diagnosis and follow-up after endovascular treatment.

Key words: pulmonary arteriovenous malformations; hereditary haemorrhagic telangiectasia; paradoxical embolism; transoesophageal bubble contrast echocardiography; catheter embolisation

Case report

A 54-year-old patient presented himself to our hospital with recurrent short episodes of paraesthesia of the left arm and a speech disorder over the last few weeks. The patient was also known for a splenic infarction of unknown origin diagnosed 6 months earlier on an abdominal computed tomography (CT) scan performed because of left abdominal pain. He suffered from frequent episodic migraine and recurrent epistaxis since adulthood. The patient had never smoked, had normal cholesterol levels, no diabetes and no arterial hypertension. He had never experienced shortness of breath. Clinical examination revealed a telangiectasia on the upper lip. There was no heart murmur. Laboratory analysis including a blood cell count, renal function, blood glucose and inflammatory markers were normal. His 12-lead ECG showed sinus rhythm. Suspecting cerebrovascular disease, magnetic resonance imaging (MRI) of the head was performed, which showed two subacute ischaemic lesions in the right hemisphere (frontal and parieto-occipital areas), and also multiple older ischaemic lesions in the cerebellum. A stroke work-up was performed. A 24-hour Holter ECG was negative for atrial fibrillation. Duplex ultrasound showed only mild atherosclerotic plaque of the right internal carotid artery. Coagulation tests were normal. Because of cryptogenic stroke and a splenic infarction in this relatively young patient we suspected multiple thromboembolic events and performed transoesophageal contrast echocardiography, which failed to show any cardiac sources of emboli. However, there was a pronounced noncardiac right-to-left shunt shortly after the intravenous application of contrast bubbles (agitated saline mixed with blood). Chest X ray and pulmonary CT (fig. 1) were performed and revealed three pulmonary arteriovenous malformations (PAVMs) with feeding artery diameters of 2, 5 and 7 mm. Paradoxical cerebral and splenic embolism caused by PAVM due to the loss of capillary filtering function was assumed. The right-to-left shunt was calculated to be 18% by arterial blood gas analysis during inhalation of 100% oxygen. Capillary microscopy of the nailfold showed megacapillaries (fig. 2). The patient met three out of four of the Curaçao criteria for hereditary haemorrhagic telangiectasia (HHT) – epistaxis, visceral arteriovenous malformation, mucocutaneous telangiectasia – but not family history of HHT. Genetic testing for HHT confirmed the diagnosis (*ACVRL1* mutation, HHT type 2). Because of symptomatic PAVM, pulmonary angiography with the option of catheter embolisation to prevent further vascular events was suggested to the patient (fig. 3). A vascular plug was placed into the feeding

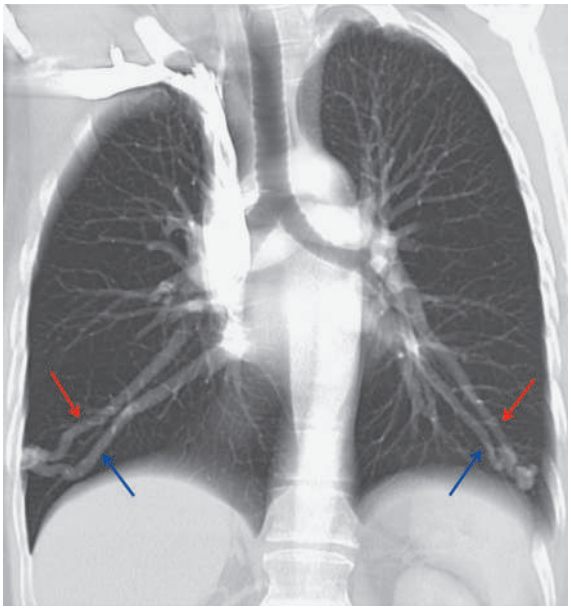

Figure 1: The two largest PAVM with feeding artery (red arrows) and venous drainage (blue arrows). Pulmonary CT reconstruction.

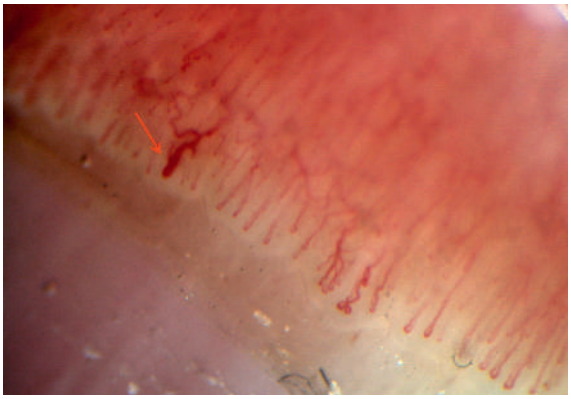

Figure 2: Nailfold microscopy with megacapillaries (red arrow).

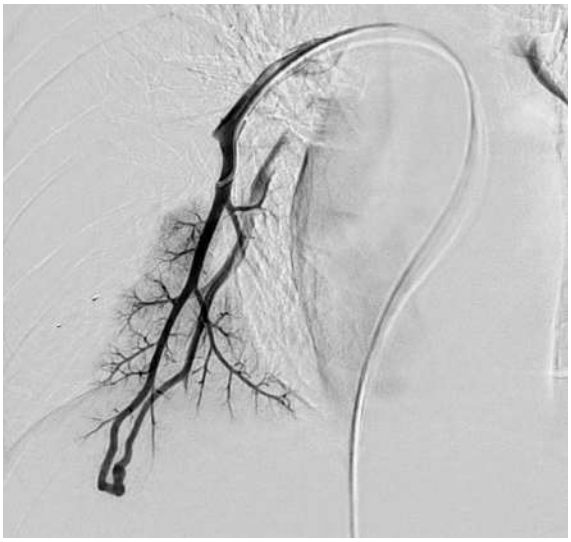

Figure 3: Pulmonary angiography before embolisation of the PAVM.

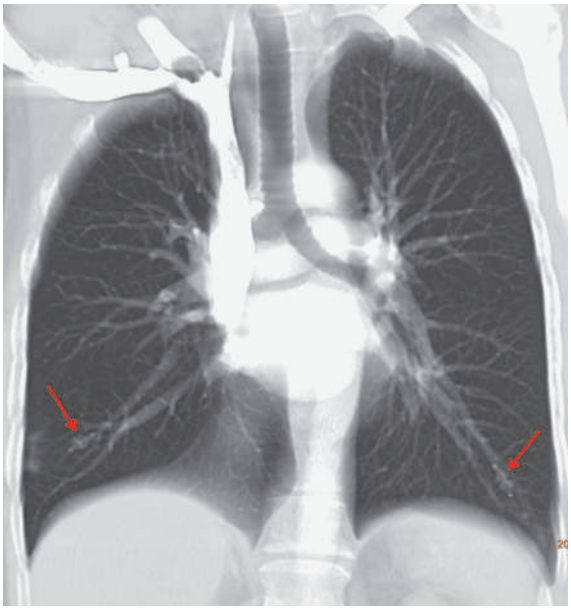

Figure 4: PAVM after vascular plug (arrows) placement. Pulmonary CT reconstruction.

arteries of all three PAVMs without complications. On the first clinical follow-up three months after the intervention the patient was asymptomatic. Pulmonary CT showed occlusion of all three feeding arteries (fig. 4). Screening of the patient's family revealed one son to have PAVM and he also underwent catheter embolisation.

Discussion

Pulmonary arteriovenous malformations (PAVMs) are abnormal communications between pulmonary arteries and veins. PAVM is a rare disorder. One study suggested a prevalence of 1:5000 at autopsy [1]. PAVMs tend to increase in size over time. The most frequent complications of PAVM are thromboembolic events (i.e., paradoxical embolism and brain abscess) due to the loss of capillary filtering function. The incidence in PAVM has been reported to be 18% for stroke, 37% for transient ischaemic attacks and 9% for brain abscess [2]. Other complications of PAVM include migraine, hypoxaemia from the right-to-left shunt and pulmonary haemorrhage. Our patient had paradoxical embolism and frequent episodic migraine. During the work-up of cryptogenic stroke, contrast echocardiography is often performed. It has a sensitivity of 100% and a specificity of 49% for detecting PAVM [3]. Because of the high sensitivity of contrast echocardiography, grading scales have been proposed to avoid unnecessary pulmonary CT scans [4]. Patients with a grade 1 shunt (<30 bubbles reaching the left ventricle) have less than a 2% chance of having a treatable PAVM. Patients

with a grade 2 or 3 shunt, including our patient, (grade 2 refers to 30–100 bubbles, grade 3 refers to >100 bubbles reaching the left ventricle) should have a pulmonary CT to search for PAVM. A method to evaluate the shunt fraction (the fraction of the cardiac output that bypasses the pulmonary capillaries) is the 100% oxygen method. The patient breathes 100% oxygen through an airtight mask. After 20 minutes an arterial blood gas analysis is performed to calculate the shunt fraction [5]. Our patient showed a relevant shunt fraction of 18% before catheter embolisation. Values above 5% are considered abnormal. However, a calculated shunt fraction <5% does not exclude PAVM. As in our patient, capillary microscopy has been shown to reveal megacapillaries in a vast majority of confirmed HHT patients (83 vs 0% in healthy controls) [6].

Screening for asymptomatic PAVM in patients with HHT is recommended worldwide for adults. Symptomatic patients or patients with a feeding artery diameter of ≥2–3 mm should be considered for catheter embolisation (grade 2C indication) [7]. Catheter embolisation is the treatment of choice, while surgery is reserved for patients with severe contrast-agent allergy or patients with pulmonary haemorrhage due to ruptured PAVM. Primary success rates are high though PAVM can recur over time. The most common post-procedural complication of catheter embolisation is pleuritic chest pain, dislocation of the device is rare. After catheter embolisation pulmonary CT is used to screen for disease progression or recurrence.

In 80–90% of cases, PAVMs are congenital and associated with HHT (also referred to as Osler-Weber-Rendu syndrome) [8]. Other causes include hepatic cirrhosis, mitral stenosis, Fanconi's syndrome and previous surgery for congenital heart disease. Our patient was diagnosed with HHT meeting three of four Curaçao criteria and by genetic testing. HHT is a rare genetic autosomal dominant trait caused by mutation of various genes that modulate the transforming growth factor-β superfamily signalling in vascular endothelial cells. The prevalence of PAVM in patients with HHT is estimated to be between 30 and 50% [9].

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Conclusion

A history of paradoxical embolism and a noncardiac right-to-left shunt on transoesophageal contrast echocardiography should raise the suspicion of PAVM. Pulmonary CT can confirm the diagnosis. Up to 55% of PAVMs do not cause symptoms. However, symptomatic patients or patients with a feeding artery diameter of ≥2–3 mm should be considered for catheter embolisation to prevent complications. Individuals with a family history should also be screened for PAVM.

Disclosure statement
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