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CASE REPORT
Adult congenital heart disease

Percutaneous closure of 'complex' multi-fenestrated atrial septal aneurysm in visceral situs inversus using a multi-device approach: a case report

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Background Percutaneous closure is nowadays still deemed challenging in patent forame ovale (PFO) associated to multi-fenestrated atrial septal aneurysm (ASA). This anatomic arrangement is still considered a significant risk factor for recurrence of paradoxical embolism. Theoretically, transcatheter approach could be theoretically even more complex in the case of dextrocardia and visceral situs inversus.

Case summary A 59-year-old man with history of migraine with aura and multiple cryptogenic strokes was referred for percutaneous closure of a PFO with associated ASA. He had been previously submitted to repeat attempt of percutaneous closure with not self-centering and self-centering devices that failed due to unfavorable anatomic characteristics (dextrocardia with situs viscerum inversus, huge ASA, multiple fenestrations, large PFO). Based on this "complex" anatomy, a sequential 2-step interventional approach aiming to reduce size and mobility of the atrial septal aneurysm with a suture-based approach (Noblestich™ EL, HeartStitch, Fountain Valley, CA, USA) and to close any eventual accessory fenestrations with a not self-centering occluding device was planned. At the end of the procedure, the ASA completely disappeared and no residual shunt was imaged at TEE bubble test.

Discussion We describe a very rare case of symptomatic ASA-PFO in dextrocardia with situs viscerum inversus as well as an innovative approach to treat such complex anatomic setting by using the suture-based closure of a PFO to reduce size and mobility of an ASA in order to deploy dedicated not-self-centering occluding devices.

Keywords Situs viscerum inversus • Patent foramen ovale • Device • Case report

ESC curriculum 7.4 Percutaneous cardiovascular post-procedure • 9.7 Adult congenital heart disease

Learning points

- To describe a patient-tailored approach in closure of a 'complex' anatomic variant of patent foramen ovale (PFO) in an unusual anatomic settings.
- To suggest a potential 'off-label' use of the Noblestitch technology in treatment of PFO with aneurysmal atrial septum.

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Introduction

Patent foramen ovale (PFO) has been consistently associated with cryptogenic stroke, and its percutaneous closure has been proved the best cost/benefit approach in secondary prevention.[1–3] Transcatheter approach is nowadays still deemed challenging in PFO associated to multi-fenestrated atrial septal aneurysm (ASA).[4,5] This anatomic arrangement is considered a significant risk factor for recurrence of paradoxical embolism, thus advising complete closure of all sites of potential right-to-left shunt.[6] Due to unusual anatomic references, percutaneous closure of PFO-ASA could be even more complex in the case of dextrocardia and visceral situs inversus.[7]

Summary figure

This paper reports on a patient with mirror-image dextrocardia in visceral situs inversus who experienced multiple cryptogenic strokes presumably due to paradoxical cardiogenic embolism through a multi-fenestrated atrial septum. He had been previously submitted to repeat unsuccessful attempts of percutaneous closure caused by mispositioning of either not self-centring or self-centring occluding devices. This anatomic setting prompted us to plan a sequential two-step approach aiming to reduce the mobility of the septal aneurysm with a percutaneous suture-based PFO closure and afterwards to close the associated fenestrations using a not self-centring occluding device.

DATE	EVENT
• Cryptogenic stroke in the left middle cerebral artery (age 40 years)	• **No treatment**
• Myocardial infarction in circumflex coronary artery territory (age 43 years)	• **Acute treatment**: systemic fibrinolysis **Echocardiography**: diagnosis of situs inversus, dextrocardia, multi-fenestrated ASA. **Coronary angiography**: no significant coronary artery disease. **Chronic treatment**: carvedilol 3.75 mg/day, atorvastatin (40 mg/day) and acetyl-salicylic acid (100 mg/day)
• Cryptogenic stroke in multiple areas of the right middle cerebral artery (age 56 years)	• **Transcranial Doppler**: massive right-to-left shunt during Valsalva manoeuver. **Treatment**: unsuccessful attempt of percutaneous PFO closure using Amplatzer PFO device. Chronic anti-coagulant therapy (warfarin 30 mg/week)
• Spontaneous discontinuation of anti-coagulant therapy (age 58 years)	• **Treatment**: Second unsuccessful attempt of percutaneous closure using Amplatzer Atrial Septal Occluder device. Chronic acetyl-salicylic acid therapy
• Transient ischemic attack at 59 years of age	• First consultation at our centre. Counseling about the planned percutaneous intervention. Further attempt of percutaneous PFO closure using a multi-device approach

Case presentation

A 59-year-old man with history of migraine with aura and multiple cryptogenic strokes was referred to our centre for consideration of percutaneous closure of a PFO with associated ASA. He has previously had an embolic stroke in the territory of the left middle cerebral artery at the age of 40 years and myocardial infarction with not critically obstructed circumflex coronary artery submitted to systemic fibrinolysis at the age of 43 years. Then, he was started on bisoprolol (3.75 mg/day), acetylsalicylic acid (100 mg/day), and atorvastatin (40 mg/day) therapy. A transthoracic echocardiogram following his myocardial infarction revealed a diagnosis of visceral situs inversus and dextrocardia without any cardiac malformation except for a huge ASA (20 mm large with 15 mm bi-directional excursion) with multiple fenestrations and a large PFO. At the age of 56 years, he represented with embolic stroke in multiple areas of the middle right cerebral artery territory at which time a trans-cranial Doppler showed a massive right-to-left shunt during a Valsalva manoeuvre. Percutaneous PFO closure was unsuccessfully attempted using an Amplatzer PFO Septal Occluder (Abbott, Plymouth MN, USA) device, and therefore, he was commenced on regular anticoagulant therapy (warfarin about 30 mg/week). After 2 years, the patient spontaneously discontinued anticoagulant therapy due to gastro-intestinal bleeding. Thus, he underwent a second unsuccessful attempt of percutaneous PFO closure using an Amplatzer Atrial Septal Occluder (Abbott, Plymouth MN, USA) device and was established on aspirin (100 mg/day). His congenital anatomic arrangement likely caused the failure of the two previous failed attempts of percutaneous treatment due to supposed instability and malposition of dedicated and off-label protheses. Unfortunately, he subsequently had a transient ischaemic attack, and was referred to our centre. This case was submitted to our Heart Team discussion, and the final decision was to attempt a third percutaneous procedure using a novel, sequential anatomic-tailored approach aiming to reduce the size of the atrial septum aneurysm with a suture-based device and closing eventual residual fenestrations with standard occluding device(s). Thus, the planned procedure was explained to the patient who signed the informed consent to the procedure.

At hospital admission, clinical examination and EKG were normal. Holter EKG did not show any arrhythmia potentially related to cardio-embolism. No deep vein embolic sources were found at vascular ultrasound examination. At transoesophageal echocardiography (TEE),

the atrial septum secundum appeared very thick and lipomatous while the septum primum was thin, aneurysmal, and mobile with bi-directional shunt at rest that was completely right-to-left during Valsalva's manoeuver through a large PFO and multiple, tiny accessory fenestrations (*Figure 1*, Supplementary material online, *Movie S1*). Cardiac MRI clearly detailed the relative position of the caval veins with respect to the atrial septum.

Based on this 'complex' anatomic setting as well as the history of multiple failures in positioning either self-centring and not self-centring devices, we decided to perform a sequential two-step interventional approach. Thus, it was planned to close the PFO using a suture-based approach (Noblestitch™ EL, HeartStitch, Fountain Valley, CA, USA), which hopefully could have been useful also to reduce size and mobility of the ASA and then to treat the accessory fenestrations with an occluding device chosen on the basis of the local anatomy resulting from the former intervention. At cardiac catheterization, the superior and inferior vena cava angiographies clearly imaged the relative position of the systemic venous drainages with respect to the huge aneurysmal septum (*Figure 2*). Then, the stitch-implantation procedure was performed in a mirror-image fashion via the left femoral vein, resulting in complete closure of the PFO and significant reduction of size and mobility of the aneurysmal atrial septum (*Figure 3*). As expected, a mild-to-moderate residual right-to-left shunt at bubble test was imaged far from the PFO, in the middle of the septal aneurysm, due to multiple fenestrations that appeared even larger than before the stitch implantation. However, they were completely closed using a 30 mm Ultrasept PFO Occluder device (Cardia Inc., Eagan, MN, USA) that nicely seated inside the aneurysm and further stabilized the septum (*Figure 4A*, Supplementary material online, *Movie S2*). At the end of the procedure, no residual shunt was imaged at TEE bubble test and the patient was uneventfully discharged under double antiplatelet therapy (clopidogrel, 75 mg/day and acetil-salycilic acid, 100 mg/day) (*Figure 4B* and *C*; *Figure 5*, Supplementary material online, Movie *S3*). At the 6 months follow-up evaluation, neither recurrence of embolic symptoms nor

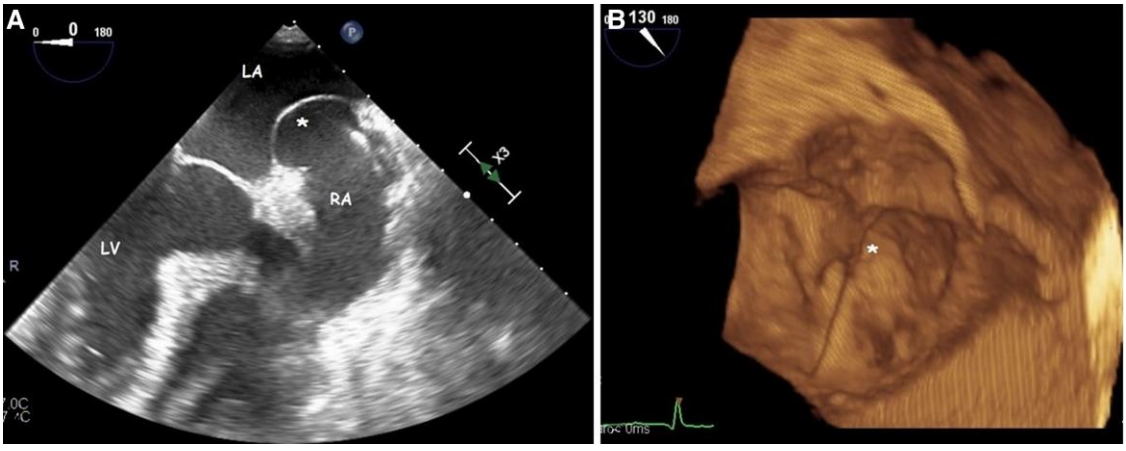

Figure 1 Thin, hyper-mobile ASA (asterisk) as imaged at 2D (*A*) and 3D (*B*) TEE echocardiography. LA, left atrium; LV, left ventricle; RA, right atrium.

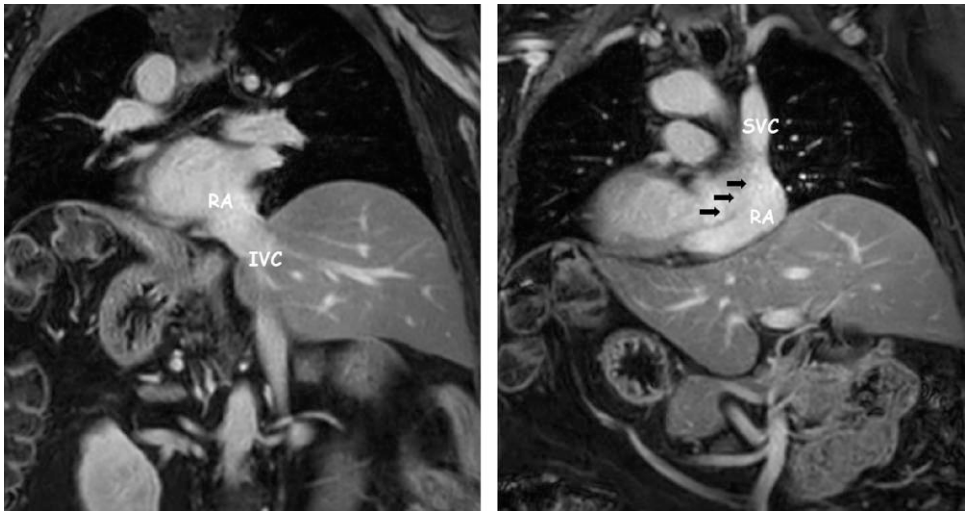

Figure 2 MRI evaluation before the interventional procedure showing the position of IVC and SVC with respect to the atrial septal aneurysm (black arrows). IVC, inferior vena cava; SVC, superior vena cava; RA, right atrium.

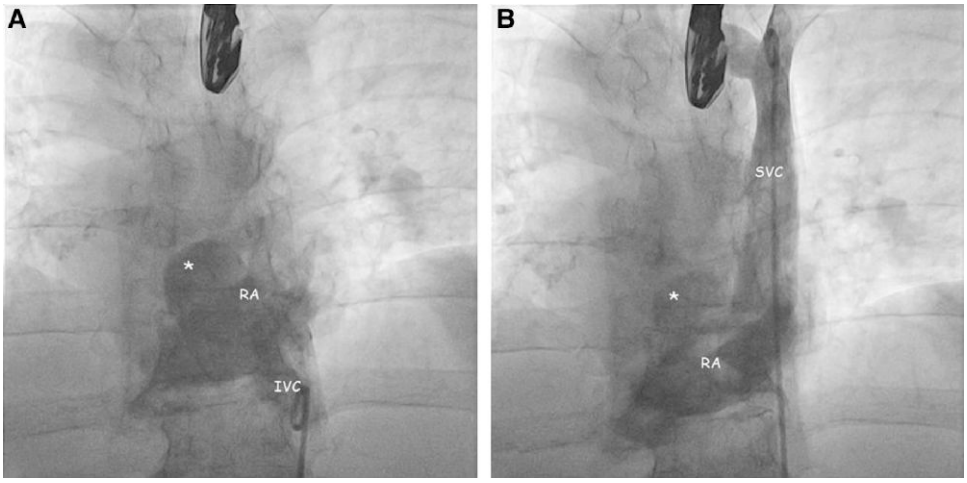

Figure 3 Inferior (*A*) and superior (*B*) vena cava angiographies showing the position and relationship between systemic venous drainage and ASA (asterisk). IVC, inferior vena cava; SVC, superior vena cava; RA, right atrium.

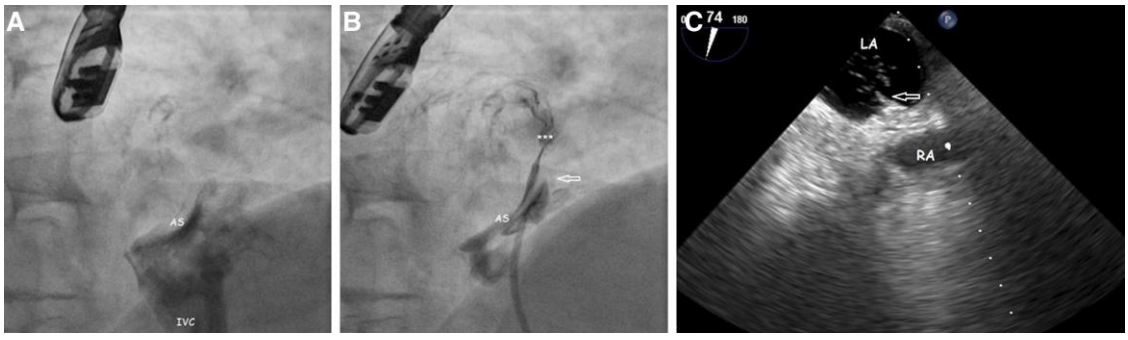

Figure 4 Atrial septum appearance after the PFO closure with the Noblestitch device, with an almost complete disappearance of the aneurysmal bulging at right atrial angiography (*A*). However, a mild-to-moderate residual right-to-left shunt (multiple arrows) still remained far from the site of the KwicKnot™ implantation (white arrow), as imaged at right atrial angiography (*B*) and bubble test TEE evaluation (*C*). AS, atrial septum; IVC, inferior vena cava; LA, left atrium; RA, right atrium.

procedure-related complications was recorded. At that time, the patient signed the informed research consent for participation in this case report as long as he remained anonymous.

Discussion

Dextrocardia and visceral situs inversus are a quite rare anatomic arrangement reported in 1:10 000 individuals.[8] It may occur without major cardiac anomalies except for the mirror-image position of the heart and great vessels. As in normal population, also in this unusual viscero-atrial arrangement, PFO should be statistically found in nearly 25% of individuals and also in this anatomic setting, it could be a potential culprit of cryptogenic systemic embolism. Percutaneous PFO closure is nowadays considered the best cost/effective treatment in secondary prophylaxis of patients with cryptogenic stroke. However, transcatheter device implantation could be challenging and potentially unsuccessful in some anatomic settings as in the case of aneurysmal, multi-fenestrated septum, even with some technical tricks and using off-label devices.[4,5] Further complexity to this percutaneous approach can be added by dextrocardia and situs inversus, as found in our patient in whom the lack of usual anatomic references, an anticipated mirror-image procedure steps, and the anatomic complexity of the atrial septum could justify the repeat failures of the previous interventional procedures. In this case, using large, stiff, not self-centring devices (PFO or Cribriform Amplatzer or Amplatzer-like occluders) might have been a simpler and less time-consuming approach. However, the use of these devices is increasingly considered a risk factor for residual shunt mainly in the case of significant difference between septum secundum and septum primum thickness.[9] In addition, residual shunt after device closure has been related to a higher risk of recurrent stroke during long-term follow-up.[10–13] Thus, we decided a sequential two-step approach aiming to deal with the aneurysmal septum and PFO and afterwards to perform an anatomic-tailored closure of any residual site of paradoxical shunt. The suture-based PFO closure was easily performed in a mirror-image fashion under fluoroscopic and TEE guidance and resulted in complete disappearance of the PFO shunt. The primary

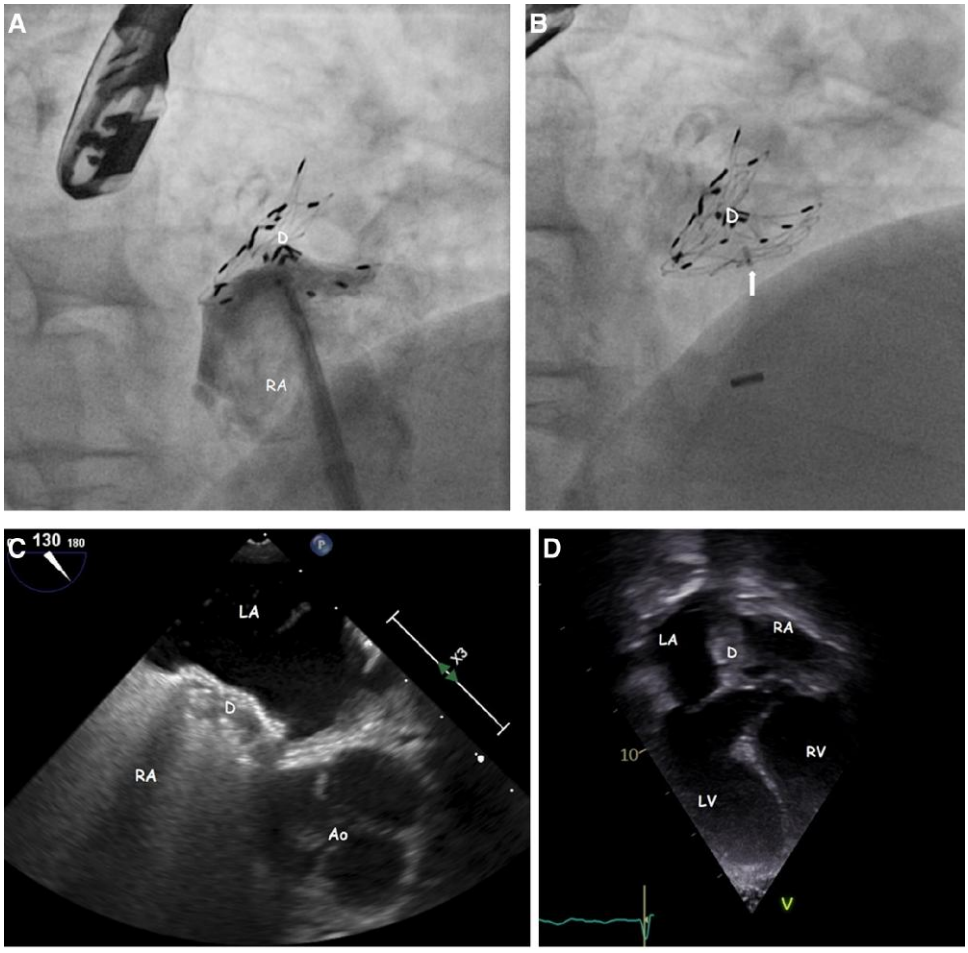

Figure 5 Final result after deployment of the Cardia Ultrasept device that nicely outlines the thick septum secundum (asterisk). No residual paradoxical shunt is imaged at angiography (*A*) and both devices (D and white arrow) appeared nicely seated inside the septum at final fluoroscopic examination (*B*). In addition, no residual shunt was found at the confirmatory bubble test TEE evaluation (*C*). At hospital discharge, transthoracic evaluation confirming the nice position of the occluding device with straightening of the atrial septum (*D*). Ao, aorta; AS, atrial septum; D, device; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

stitch deployment was performed quite far from the secondary stitch previously implanted to straighten up as much as possible the atrial septum. This manoeuver likely stretched the accessory fenestrations located inside the septal aneurysm. However, a careful evaluation of the final appearance of the atrial septum by TEE was made possible to choose the most effective occluding device. Our choice was the Cardia Ultrasept PFO device, a soft, not self-centring device with high grasping capacity and, in our opinion, a favourable compromise between cardiac electro-mechanical impact and occluding capacity.

Conclusions

Detailed imaging of local anatomy is crucial in successful treatment of complex, unusual types of PFO. This novel approach based on the combined use of the Noblestitch technology to decrease the size of an aneurismal septum and a standard double-disk device to seal any residual/accessory fenestration could be effective in achieving complete closure of complex aneurismal, multi-fenestrated atrial septum.

Lead author biography

Silvia Scalera graduated at the University 'Tor Vergata' of Rome, Italy and is currently in her final year of specialty degree in Cardiology at the University of Pisa, Italy. She is full-time involved in training programme of paediatric cardiology and adult congenital heart disease at the Heart Hospital 'G. Pasquinucci', National Research Council-Tuscany Foundation 'G. Monasterio', Massa, Italy.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Consent: The patient signed a written consent to publish his data.

Conflict of interest: S.S.: no conflicts of interest, A.P.: no conflicts of interest, P.M.: no conflicts of interest; G.S. is proctor for Abbott, Italy, WL Gore, Italy, and Occlutech, Italy.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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