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Index words

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Abstract

This case describes the successful implantation of an Occlutech Atrial Flow Regulator® in a young child with idiopathic pulmonary hypertension and recurrent syncope despite targeted combination therapy, with subsequent relief of symptoms.

Introduction

Pulmonary arterial hypertension (PAH) is a rare but life threatening condition in children. (1). Most common types in children are idiopathic, hereditary and congenital heart disease associated PAH. Patients may present at all ages with nonspecific symptoms such as fatigue, failure to thrive, dyspnea and even syncope (2). Compared to adults, right heart failure is a late presentation and episodes of severe PAH with syncope are more common in children (1). With current treatment options, the 5-year survival rate for patients diagnosed with idiopathic PAH is 75% (2). Calcium channel blockers, endothelin receptor antagonists, phosphodiesterase 5 inhibitors and prostacyclins are the main targeted medical treatment options for children (1, 2). Atrial septostomy should be highly considered in drug resistant patients with persistent PAH-related syncope or with progressive PAH, elevated atrial pressure and low cardiac output (2, 3). Treatment options for a permanent atrial septostomy are creating and stenting an atrial septum defect with risk of stent migration and occlusion, or implantation of a custom made fenestrated ASD device complicated by high occlusion rates (4-6). In adults the recently introduced Occlutech Atrial Flow Regulator® is used with success for pulmonary hypertension (7). We report a case in which a smaller version of the AFR was implanted in a 2-year old boy with idiopathic pulmonary hypertension.

Case report

This case describes AFR implantation in a 2 year old boy with idiopathic PAH.

Idiopathic PAH was diagnosed at the age of 1,5 years old after presentation with recurrent syncope and cyanosis. At initial presentation, NTproBNP was elevated (2430 pg/mL) and

echocardiogram showed right ventricular dilation and hypertrophy with elevated tricuspid regurgitation in a structural normal heart. Because of the recurrent syncope and young age, sildenafil was immediately initiated with gradually increasing dose with only temporary clinical effect. A cardiac catheterization was performed confirming PAH with a mean pulmonary artery pressure (mPAP) of 32 mmHg (2/3 systemic pressure) and a pulmonary vascular resistance index of 6 WU*m². Acute vasoreactivity testing (AVT) with NO 20ppm showed a 30% decrease of the mPAP to 22 mmHg (table 1). A temporary atrial septostomy was made during the same procedure using a 6 mm Powerflex Balloon (Cordis® – Cardinal health®, California, USA) in an attempt to stop syncope, while optimizing medical therapy to reduce pulmonary hypertension. Because of positive response to AVT, a calcium channel blocker (diltiazem) was associated. The boy remained well for a few months, until pre-syncope reoccurred. Echocardiography at that time showed spontaneous closure of the atrial septal defect (ASD). Medical therapy was optimized with bosentan, an endothelin antagonist. Over time, while the child remained in NYHA functional class II, episodes of pre-syncope reoccurred. During one of these episodes, echocardiography showed an acute and severe dilation of the RV with compression of the left ventricle (LV), confirming a pulmonary hypertensive crisis. Additional therapy was discussed and we preferred an atrial fenestration instead of IV prostacylins, since our patient was still in NYHA class II and syncope was his most important complaint. In order to create a permanent interatrial fenestration, implantation of the novel AFR device (Occlutech®, Sweden) was chosen (Figure 1).

We chose an AFR device with a fenestration diameter of 6 mm and disc diameter of 18 mm. Since this small sized device was not CE approved and provided for compassionate use, approval of the local health authority (FAGG) and the local Ethics Committee (UZ Ghent) was obtained as well as informed consent from both parents.

During induction of anesthesia, the child suffered from a severe pulmonary hypertensive crisis which responded well to NO 20 ppm inhalation. The interatrial septum was perforated with a transseptal puncture needle (St. Jude Medical®, Minnesota, USA) under TEE guidance, and after predilation of the puncture hole with a 8 mm diameter powerflex balloon, a 10 Fr Mullins

transseptal introducer sheath (Medtronic®, Minneapolis, USA) was inserted in the left atrium and the AFR device with 6 mm fenestration (Occlutech®, Sweden) was successfully deployed. After confirming adequate oxygen saturation of >85% and stable hemodynamics according to the Occlutech AFR® implantation guideline, the device was released successfully. TEE confirmed a 5-6 mm left-to-right color flow through the device.

After successful implantation, targeted medical therapy was continued and anticoagulation with warfarin was switched to dual antiplatelet therapy (aspirin and clopidogrel) after a few weeks. Antiplatelet therapy will be continued as long as device patency is necessary. Until today, 5 months after the AFR implantation, the patient remains well without syncope and with a left-to-right shunt over a stable 5 mm fenestration in the AFR device on echocardiogram.

Discussion

Children with PAH suffer more frequently from syncope than adults (8, 9). The etiology for syncope in children with PAH is more related to hemodynamic changes than to arrhythmia. An acute and severe increase of pulmonary vascular resistance results in an insufficient transpulmonary blood flow with massive dilation of the RV and subsequent compression of the LV, low stroke volume and low blood pressure (8). At presentation our patient showed a mixed risk profile according to pediatric risk stratification tables (10). Despite targeted combination therapy and although the patient remained in NYHA functional class II, syncopal episodes persisted. Because of the preserved functional status, the important side-effects and the potential risk of catheter sepsis, we did not start triple combination therapy with IV prostacyclins (1). Oral triple therapy with the use of a prostacyclin receptor agonist with proven benefit for PAH treatment (selexipag) was another possibility, but is not reimbursed for children in Belgium and our patient was too young to be included in the upcoming randomized control trial (11). Because the recurrent syncope was affecting the quality of life, we decided in team and in consultation with the parents for a permanent atrial septum fenestration.

Atrial septostomy is recommended in adults with high risk PAH as a bridge-to-transplant or as destination therapy in patients with limited access to targeted combination therapy or

transplant option. It is also proven to reduce symptoms of syncope (12, 13). In patients with severe crises of pulmonary hypertension and consequently syncope, creation of an atrial septum defect will allow right-to-left shunting with preservation of left ventricular filling and systemic cardiac output. However cyanosis may be the result of the right-to-left shunt and systemic oxygen saturation will depend on the amount of shunting. Therefore the final size of the septal defect is crucial (12). Preprocedural oxygen saturations below 85-90% and RA pressure above 20 mmHg are so far contra-indications for atrial septostomy (10, 13).

Several procedures are used for the creation of an atrial septal defect. Graded balloon atrial septostomy is the technique mentioned in the ESC guidelines for adult patients with PAH (1). The technique is safe in experienced hands and allows gradual dilatation of the created defect reducing the risk of overshunting. This technique is associated with largely favorable hemodynamic outcomes in carefully selected patients with PAH (13). However, spontaneous closure of the atrial septal defect occurs in up to one quarter of the patients (13). Therefore several other techniques have been proposed varying from custom made fenestrations in commercially available ASD occluders, stent insertions with different configurations and delivery techniques and an extracardiac Potts shunt (4-6, 12). All these alternative techniques have their disadvantages such as unpredictable size of the fenestrations, spontaneous closure, stent embolization and unpredictable right-to-left shunt with severe cyanosis as consequence (4, 6, 12).

Since 2019 the Atrial Flow Regulator (Occlutech®, Sweden) with fenestration diameter of 8 or 10 mm is authorized in adults with severe and drug-resistant PAH and heart failure. The AFR device, a fenestrated self-expandable double-disc, is developed to allow for a controlled interatrial right to left blood flow with decompression of the right ventricle and improvement of the cardiac output without significant systemic desaturation when device size is well chosen for the patient (6). Clinical trials have shown that the AFR is easily implanted with a single attempt and without major complications in adults (7). The procedure is comparable to the implantation of a double disc ASD device, which is a common and safe procedure in children without pulmonary hypertension (6, 14). A positive long term outcome with an improvement of

the cardiac index, very low occlusion rate and no relapse of syncope has been shown in adults (table 2) (7). Larger clinical trials with longer follow up are necessary, but the first results are promising.

In children the experience is limited to a few case reports and small series describing patients with PAH based on different etiology (7, 15). Smaller AFR sizes (4 and 6 mm fenestrations) are not yet CE approved. We successfully deployed an AFR with a 6 mm fenestration in a small child in a compassionate use program (Figure 1). The device placement and deployment were a lot easier than stent implantation. The result was satisfying with adequate oxygen saturation and disappearance of clinical symptoms.

Conclusion

Implantation of the AFR device is proven to be a safe and effective percutaneous procedure for treatment of severe and drug-resistant pulmonary hypertension in adults, especially in those with recurrent syncope. Although clinical trials and follow-up are limited, the results are promising compared to other devices creating a permanent atrial septal patency. The small size AFR devices are not yet CE approved and data of the use in children are scarce. In this case, we show the successful percutaneous implantation of an AFR device in a young child with idiopathic pulmonary hypertension and syncope. More cases with longer follow up should be analyzed to prove safety and efficacy in children.

Conflicts of interest

None.

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Figure legends

Figure 1. a) Occlutech Atrial Flow Regulator® device. b) Postprocedural radiograph showing the implanted double-disc Atrial Flow Regulator® with fenestration. c) Perprocedural transesophageal echocardiography image of the implanted Atrial Flow Regulator® device through the interatrial septum with a left-to-right color flow through the device.

Table legends

Table 1. Cardiac catheterization measurements

AVT = acute vasoreactivity testing, mRA = mean right atrial pressure, sRV = systolic right ventricle pressure, sPA = systolic pulmonary artery pressure, dPA = diastolic pulmonary artery pressure, mPA = mean pulmonary artery pressure, Qp/Qs = cardiac pulmonary output/cardiac systemic output, Rp/Rs = pulmonary vascular resistance/systemic vascular resistance, PVRi = pulmonary vascular resistance index

Table 2. Current literature AFR implantation in patients with pulmonary hypertension

NYHA class = New York Heart Association functional class, 6MWT = six minute walk test

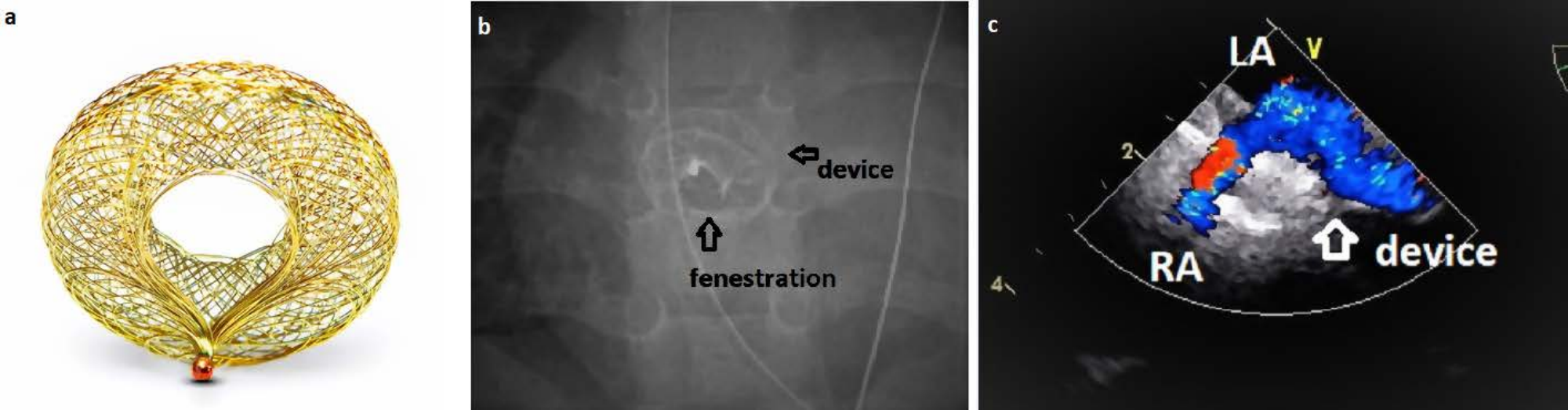
a
b
device
fenestration
c
LA
V
2
RA
4
device

Table 1. Cardiac catheterization measurements

	Basal	Post AVT
mRA (mmHg)	9	7
sRV (mmHg)	50	38
sPA (mmHg)	49	35
dPA (mmHg)	18	11
mPA (mmHg)	32	22
Qp/Qs	1	1
Rp/Rs	0,45	0,35
PVRi (WU*m²)	6	4,65

AVT, acute vasoreactivity testing; mRA, mean right atrial pressure; sRV, systolic right ventricle pressure; sPA, systolic pulmonary artery pressure; dPA, diastolic pulmonary artery pressure; mPA, mean pulmonary artery pressure; Qp/Qs, cardiac pulmonary output/cardiac systemic output; Rp/Rs, pulmonary vascular resistance/systemic vascular resistance; PVRi, pulmonary vascular resistance index

Table 2. Current literature AFR implantation in patients with pulmonary hypertension

Author	Title	Patients (n)	Symptoms	Complications	Duration follow-up	Results
Patel et al.	Implantable atrial flow regulator for severe, irreversible pulmonary arterial hypertension	1	NYHA class III Impaired 6MWT Progressive ascites and pedal pitting edema	None	6 weeks	Improvement of 6MWT Relief of ascites and pedal edema Subjective symptomatic improvement Mean resting saturation of 98%
Rajeshkumar et al.	Atrial septostomy with a predefined diameter using a novel occlutech atrial flow regulator improves symptoms and cardiac index in patients with severe pulmonary arterial hypertension	12	NYHA class III (9/12) NYHA class IV (3/12) Syncope or pre-syncope (12/12) Angina (3/12) Palpitations (3/12)	Perprocedural atrial flutter (1/12) Postprocedural hypoxia warranted continued oxygen supplementation for 48–72 hr (6/12)	Median follow-up 189 days (range 10–296 days)	Improvement NYHA class (12/12) Relief of syncope (12/12) Subjective symptomatic improvement (12/12) Significant improvement 6MWT Preserved device patency (12/12) Mean resting saturation of 92%
Janus et al.	Atrial flow regulator as a bridge to lung transplant in a young patient with drug-resistant idiopathic pulmonary arterial hypertension	1	WHO functional class IV Impaired 6MWT Ascites and pedal pitting edema	Postprocedural hypoxia warranted continued oxygen supplementation	8 weeks	Improvement WHO functional class Improvement 6MWT

Dąbrowska-Kugacka et al.	Atrial flow regulator for severe drug resistant pulmonary arterial hypertension after congenital heart defect correction	1	WHO functional class IVa Recurrent syncope Ascites and pedal pitting edema	None	6 weeks	Improvement WHO functional class Relief of syncope Relief of edema
Recruiting	The Prophet Trial - Pilot Study to Assess Safety and Efficacy of a Novel Atrial Flow Regulator (AFR) in Patients With Pulmonary Hypertension					

NYHA class, New York Heart Association functional class; 6MWT, six minute walk test