CASE REPORT

A large pulmonary arteriovenous malformation causing cerebrovascular accidents

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SUMMARY

The incidence of pulmonary arteriovenous malformations (PAVMs) is 2.5 in 100 000. 80% are associated with Osler-Weber-Rendu syndrome or hereditary haemorrhagic telangiectasia. We report the case of a 70-year-old man with a 6 cm spherical mass incidentally found on chest X-ray. There was a localised systolic bruit over the right lower zone posteriorly; however, he was asymptomatic. He had suffered a stroke, affecting his right hand and his speech, from which he recovered. He experienced regular transient ischaemic attacks, on an average of every 2 months. He underwent a right lower lobectomy and on ligating the right lower lobe pulmonary artery the saturations of oxygen rose from 92% to 97%, demonstrating a significant right to left extracardiac shunt. Postoperative recovery was excellent and 1 year later the patient reports no further neurological symptoms. 40% of such lesions exhibit symptoms, however, only one-third are neurological. Treatment should be by percutaneous embolisation.

BACKGROUND

Pulmonary arteriovenous malformations (PAVMs) are direct communications between pulmonary arteries and veins without an intervening pulmonary bed. Varied nomenclature exists, such as pulmonary arteriovenous fistula, pulmonary arteriovenous aneurysm, pulmonary angioma, arteriovenous angiomas, cavernous haemangiomas and pulmonary hamartomas. Most are congenital malformations, and although they may increase in size, they are always benign. The nomenclature varies to represent the spectrum of different combinations of such malformations. Some lesions have visible aneurysmal arterial dilation with venous connections, whereas others have a network of arteriovenous connections with anomalous venous drainage.¹

The incidence is around 2.5/100 000 and more than 80% are congenital. Of these congenital PAVMs the majority occur as part of Osler-Weber-Rendu syndrome or hereditary haemorrhagic telangiectasia (HHT). The genetic abnormality in some forms of HHT is in a gene on chromosome 9, which also codes for endoglin (a membrane glycoprotein of vascular endothelial cells), and in the ALK-1 gene, which explain the frequent association between these two conditions.² The Curaçao criteria is used to determine likelihood of HHT, and genetic testing for endoglin (HHT1) or ALK-1 (HHT2) mutations will confirm the diagnosis. The addition of the presence of PAVMs with larger shunt grades to the Curaçao criteria, with the exclusion of those with lower shunt grades has been shown to

increase the sensitivity and not affect the specificity of the Curaçao criteria.³

Age at diagnosis may range from newborn to 70 years old. They may be single lesions but multiple simultaneous lesions are slightly more common. The majority of PAVMs are located in the lower lobes, with presence in the left lower lobe being more common than in the right.^{4–6}

The spectrum of different PAVMs is classified according to their anatomical variations. The case we discuss below is a peripheral, large arteriovenous aneurysm with no anomalous venous drainage, with right to left arteriovenous shunting through the aneurysm cavity.

CASE PRESENTATION

A 71-year-old man, an accountant, was referred to the cardiothoracic clinic after a routine examination revealed a systolic bruit over the lower aspect of the right side of the posterior chest wall. He was known to have a spherical lesion in the right lower zone on chest X-ray (figures 1 and 2), which had no suspicious features and had remained within 61–64 mm in size for over 20 years. The patient had been aware of this lesion as far back as he could remember and was always told the lesion was harmless and need not be resected. A sputum cytology result from 1988 showed no malignant cells. The patient was no longer followed up for this condition.

Figure 1 Plain chest radiographs (anteroposterior and lateral view) showing the spherical lesion in the right lower lobe.

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Figure 2 Plain chest radiographs (anteroposterior and lateral view) showing the spherical lesion in the right lower lobe.

He was virtually symptom free besides occasional cough productive of yellowish sputum and rare minor episodes of haemoptysis. He was not short of breath at rest despite saturations on air never rising above 92%. As a young adult he was very physically active, and competed in tennis and other sports with no limitation.

His history includes a cerebrovascular accident (CVA) affecting his left arm in 1999, two myocardial infarcts in 1993 and 2003, a transient ischaemic attack (TIA) affecting gait and vision for 45 min in 2006, a coronary artery bypass graft in 2004 and recurrent ischaemic heart disease requiring percutaneous coronary stenting in 2012. He described multiple episodes of dizziness, confusion and loss of balance, which had been diagnosed as TIAs by the neurologist. There was no history of oral or nasal telangiectasia or gastrointestinal bleeds.

He was diabetic on oral hypoglycaemics. The patient had quit smoking 12 years prior but previously used to smoke 30 cigarettes a day. His family history was unremarkable. Direct family members were screened for arteriovenous malformations or telangiectasia, none were found. Using the Curaçao criteria, this patient only receives one of the four available points and therefore is unlikely to have HHT.

Clinically, there was moderate weakness and tremor of the left hand following the CVA, low pulse oximetry saturations and this audible bruit over the right lower chest posteriorly.

INVESTIGATIONS

Transthoracic echocardiography and bilateral carotid Doppler scans were performed at the time of presentation with stroke to search for sources of emboli. Contrast echocardiography should have been used but was not and the lesion on chest X-ray was ignored completely.

On referral to the cardiothoracic unit, a CT scan of the chest was performed. It confirmed that this 6 cm lesion in the lower lobe of the right lung was an arteriovenous malformation (figures 3 and 4), and the three-dimensional reconstruction clearly shows the large feeding vessels (figure 5).

Figure 3 CT scan with intravenous contrast. Cut at different levels showing communication with large vessels and lesion filled with contrast.

TREATMENT

The patient underwent an open right lower lobectomy in March 2013. On ligating the right lower pulmonary artery, the oxygen saturation rose from 92% to 97%.

On histological examination of the right lower lobe, there was a blood-filled 5 cm cystic space close to a main feeding vessel 5 mm beneath the pleural surface peripherally. A large thick-walled vessel communicated with this cystic space, which was itself lined with thickened tunica intima and media, and a normal endothelial layer. This further confirms the fistula as a peripheral arteriovenous aneurysm between the right lower pulmonary artery and vein, with no anomalous venous drainage (Anatwabi classification: group II).

OUTCOME AND FOLLOW-UP

The patient has recovered fully from the operation and is asymptomatic. Oxygen saturation on air remains 97% or higher.

Figure 4 CT scan with intravenous contrast. Cut at different levels showing communication with large vessels and lesion filled with contrast.

Figure 5 Three-dimensional CT reconstruction. Note large artery and vein entering aneurysm.

The mild cough has resolved and no further TIAs have occurred throughout the year since surgery.

DISCUSSION

The fundamental defect is a right to left shunt. In the majority of cases, this rarely causes significant haemodynamic upset; however, if the shunt is greater than 20% of the systemic cardiac output or in the context of severe anaemia, the patient may become symptomatic.

Many are asymptomatic (60%), although signs of right to left shunt may include exertional dyspnoea, cyanosis and clubbing in severe cases, or haemoptysis. As in our patient, there may be mildly decreased oxygen saturations with occasional non-specific symptoms. Of the symptomatic patients, up to 33% may present with neurological features. These may be secondary to paradoxical embolisation or intracranial haemorrhage from ruptured cerebral PAVMs.³ Half the lesions have audible vascular bruits, as in this case. It is worth mentioning that the polycythaemia caused by hypoxia can be masked by the venesection effect of epistaxis caused by telangiectasia.¹ There is an association with PAVMs causing brain abscesses and this should be excluded in such conditions.⁷

Chest X-ray is usually the initial investigation. It may show an isolated spherical lesion of varying radio-density in the lung fields, although the lesion may not be visible at all as the sensitivity is 28% and the negative predictive value is 85%.⁸ The lesion may also be mistaken for a solid tumour, and a CT of the thorax is the usual second-line investigation. While CT with intravenous contrast will usually secure the diagnosis of a PAVM, it is not the preferred investigation. The use of transthoracic contrast echocardiography (TTCE) is the new gold standard diagnostic modality, and its results are comparable to those of CT even at calculating shunt size.⁹ This was not available at the time this lesion was being investigated; being such a rare condition, it was locally investigated using CT prior to its diagnosis. Saline-contrast containing relatively large air bubbles can be used and is injected into a peripheral vein; normally, all bubbles are eliminated in one circulation through the lung bed. Therefore, the delayed appearance of contrast bubbles in the left heart chambers on echocardiography confirms a pulmonary

arteriovenous right to left shunt. Transoesophageal echo can localise the area of shunting by viewing individual pulmonary veins before and after contrast injections.^{10–12} As highlighted in Velthuis *et al*,⁹ TTCE can also establish the grade of shunting, which is a good predictor of size and helps the decision for treatment. All 772 patients with possible or definitive HHT underwent TTCE with any shunt graded into grades I, II or III. The positive predictive values of TTCE correlating to findings on CT were 13.4% for grade I, 45.3% for grade II and 92.5% for grade III. They conclude that in grade I shunting, percutaneous embolectomy is not usually possible, and the lesions are often too small to be characterised on CT, therefore this investigation may be withheld following TTCE.⁹

Currently, the preferred management option is percutaneous embolisation. This can be carried out as part of the investigative pulmonary angiography.¹³ The feeding artery may be occluded with coils. In the case of multiple feeding arteries being present, they must all be occluded individually in order for successful resolution to occur.⁷ Surgery was once more common for such malformations, however, it has now been superseded by embolisation even in the context of neurological complications; surgery is rarely required anymore. Embolectomy is advisable in all PAVMs with a feeding artery diameter of over 3 mm, which should include 88% of all PAVMs; as described in Velthuis *et al*,⁹ all these cases treated by embolectomy had a shunt grade of II or III.

Many variations of PAVMs exist, hence the different nomenclatures discussed earlier. The most recognised classification system is that described by Anabtawi *et al*,¹⁴ where the malformations are classified anatomically. Group 1 is made up of multiple small AV fistulas without aneurysms. Group 2 comprises of large peripheral AV aneurysms, as in our case. Group 3 comprises of large central AV aneurysms (type A), large AV aneurysms with anomalous venous drainage (type B) and multiple small AV fistulas with anomalous venous drainage (type C). Group 4 includes large venous aneurysms with systemic artery communication (type A) and large venous aneurysms without fistulas (type B). Group 5 has anomalous venous drainage without fistulas.¹⁴

Our patient was over the usual age range at the time of surgery. Although chest X-rays showed the lesion in 1986, the patient was advised that no management was necessary. Medical notes revealed no mention of its diagnosis or the other possible aetiologies at that time. The lesion was present in the right lower lobe, the second most common location. This highlights the lesson that rare conditions were mistakenly left untreated in times of fewer diagnostic modalities and were often lost to follow-up or ignored when re-presenting. In this case, our patient presented to neurologists with a stroke and then subsequent TIAs, and was not referred for investigation of this lesion on chest X-ray. It was only after a routine visit to his community doctor that a bruit was discovered and he was referred. A major significant CVA could have occurred in this time period, which would have been prevented by treatment of this PAVM.

CVAs were believed to be a rare complication of PAVMs, but a series of 219 patients published in *Thorax* in 2008 showed that, on imaging, 57 of these patients had ischaemic stroke even prior to diagnosis of the PAVM. No correlation was found between the size of the PAVM and the occurrence or severity of the CVAs.¹⁵ However, in a study of 1038 patients being screened for HHT, the incidence of neurological complications was 8.3% in those with pulmonary shunting and 1.4% in those without. The extent of shunting also correlated with the occurrence of neurological complications, the lowest grade of

shunting giving cerebral manifestations in 1.4% and the highest grade in 20.9% of cases.¹⁶ This is in keeping with our case having a large AV malformation with significant shunt, as shown by the change in oxygen saturation on treatment, and recurrent thromboembolic events. Reports of other similar cases highlight the rarity of stroke occurring secondary to PAVMs but share the similarity of significant shunting occurring in those cases who suffered CVAs.^{17 18}

No other sources of emboli were detected, the patient was in sinus rhythm, echocardiography was normal and carotid Doppler showed no significant stenosis. The only explanation for these recurrent CVAs is paradoxical embolisation through the fistula. One year on since his lobectomy, the patient has suffered no further attacks. Up to 33% of complications of PAVMs are CVAs secondary to paradoxical embolisation.⁷ The most common neurological features are headaches, dizziness, tinnitus, convulsions and hemiplegia. In this case, the common symptoms of dizziness and confusion were experienced during the transient attacks, and the single occurrence of left arm weakness eventually improved. Many theories for these neurological symptoms exist, such as cerebral hypoxia from shunting and its associated polycythaemia, as well as the possibility of cerebral angiomatous malformations.^{19 20} In this case, there was little hypoxia and no polycythaemia, and a CT of the brain showed no malformations. The possibility of emboli arising in the cystic cavity itself and then proceeding to cerebral circulation was eventually dismissed, as no thrombus was found on multiple

histological examinations of these fistulas.²¹ Recent research into strokes has outlined iron deficiency anaemia as a risk factor for strokes, as it causes enhanced platelet adherence in the setting of elevated plasma serotonin/5HT. This research led to the analysis of patients with PAVMs as examples of this occurrence. The theory was raised that perhaps this is not a case of emboli formed peripherally being transmitted paradoxically to the systemic circulation but rather a disease of the neurovascular lining. The usual pulmonary capillary blood filtration is breached and therefore platelet-serotonin aggregates are allowed passage through to the systemic circulation where they then trigger thrombotic events.²²

Competing interests None declared.

Patient consent Obtained.

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Learning points

- Large spherical lesions found incidentally on chest X-ray may be pulmonary arteriovenous malformations (PAVMs) (sensitivity 28%). They may be asymptomatic but one must question specifically for any neurological symptoms.
- There is a strong association between these malformations and other vascular conditions such as Osler-Weber-Rendu syndrome and hereditary haemorrhagic telangiectasia.
- Paradoxical thromboembolisation from peripheral veins through pulmonary AV malformations is a cause of cerebrovascular accidents (CVAs). When no obvious cause for stroke is identified one should screen for such lesions. Contrast transthoracic echocardiography is the gold standard screening tool, however, transoesophageal echocardiography may also be helpful.
- PAVMs should be treated when the risk of CVAs is high, indicated by a large shunt grade on transthoracic contrast echocardiography. Not all PAVMs require treatment, especially if small shunts and narrow diameter of feeding artery are seen, or if technical difficulties are faced. CVAs could be small and clinically silent, but will eventually lead to ischaemic atrophy and dementia. Treatment is by percutaneous coil embolisation, and although this case was treated surgically, this should only be a last resort.
- As highlighted in this case, the consequences of the lesion not being treated on its discovery was a stroke. Furthermore, it was still left untreated with several transient ischaemic attacks occurring. The significance of this could have been far worse for our patient, who luckily made a full recovery. All such lesions discovered incidentally should be investigated.

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