

Reminder of important clinical lesson

Aneurysmal 'pepper-pot' atrial septal defect in an older gentleman with multiple cerebrovascular attacks

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Summary

Our patient presented to a large university teaching hospital with a history of light-headedness, falls and multiple cerebrovascular ischaemic events. This caused a right sided hemiplegia and the patient experienced significant functional limitation. Extensive investigations were carried out to exclude any causative factors such as carotid artery disease and the patient had all identifiable cardiovascular risk factors identified and modified. No significant pathology was found and a referral was made to the cardiology service. Transthoracic echocardiography revealed a complex type 3 perforate 'pepper pot' atrial septal aneurysm with associated thrombus. The patient was commenced on warfarin and appropriate rate limiting medication. After discussion of all interventional modalities, the patient opted for conservative management.

BACKGROUND

Atrial septal defects (ASD) are an important cause of thromboembolic cerebrovascular attacks (CVA). In cases of CVA where the patient has a simple ASD, the two pathologies are likely to be unrelated. But when there are further congenital abnormalities in addition to an ASD, the prevalence of CVA is significantly increased. This has been reflected in studies outlining the association of atrial septal aneurysm (ASA) with cerebral ischaemia in patients with normal carotid vasculature. This association is seen in approximately 27% of patients and is much higher than previously thought. In one such study of over 200 patients under the age of 45 presenting with acute CVA, an ASA was found in 86%.

We discuss here the different morphologies of aneurysmal ASD, the formation of the aneurysm and the pathophysiology of CVA. We look specifically at aneurysmal ASD and the significant increase in the incidence of CVA in these patients.

CASE PRESENTATION

An 83-year-old man presented to a large university teaching hospital in Liverpool. The patient's initial presentation was due to 'constriction of his chest' on exertion associated with

dizziness and collapse. These symptoms were mild but causing significant effects on everyday activities. Medical history included paroxysmal atrial fibrillation, dyslipidaemia, hypothyroidism and multiple previous transient ischaemic attacks (TIA). The calculated CHA2D2-VASc score of 2 indicated a risk of cerebral thromboembolic events in the next 12 months of 4% (95% CI).¹ He was commenced on rate limiting treatment and formally anticoagulated with warfarin. Following extensive investigation a complicated type 3 ASD with aneurysm was identified.

Unfortunately, the patient had further TIAs despite having a therapeutic INR value and it was felt highly likely that

the ASA was responsible for his numerous previous cerebral ischaemic events. It is possible that some of the previous cerebral events were secondary to thromboembolic foci from the left atrium secondary to underlying atrial fibrillation but there was significant distortion to the normal cardiac anatomy; the calculated annual thromboembolic risk is likely to be significantly underestimated in this demographic given this degree of distortion. The possible treatment options available were discussed including remaining on current therapy or attempting interventional closure. The patient decided he would prefer conservative management.

INVESTIGATIONS

All of the usual investigations for such a presentation were performed with no pathology identified. Following thorough cardiovascular investigations a perforated ASA was identified on transthoracic echocardiography and confirmed on transoesophageal echocardiography (TOE). Most recent echocardiography in February 2010 demonstrated an appearance consistent with an ASA with lipomatous hypertrophy of the basal segment of the septum. The septum itself appeared thinned and aneurysmal with a spherical structure seen adjacent to the right atrial cavity. Colour flow was detected across the interatrial septum flowing from left to right seen as two adjacent high velocity jets (figures 1 and 2). In addition, mild to moderate mitral and tricuspid regurgitation with preserved left atrial size was noted. The pulmonary arterial pressure was 19 mm Hg indicating normal pulmonary arterial pressure. Using transthoracic and TOE a bubble contrast enhanced study can be performed. When a defect has already been visualised or suspected this additional manoeuvre can be used to determine if there is a significant volume of blood crossing the defect. With attention to the subcostal view in transthoracic echocardiography we used colour doppler to identify flow but could not fully appreciate the true fluid dynamic across the defect.

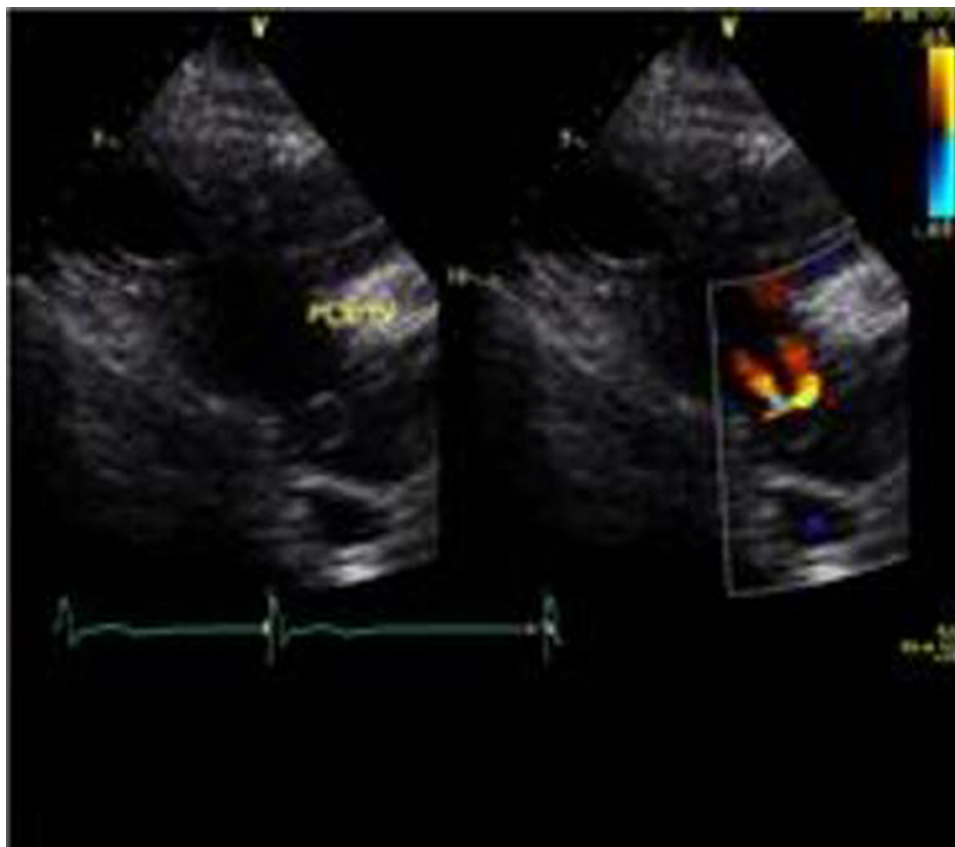


Figure 1 Two jets of high velocity colour flow across the atrial septum in parasternal demonstrated.

Bubble contrast studies are performed by injecting saline or aggregated blood from the patient into a peripheral vein and increasing venous return to the right atrium by deep inspiration. This opacifies the right atrium and ventricle with microbubbles, which reflect the ultrasound waves from the echo probe.

Where there is flow from the right to left atrium across a defect then bubbles will be seen in the left atrium. By instructing the patient to perform a valsalva manoeuvre the right atrial pressure is increased, allowing the practitioner to get a true appreciation of flow. Unfortunately, patients undergoing TOE often receive sedation and the coordinated movement required to perform adequate valsalva manoeuvre can be suboptimal.

DIFFERENTIAL DIAGNOSIS

Classification of aneurysms of the perforated atrial septum

The diagnostic criteria for ASA can vary greatly as there is currently no consensus. The common criteria employed to define an ASA seems to be the identification of a dilatation of the atrial septum, with a base width and depth in excess of 15 mm by 15 mm in adults (or 8 mm/m² body surface area in children) or if there is an oscillating membrane with lateral movement of 15 mm or more. Perforated aneurysms can then broadly be divided into four subgroups, which then influence the management of the patient.²

Type 1 Aneurysm with a persistent foramen ovale (PFA) closed with a large PFO occluder for example, star closure device.

Type 2 Aneurysm with a single ASD, occluded with an Amplatzer ASD occluder.

Type 3 Aneurysms with two or more perforations located in no more than two clusters and not treatable with a single device, treated with an occlusion device appropriate to the size of the defect.

Type 4 Multiple perforations spread irregularly over the aneurysm leading to surgical closure or conservative treatment with anticoagulants.

There are a multitude of varying morphologies of interatrial communications. With attention to that of the secundum-type ASD, the possible management options with regards to percutaneous closure using Amplatzer septal occluder (ASO) devices are heavily influenced by the structural characteristics. One hundred and ninety patients who underwent either percutaneous or surgical closure of this kind were studied and the morphology detailed. Centrally placed defects were observed in 24.2%. Morphological variations of secundum-type ASD were detected in 75.8%. 79.5% underwent percutaneous closure using ASO. 20.5% underwent surgical closure. It was deemed that centrally placed defects, defects with deficient superior anterior rim, multiple defects and perforated aneurysms of the interatrial septum are all morphological variations of secundum-type ASD suitable for percutaneous closure using ASO.³

In a further study analysing the echocardiographic characteristics of isolated secundum-type ASD (ASD II), 64 patients were evaluated using both transthoracic and TOE.



Figure 2 Aneurysmal 'pepper-pot' appearance of the atrial septal defect. Note the lipomatous hypertrophy of the atrial septum seen at the base of the perforate aneurysm.

Defects in 45.3% fulfilled the echocardiographic criteria for percutaneous closure. Thirteen separate variations in morphology of ASD II were identified. A statistically significant correlation between defect size and the number of deficient defect rims was found. Importantly it has been demonstrated that ASDs (II) are not static defects with fixed morphology but in fact can 'grow' and evolve. With this 'growth' the clearly defined borders of the defect that at one time were present meaning that the defect could be closed with a percutaneous device become eroded or attenuated. It is postulated that this process is responsible for the huge variety of morphologies encountered. It may well be that these observations represent various snapshots in time at different stages of the evolution of this process. With better understanding of the natural history of this condition we can better classify the characteristics and therefore understand which patient cohorts will respond best to intervention.⁴

OUTCOME AND FOLLOW-UP

Unfortunately, despite medical treatment with appropriate rate limiting medication and anticoagulation with warfarin, the patient went on to have further TIA and a cerebrovascular event with left-sided hemiplegia. The patient continues to maintain that he does not wish to be referred for interventional therapy. Overall, while our patient preferred conservative management his recurrent events and closely linked defects would have made him an ideal candidate for defect closure.

DISCUSSION

Pathophysiology of CVA in this circumstance

Importantly the pathophysiology and causality of cerebrovascular accident in this cohort is quite different from that caused by deep venous thrombosis with paradoxical embolus. In this particular group of patients it is not unheard of for patients to have a number of 'herald' TIA before CVA. This is reflected in studies outlining the prevalence of ASA in those with cerebral ischaemia and normal carotid vasculature to be much higher than previously thought at 27%.⁵

While the morphology and position of defects in the atrial septum are of great interest, the most important issue is the high thromboembolic potential. While the exact mechanism of this increased risk is open to question, there have been suggestions that thrombi can form in the aneurysmal sac that can be transmitted through a defect such as a PFO or ASD. For the physician caring for these patients and deciding on management such as interventional closure there is little information on how to accurately assess the potential embolic risk. In two studies so far the only factor associated with additional stroke risk was a thickness of greater than 5 mm of the aneurysmal membrane.^{6 7} There is no validated protocol for which this thickness should be reproducibly measured. The precise constellation of structures from which this value is established from echocardiography is left entirely to operator discretion which of course introduces interoperator variability. It would be our recommendation that

the value is established from what appears to be the thickest segment by eye.

It is postulated that microthrombi formation takes place at the base of the perforated aneurismal defect. This walled structure will shelter the developing thrombi from turbulent high velocity flow. It may be that increased aneurismal membrane thickness is better able to shield developing thrombus as it develops in the aneurismal sac. It is the swinging of this mobile 'pepper-pot' ASD through the cardiac cycle, not to dissimilar to that of a swinging chandelier, which leads to the displacement of the thrombus across the ASD with the eventual repercussions. It is for this reason that CVAs are strongly associated with ASA and this clinical hypothesis has since been confirmed by autopsy.⁸ Importantly, it should be acknowledged that in this circumstance other unusual complications can be encountered. Additionally, patent foramen ovale (PFO) is also associated with CVA, mostly when associated with ASAs. Unusual systemic associations such as cerebellar abscess have been documented secondary to gemella morbillorum infection, a commensal of the oropharynx and upper respiratory tract.⁹

Formation of aneurysmal ASD

While there is little known about the precise nature of how ASA come to be, there are data from a number of multi-centre observational trials that search for associated anomalies. The results clearly demonstrate that the most common associated cardiac malformation with regard to ASA is the presence of a PFO.⁵ In one such study of over 200 patients under the age of 45 with stroke, an ASA was found in 86% but in only 10% of the general population.⁵ This association has been confirmed in other studies looking at causes of stroke.^{6-7 10}

2D transthoracic echocardiography has become one of the routine initial investigations performed in the diagnosis and management of TIA or CVA, usually to exclude the possibility of intraventricular thrombus. As demonstrated in this patient there are other important cardiac pathologies that may be responsible for acute vascular neurological pathology. It would be our recommendation that patients with recurrent TIA with normal carotid Doppler studies and few identifiable atherosclerotic risk factors, that a 2D transthoracic echocardiogram with valsalva and bubble contrast be performed to exclude the possibility of PFO or ASD. It must be remembered that TOE is a more detailed investigation with greater spatial resolution of structural pathology. This investigation should be reserved for those patients where transthoracic images are of limited diagnostic quality.⁷

Early recognition and delineation of the precise structural pathology of an ASD with aneurysm may influence the management of the patient as discussed above. ASDs may be missed as a possible cause of CVA when not as obvious as in this case and so we should have a low threshold for investigation.

A major advancement recently was a greater appreciation of the management of patients with PFO. The CLOSURE-1 trial completed in 2010 was the first randomised controlled trial with a cohort of 909 patients over three independent centres. This trial studied PFO closure using the STARFlex closure device with the patient receiving 6 months of aspirin and clopidogrel plus an additional 18 months of aspirin

versus best medical therapy defined as aspirin or warfarin on the basis of CHADS2 score. After 2 years of study, the rates of stroke and TIA were very similar between the two study groups but statistical significance was not achieved. Major adverse vascular complications and incidence of further atrial fibrillation were statistically higher in the interventional group. It is essential to emphasise that this does not negate the merit of intervention but suggests that further study is required to refine selection criteria. We would hope that positive criteria rather than a lack of criteria can be identified and distributed in a format that is easy to follow without confusion. This will allow patients to be reassured with confidence. Current indications for interventional closure include:

- ▶ Infarction in both cerebral hemispheres
- ▶ Anterior and posterior circulation involvement
- ▶ Cerebrovascular event with silent renal or splenic infarction.

Other indications for percutaneous closure of interatrial communications of this kind outside of that documented following CVA include hypoxia due to persistent or intermittent right-to-left shunting,¹¹ dilated right ventricle,¹² peripheral embolic event, disabling migraine with aura, professional scuba diving and severe platypnea-orthodoxia syndrome.¹³ Whenever undertaking an interventional procedure the potential risks of the procedure versus the benefits in terms of primary and secondary prevention plus of course any symptom benefit must be weighed. While symptom benefit is of paramount importance to the patient, when the potential cost although rare may include arrhythmias (specifically supraventricular tachycardia), pericardial effusion, thrombus formation on the left atrial disc with systemic embolisation and right iliac vein dissection with retroperitoneal and groin haematoma, we must ensure the patient is fully aware of these potential complications and in the first instance that the circumstances are such that intervention can be justified.¹⁴

Learning points

- ▶ There are causes of common conditions/presentations such as TIA/CVA which are unknown to junior doctors. In the younger demographic with TIA/CVA ASA have been shown to be more prevalent than previously thought.
- ▶ We must be aware of pathologies although previously thought to be uncommon which research dictates is more prevalent than we perceive. We must use imaging modalities available (not involving radiation or contrast material where possible) in aiding diagnosis. By doing this we minimise risk to our patients while identifying pathology which may be amenable to intervention.
- ▶ It would be our recommendation that patients with recurrent TIA with normal carotid Doppler studies and little identifiable atherosclerotic risk factors, that a 2D transthoracic echocardiogram with valsalva and bubble contrast be performed to exclude the possibility of PFO or ASD.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Gage BF**, Waterman AD, Shannon W, *et al.* Validation of clinical classification schemes for predicting stroke. Results from the national registry of atrial fibrillation. *JAMA* 2001;**285**:2864–70.
2. **Ewert P**, Berger F, Vogel M, *et al.* Morphology of perforated atrial septal aneurysm suitable for closure by transcatheter device placement. *Heart* 2000;**84**:327–31.
3. **Podnar T**, Martanovic P, Gavora P, *et al.* Morphological variations of secundum-type atrial septal defects: feasibility for percutaneous closure using Amplatzer septal occluders. *Catheter Cardiovasc Interv* 2001;**53**:386–91.
4. **Prokselj K**, Kozelj M, Zadnik V, *et al.* Echocardiographic characteristics of secundum-type atrial septal defects in adult patients: implications for percutaneous closure using Amplatzer septal occluders. *J Am Soc Echocardiogr* 2004;**17**:1167–72.
5. **Tchana B**, Hagler DJ, Carano N, *et al.* Device closure of fenestrated atrial septal aneurysm: difficulties and complications with implantation of two devices. *J Invasive Cardiol* 2004;**16**:532–4.
6. **Mattioli AV**, Aquilina M, Oldani A, *et al.* Atrial septal aneurysm as a cardioembolic source in adult patients with stroke and normal carotid arteries. A multicentre study. *Eur Heart J* 2001;**22**:261–8.
7. **Schneider B**, Hanrath P, Vogel P, *et al.* Improved morphologic characterization of atrial septal aneurysm by transesophageal echocardiography: relation to cerebrovascular events. *J Am Coll Cardiol* 1990;**16**:1000–9.
8. **Mattioli AV**. [Study of the interatrial septum using transthoracic echocardiography]. *Cardiologia* 1997;**42**:257–64.
9. **Lopes A**, Providencia R, Pais RP, *et al.* Cerebellar abscess by Gemella morbillorum in a patient with inter-atrial communication. *Arq Neuropsiquiatr* 2007;**65**:1022–5.
10. **Silver MD**, Dorsey JS. Aneurysms of the septum primum in adults. *Arch Pathol Lab Med* 1978;**102**:62–5.
11. **Ilkanhoff L**. Transcatheter device closure of interatrial septal defects in patients with hypoxia. *J Interv Cardiol* 2005;**18**:227–32.
12. **Egred M**, Andron M, Albouaini K, *et al.* Percutaneous closure of patent foramen ovale and atrial septal defect: procedure outcome and medium-term follow-up. *J Interv Cardiol* 2007;**20**:395–401.
13. **Lisignoli V**, Lanzone AM, Zavalloni D, *et al.* Closure of patent foramen ovale: when and how? *Curr Vasc Pharmacol* 2007;**5**:322–7.
14. **Chessa M**, Carminati M, Butera G, *et al.* Early and late complications associated with transcatheter occlusion of secundum atrial septal defect. *J Am Coll Cardiol* 2002;**39**:1061–5.

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