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Research Article

Management of Severe Clinical Intravascular Hemolysis Following Percutaneous Transcatheter Closure in Adulthood

Ata Firouzi[1], Mohammad Javad Alemzadeh Ansari[1,3], Zahra Khajali[2], Majid Maleki[1], Bahram Mohebbi[1,3], Sedigheh Saedi[2], Zahra Hosseini[1], Parham Ostovan[4], Mohammadreza Baay[2], RaanaAsghari[5], Seyed Ehsan Parhizgar[1]

[1]Cardiovascular Intervention Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran;[2]Department of Cardiovascular Medicine, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran;[3]Cardio-Oncology Research Center, Rajaie Cardiovascular Medical and Research Center, Tehran, Iran;[4]Cardiovascular Intervention Fellow-ship, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran;[5]Department of Cardiovascular Medicine, Shafa General Medical Center, Ghazvin University of Medical Sciences, Ghazvin, Iran.

ABSTRACT

One of the rare complications of transcatheter closure of structural heart defects and recently advanced procedures in other conditions like valvular interventions, is intravascular subclinical and clinical hemolysis. The accurate incidence, etiology, management and approach to these patients are not really known. In this retrospective, mono-centric study, we recruited all the patients who underwent the transcatheter closure of Atrial Septal Defects (ASDs), Patent Foramen Ovales (PFOs), Ventricular Septal Defects (VSDs), Patent Ductus Arteriosus (PDAs), Sinus of Valsalva Ruptures (SVRs) and Paravalvular Leakages (PVLs) in the time period between 2017 and 2019. We evaluated the incidence and our approach to management (either conservative or invasive approaches) of this infrequent side effects among 675 patients in this time period.

Keywords: Transcatheter closure; Subclinical and clinical hemolysis; Conservative approach; Invasive approach

INTRODUCTION

Congenital heart diseases include a variety of lesions that cause intra-cardiac shunts. The most common causes of Left to right shunts are Patent Ductus Arteriosus (PDAs), Ventricular Septal Defects (VSDs) and Atrial Septal Defects (ASDs). They might lead to volume overload, heart failure, and irreversible complications such as the Eisenmenger syndrome [1]. Transcatheter defect closure with implantable devices is now the main approach toward such defects. Recent years have also witnessed greater interest in the application of device closure for paravalvular leakages (PVLs), iatrogenic or traumatic VSDs, Transcatheter aortic valve implantation, valve-in-valve and post–myocardial infarction ventricular septal ruptures.

Despite the safety and effectiveness of percutaneous transcatheter closure (TCC) in comparison with surgical repair, this approach is associated with some rare complications. One of these scarce side effects is hemolysis in between 1% to 3% of cases following device closure. The underlying causes of this phenomenon have yet to be fully elucidated, but the few published cases suggest such reasons as incomplete closure and residual shunting, the abnormal configuration of the device, and the mechanical exposure of the devices to the blood flow [2].

The signs and symptoms of hemolytic anemia usually manifest themselves within 24 hours to 2 weeks after the procedure. Severe anemia, a change in urine color, hemolytic evidence in the peripheral blood smear, and increased lactate dehydrogenase (LDH), reticulocyte count, and bilirubin are all signs of hemolytic anemia. Most cases of hemolysis are subclinical and self-limiting. Even in clinical cases, most patients respond appropriately to conservative management. There are patients with refractory hemolysis and ongoing hemoglobin drops that require multiple blood transfusions, renal replacement therapy or multiple-organ failure. In these group of patients, it is vital that any residual shunt be completely eliminated either through device removal via invasive interventions (i.e., transcatheter and surgical), or the implantation of another device [3].

In light of the above mentioned introduction, we performed the

Correspondence to: Zahra Hosseini, Cardiovascular Intervention Research Center, Tehran, Iran, Tel: +0098912327011; E-mail: Hosseini.zahra64@gmail.com

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present retrospective, single-center study to assess the common approaches to this occasional complication.

METHODS

The present retrospective, single-center study consecutively recruited all the patients who underwent the transcatheter closure of ASDs, Patent Foramen Ovales (PFOs), VSDs, PDAs, Sinus of Valsalva Ruptures (SVRs) and PVLs in the time period between 2017 and 2019 Clinical data were obtained before and after the catheterization. The study protocol was approved by the institutional ethics committee, and written informed consent was obtained from all the patients for follow-up. The inclusion criteria were minimum age of 18 years and the transcatheter closure of ASDs, PFOs, PDAs, VSDs, SVRs and PVLs between the year 2017 and 2019. Patients with a pervious history of any type of hemolytic anemia were excluded.

Significant intravascular hemolysis criteria

There is no single specific definition of hemolytic anemia. However, the diagnosis of hemolytic anemia is usually established if 3 major criteria are present: unexplained anemia, a high reticulocyte count, and signs of Red Blood Cells (RBCs) destruction (i.e., elevated unconjugated bilirubin and LDH as well as low Haptoglobin). The term "sub-clinical hemolysis" is used to describe patients who meet the latter 2 criteria but do not have anemia. In these patients, the bone marrow adequately compensates for the hemolysis and maintains a normal hemoglobin level [4].

RESULTS

During the study period, 675 patients underwent TCC. Of them, 531 patients underwent ASD or PFO closure, 68 PDA, 58 VSD [5]. Sinus of Valsalva rupture, and 13 Paravalvular leakage. In the following section, we will describe adult patients with severe clinical intravascular hemolysis after percutaneous device closure (0.88%) [6] (Table 1). Although the majority cases which undergoing TCC were in ASD or PFO closure, none of them experience clinical hemolysis following procedure. In Table 2, demographic data, treatment options, and follow up of patients with clinical hemolysis following TCC is shown. In the following, details of patients are described [7].

Case 1

A 24 years old man, presented with complaints of exertional dyspnea and palpitation (Table 2). In physical examination, he had a wide pulse pressure with continuous murmur at the upper left sternal border with no right ventricular heave or loud P2. No signs of the Eisenmenger syndrome was detected.

Transthoracic echocardiography revealed mild to moderate left ventricular enlargement with mild dysfunction, normal RV size and function, and no valvular heart disease. Additionally, a large PDA (8 mm) was detected between the descending aorta and the left pulmonary artery with a turbulent continuous flow [8].

Cardiac catheterization showed: (LVP: 140/0-15 mmHg, PAP: 40/20 [mPAP: 26 mmHg], RVP: 40/0-7 mmHg, mRA: 5 mmHg, and Qp/Qs ratio: 2.5).

The patient underwent angiography, followed by transcatheter PDA closure with an Occlutech ductal occluder [10/12 mm] (Figure 1).

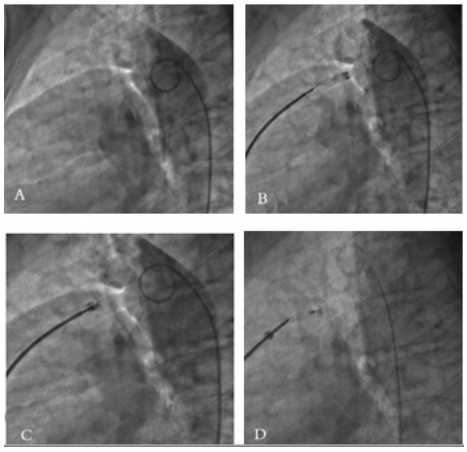

Figure 1(A, B, C, D): A large conical shaped PDA is seen which by aortography, pulmonary artery is filled (Figure A).Via antegrade approach, aortic skirt of ductal Occluder 10/12 is deployed with full traction on the whole system (Figure B). The pulmonary disk is deployed. In aortography, moderate residual shunt is visible (Figure C). After releasing the device, proper position of the device is demonstrated (Figure D).

The final angiography showed moderate residual shunting, which was subsequently confirmed in TTE.

Twenty-four hours after the procedure, the patient complained of urine color change (brownish) and icteric sclera. The follow-up lab data are presented in Table 3.

Table 1: Number of patients with clinical hemolysis following percutaneous trans catheter closure.

Number of patients with Clinical hemolysis following percutaneous trans catheter closure					
Atrial septal defect/ patent foramen ovale (531 patients)	Patent ductus arteriosus (68 patients)	Ventricular septal defect (58 patients)	Sinus of Valsalva rupture (5 patients)	Paravalvular leakage (13 patients)	Total (675 patients)
0	2 cases	2 cases	1 case	1 case	6 case (0.88%)

Table 2: Patients with clinical hemolytic anemia (demographic data, treatment, and follow up).

Patients with clinical hemolytic anemia (demographic data, treatment, and follow up)						
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age (yr.)	24	44	31	35	70	41
Sex	Male	Male	Female	Female	Male	Male
Cardiac shunt or defect	PDA	VSD	ruptured non-coronary sinus of the Valsalva	PDA	Severe PVL from medial side of prosthetic mitral valve	VSD
Device	Occlutech ductal occluder [10/12 mm]	Occlutech PM-VSD 12 mm	Occlutech Muscular VSD 12 mm	Occlutech Muscular VSD 20 mm	Occlutech Muscular VSD 8 mm	Occlutech Muscular VSD 14 mm
Immediate residual flow	Moderate	Mild to moderate	Mild	Moderate	Mild to moderate	Tiny
Time from the procedure to clinical hemolysis (hours)	24 hr	72 hr	24 hr	24 hr	48 hr	24 hr
Admission days	10	14	6	12	18	15
Days from the procedure to improved clinical hemolysis and no more hemoglobin drop	5	After surgical intervention	3	7	After redo TCC	6
Days from the procedure to stop clinical hemolysis	7	6	5	11	4	10
Packed RBC cells transfusion (Units)	No	2	No	1	2	1
Kinds of treatment for clinical hemolysis	Conservative	Surgical device removal and defect repair	Conservative	Conservative	TCC (another Amplatzer Muscular VSD 6 mm)	Conservative
Follow up after discharge (days)	30	30	30	7	30	7
Residual flow after discharge in follow up echocardiography	Mild	No	No	Mild	Mild	Tiny
Kinds of treatment for clinical hemolysis	Conservative	Surgical device removal and defect repair	Conservative	Conservative	TCC (another Amplatzer Muscular VSD 6 mm)c	Conservative

Table 3: Hospitalization course.

Days post Procedure																		
Variable	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6											24	24
	1st	3nd	7th	3rd	7th	8th	1st	3rd	5th	1st	3rd	12th	2nd	4th	5th	2nd	4th	15th
Hemoglobin	15.8→14	12	12	12→														
11	9	8.7	13→11.6	9.7	10.6	13.5→11.8	9.3	11	11.7→10.5	8.4	8	13.3→11	8	11				
Lactate dehydrogenase	333→1370	3808	2000	300→1200	5855	6936	250→1180	1760	1658	393→1189	5930	4220	430→1146	6700	7540	411→3645	5571	2800
Indirect bilirubin	5.5	9	5	1.5	5	5	1.6	3.2	1	0.9→2.4	6.2	4.5	3	7	10	0.4	5	1
Blood Urea Nitrogen	17	25	18	14	47	67	12	25	20	9→13	20	15	28	40	52	15→20	46	35
Creatinine	0.9	1.8	1.2	0.9	3	3.5	0.8	1.5	1.2	0.7	1.5	0.7	1.2→					
1.5	2.5	3	1□2	5	2													
Reticulocyte count	2%	_	3%	1.50%	6%	5%	1.50%	2.20%	1.50%	1.50%	2.20%	2.50%	2%	4%	5%	1.20%	3%	1.50%

The patient's hemodynamic status was stable. Massive hydration, beta-blocker therapy, and hydrocortisone therapy were started. The peak hemoglobin drop was on the fifth day, but no blood transfusion administered. Under close hemodynamic monitoring and conservative management, finally on the seventh day, the levels of LDH and bilirubin decreased, and the urine color became brighter. Ultimately, the patient was discharged in good condition on the 10th day.

One month later, the patient had normal lab tests and the follow-up TTE showed proper device position with mild residual shunting.

Case 2

A 44-years old man, who has been diagnosed with endocarditis 1 month previously, referred to our center (Table 2). The transesophageal echocardiography (TEE) at the time of diagnosis had revealed a large VSD; consequently, the patient was placed on antibiotic therapy. After eradication of infection, the patient scheduled for percutaneous VSD closure. In physical examination, he had normal S1 and S2, loud holosystolic murmur at the left sternal border, no RV heave, without evidence of cyanosis.

TTE demonstrated normal LV size and function, normal RV size and function, no evidence of vegetation, a large perimembranous VSD that was restricted by the septal pouch of the tricuspid leaflet, and 2-residual defects. The distance between the VSD and the aortic valve was 3 mm. Additionally, mild aortic insufficiency and moderate tricuspid regurgitation were detected [9] (Figure 2).

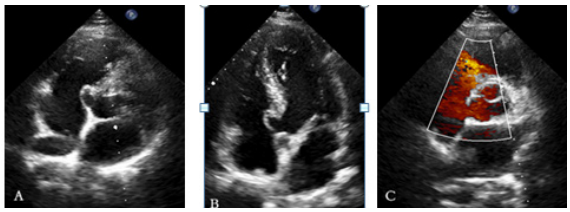

Figure 2(A, B, C): In TTE, in 4-chamber view, a perimembranous VSD which is restricted by septal leaflet of tricuspid valve is seen (Figure A). In 4-chamber view, the distance of the larger defect to the aortic valve is demonstrated (Figure B). In color echocardiography, 2 residual defects (a large one and another small one) is visualized (Figure C).

Cardiac catheterization revealed: (LVP: 130/0-10mmHg, RVP: 30/0-7mmHg, PAP: 25/10mmHg, and Qp/Qs ratio: 1.6).

The patient underwent angiography, followed by the transcatheter closure of the perimembranous VSD with an Occlutech PM-VSD 12 mm occluder device; (Figure 3).

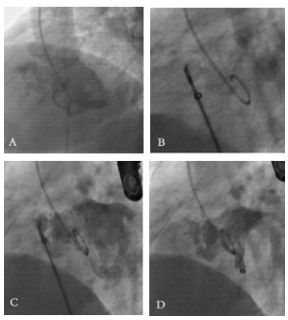

Figure 3(A, B, C, D): LV injection showed, mild LV enlargement with 2 perimembranous defects (the upper one is larger) with concomitant right ventricle opacification (Figure A). Via antegrade approach, LV and RV disk of PM VSD device 12 mm, are deployed (Figure B). LV injection showed mild residual shunting at the site of the device and moderate residual shunting in the lower non closed defect (Figure C). After releasing the device, moderate residual shunting is visualized with proper device position (Figure D).

During the procedure, after the closure of the larger defect, multiple attempts were made to wire the smaller defect, but to no avail. As a result, the procedure was terminated. The final angiography and TEE showed: mild to moderate residual shunting at the site of the device deployment and at the site of another separated small defect bellow the device position [10]. On the third day, the patient developed gross hematuria. The follow-up lab data are depicted.

Despite of close monitoring of the patient in the Intensive Care Unit (ICU), massive hydration, the transfusion of 2 units of packed RBCs, high-dose prednisolone, and beta-blocker therapy, the patient suffered continuous drops in hemoglobin and elevations in creatinine and LDH after 6 days of observation. Accordingly, he was scheduled by the heart team for surgical device removal.

After device removal and VSD repair, in the postoperative course, the levels of LDH, bilirubin and creatinine were reduced significantly (1200, 2, and 1.8 respectively). Ultimately, the patient was discharged in acceptable condition. The follow-up TTE after 1 month, showed no residual shunting, but there were mild aortic insufficiency and moderate tricuspid regurgitation.

Case 3

A 31-years old woman referred to the emergency department with complaints of atypical chest pain, dyspnea, and orthopnea of 3 weeks' duration (Table 2). In physical examination, she had a wide pulse pressure, normal S1 and S2, continuous murmur with trill in the lower left sternal border [11].

TTE demonstrated moderate LV enlargement with normal systolic function, normal RV size and function, and an aneurysmal and ruptured non-coronary sinus of the Valsalva with a typical Windsock appearance to the right atrium. No AI, No VSDs, or other anomalies were detected.

Cardiac catheterization showed: (LVP: 120/0-12mmHg, RVP: 50/0-7mmHg, PAP: 50/15 [mPAP: 26mmHg], and Qp/Qs ratio: 1.8).

The patient underwent angiography, followed by the transcatheter closure of the ruptured sinus of Valsalva with the Occlutech Muscular VSD 12 mm occluder device; (Figure 4).

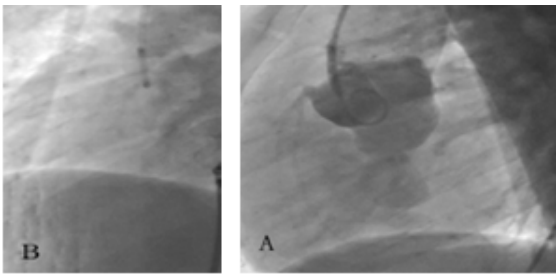

Figure 4(A, B): Aortic root injection showed, ruptured non-coronary cusp of aortic valve to the right atrium (Figure A). Via antegrade approach, LV and RV disk of muscular VSD device 12 mm, was deployed. After releasing the device, mild residual shunting is notable with good device position and no AI (Figure B).

The final angiography and TEE illustrated an appropriate device position with mild residual shunting. Within 24 hours, however, the patient developed gross hematuria and hemoglobin drop. The follow-up lab data are noted.

Immediately, massive hydration was commenced under close monitoring. On the second day, prednisolone and beta-

blocker therapy were started. On the 3rd day, with conservative management, the patient's condition improved and her urine color changed gradually from Coca-Cola to normal. Finally after 6 days, she was discharged home in good condition.

TTE demonstrated moderate LV enlargement with normal systolic function, normal RV size and function, and an aneurysmal and ruptured non-coronary sinus of the Valsalva with a typical Windsock appearance to the right atrium. No AI, No VSDs, or other anomalies were detected.

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Case 4

A 35 years old lady, presented with exertional dyspnea and palpitation (Table 2). In physical examination, she had, normal S1 and loud P2, lateral deviation of the LV apex, with a continuous murmur at the upper left sternal border. No sign of cyanosis was apparent.

TTE showed sever LV enlargement and dysfunction (EF: 30%), mild RV enlargement and dysfunction, severe left atrium enlargement, Tricuspid aortic valve, moderate aortic insufficiency, dilated ascending aorta (4.3cm), and a high turbulent flow from the descending aorta to the left pulmonary artery, suggestive of a large tubular type PDA with significant left to right shunt.

Cardiac catheterization demonstrated (LVP: 100/0-18mmHg, RVP: 60/10mmHg, PAP: 60/25 [mPAP: 36mmHg], Qp/QS ratio: 2.6, and PVR: 4 Woods units).

The patient underwent angiography, followed by the transcatheter closure of PDA with Occlutech Muscular VSD 20 mm occluder device; (Figure 5).

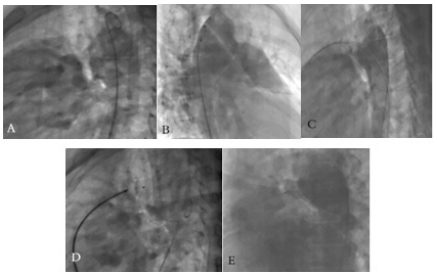

Figure 5(A, B, C, D, E): A large tubular shaped PDA is seen in aortography in LAO and RAO projections with significant pulmonary artery filling (Figure A and B). After passage of the long sheath, the shape of the PDA is better visualized (Figure C). Left and right disk of Muscular VSD device 20 mm, is deployed (Figure D). Moderate residual shunting with proper device position is delineation (Figure E).

The final angiography showed moderate residual shunting.

After 24 hours, the patient developed gross hematuria and icteric sclera. The follow-up lab data are noted below (within 12 days admission). Under close hemodynamic monitoring, massive hydration, high-dose prednisolone and beta-blocker therapy, she underwent conservative management and received 1 packed RBCs, finally on the 12th day, she discharged with clear urine color and diminished icteric appearance. A week later, follow-up TTE showed, proper device position with a mild residual shunting.

Case 5

A 70 years old man, known case of mitral valve replacement (MVR) 16 years ago, presented with refractory dyspnea (New York Association functional class III/IV) of 3 months' duration (Table 2).

TEE revealed mild to moderate LV enlargement with mild dysfunction, mild RV enlargement with moderate dysfunction, and a severe PVL from the medial side of a swing ring with normal leaflets motion.

Given the patient's comorbidities and high logistic EuroSCORE (36.83%), he was adjudged high risk for re-do mitral valve replacement. He scheduled by heart team for interventional device closure. The patient underwent angiography, followed by the transcatheter closure of the defect through the trans-septal approach with Occlutech Muscular VSD 8 mm occluder device; (Figure 6).

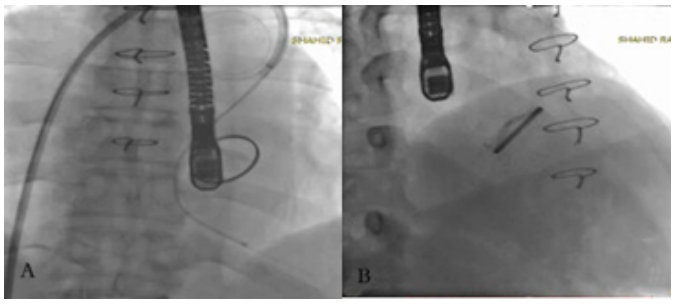

Figure 6(A, B): Via trans-septal approach, wiring of the defect is performed (Figure A). Muscular VSD device 8 mm, is deployed successfully (Figure B)

At the end of the procedure, TEE showed mild to moderate residual paravalvular leakage (Figure 7).

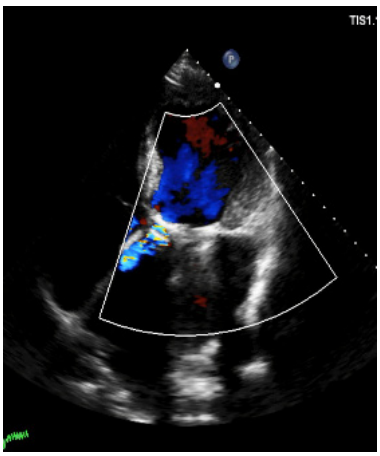

Figure 7: In 4 chamber view, mild to moderate paravalvular leakage is remarkable with appropriate position of the device.

Forty-eight hours later, the patient exhibited signs of hemolysis, and his urine color was brownish and he was icteric. The follow-up lab data are presented.

Despite 4 days of conservative management (massive hydration, high-dose hydrocortisone, beta-blocker therapy, and blood transfusion), the patient's progressive and refractory hemolysis course, prompted the heart team to schedule him for a re-interventional procedure. In percutaneous re-intervention, another Amplatzer Muscular VSD 6mm occluder device was deployed just behind the pervious device (Figure 8).

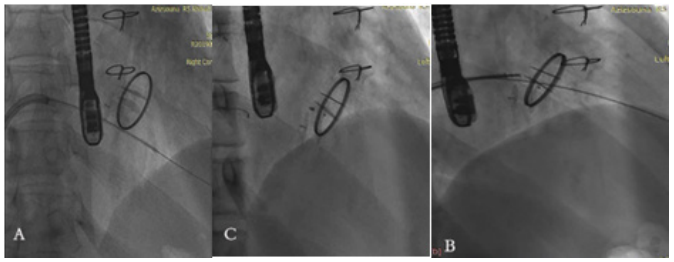

Figure 8(A, B, c): Through trans-septal approach, wiring of the residual defect is performed (Figure A). Another Muscular VSD 6 mm deployed just beside the pervious device (Figure B). After releasing the device, nice position of both devices without interaction with leaflets motions is visualized (Figure C).

The final TEE revealed a mild residual paravalvular leakage with normal leaflets motion (Figure 9).

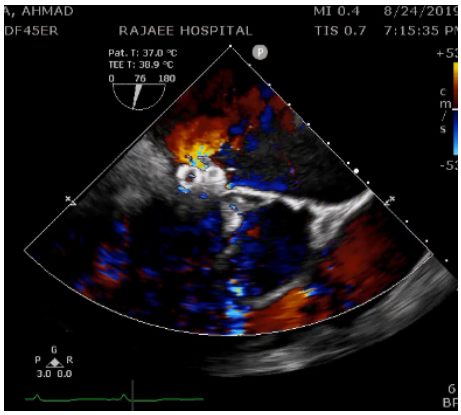

Figure 9: The final TEE showed proper position of both devices with no interaction with leaflets motion and mild residual leakage.

Two days later, the final lab data demonstrated: BUN: 15, Creatinine: 1.4, total bilirubin: 3.4, indirect bilirubin: 1, and hemoglobin: 10.3. Eventually, the patient was discharged in well condition.

At 1 month's Follow-up, TTE showed mild residual paravalvular regurgitation. Any more hemolysis evidence was detected in the follow-up lab tests.

Case 6

A 41 years old man presented with complaints of atypical chest pain and exertional dyspnea (Table 2). In physical examination, he had, normal S1, loud S2, a holosystolic murmur in left sternal border and apex and no sign of the Eisenmenger syndrome.

TTE revealed mild LV enlargement with normal systolic function, mild RV enlargement and dysfunction, and a moderately-sized perimembranous VSD. The distance between the VSD and the aortic valve and the tricuspid valve was 10 mm and 8 mm, respectively.

Cardiac catheterization demonstrated: (LVP: 130/0-12 mmHg, RVP: 50/0-6 mmHg, PAP: 50/20 mmHg, Qp/Qs ratio: 1.7, and PVR: 4 Woods).

The patient underwent angiography, followed by the closure of the perimembranous VSD with an Occlutech Muscular VSD 14 mm occluder device (Figure 10).

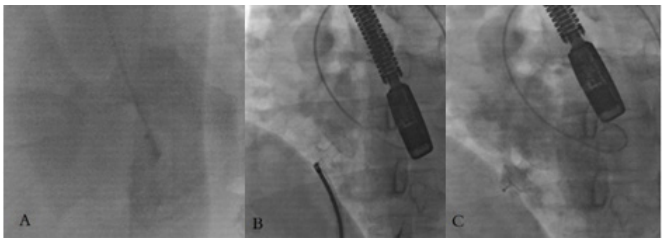

Figure 9 (A, B, C): LV injection showed mild to moderate LV enlargement with a large perimembranous VSD and opacification of right ventricle (Figure A). Via antegrade approach, Muscular VSD 14 mm is deployed (Figure B). After releasing the device, in LV injection, mild residual shunting is noted (Figure C).

The final angiography and TEE showed a tiny residual shunt.

Twenty-four hours after the procedure, the patient developed gross hematuria and suffered a hemoglobin drop. The follow-up data are presented.

Immediately, the treatment (massive hydration, high-dose prednisolone, beta-blocker therapy, and the transfusion of 1unit packed RBCs) was began. The patient was scheduled for hemodialysis on the fourth day. Fortunately, however, his condition showed improvement the next day. In the ICU, his hemodynamic status was closely monitored; finally on the 10th day, the urine color appeared brighter and his LDH level decreased. On the 15th day, he discharged in stable condition. One week later, TTE demonstrated a tiny residual shunt with acceptable device position.

DISCUSSIONc

The transcatheter device closure of anatomically suitable congenital or acquired cardiac defects is gaining further interest within the medical community as long-term outcomes trials have shown similar results in comparison with surgical repair even with fewer complications. Despite its low rate of major complications, however, the transcatheter device closure is associated with a very rare side effect (1%-2%): subclinical and clinical intravascular hemolysis.

The rate of the immediate complete closure of cardiac defects without residual shunts post procedure in most studies is between 80% and 90%. What is not known, nonetheless, is the incidence rate of subclinical hemolysis with RBC morphology changes, because most of such alterations are asymptomatic and goes unevaluated. Of course, in patients with severe clinical intravascular hemolysis, usually within 2 days to 2 weeks, clinical symptoms such as icteric changes, brownish urine color, gross hematuria and pallor manifest themselves.

In our retrospective, single-centric study, conducted over a 2 year-period, among 675 patients with TCC, 6 (0.88%) patients demonstrated severe clinical hemolysis within 24-72 hours post-procedurally. Four patients were managed conservatively. In these patients, the peak of the drop in the level of hemoglobin, and the

rise in the levels of creatinine and bilirubin was on the fifth to seventh post procedural day. One patient was referred for surgical device removal because of refractory hemolysis and our inability to close another separated small defect bellow the device position in the first procedure. Also, one patient was managed with the implantation of another device at the site of a residual defect. Four patients with conservative management, had improved clinical hemolysis and stop drop in hemoglobin, during first week after the procedure (ranged 3-7 days). Additionally, all of them had completely stopped hemolysis within 2 weeks (ranged 5-11 days).

Clinical hemolysis has also been reported early after VSD device closure or coil embolization. Mulvaney et al 9 concluded that hemolysis after transcatheter VSDs closure could be induced by residual high-velocity shunts from the device wires and the ensuing mechanical destruction of RBCs. They also stated that the incidence rate of hemolysis after transcatheter VSD closure ranged from 0.7%–15%. There are a few reports regarding intravascular hemolysis after the used of off-label ASD Amplatzer devices for VSDs closure. These studies have stated that the off-label application of devices might prevent their optimal configuration, and result in their deformation. Therefore, a high-pressure flow from the Amplatzer mesh can lead to erythrocyte fragmentation and hemolysis [10]. In a retrospective study, on 412 cases of transcatheter VSDs closure, Walavalkar et al [11], reported no hemolysis and found no significant association between device failure and complications and the type of VSD or device. They also recommended the use of ductal devices for VSDs in membranous/upper muscular locations, muscular VSD devices for muscular VSDs, and the ADOII with its softer profile for VSDs in proximity to the aortic valve. In our study, of 58 cases of VSDs closure, we had 2 patients with severe hemolysis: one of them had a perimembranous VSD, which was closed with PM VSD device with a moderate residual shunt, and the other one was closed with Muscular VSD, which was closed with a tiny residual shunt.

A prospective study on 134 patients (age<18 y) undergoing the closure of ASDs, VSDs and PDAs showed that 3% of the patients developed clinically intravascular hemolysis, and 8% developed residual shunts early after the procedures. Among 10 patients who had residual flows after the closure, only 2 patients developed hemolysis, but another 2 patients who had no residual blood flow also developed hemolysis. It makes sense that the collision of RBCs with the device wires or networks might cause mechanical cellular destruction and hemolysis, even in the absence of residual shunts.

Some authors believe that presoaking the device with the patient's own blood for about 15–20 minutes can reduce residual shunts and improve immediate complete closure [12].

One complication of paravalvular leakage is hemolytic anemia. The correlation between the size of the leak and the severity of hemolysis is unclear. Small holes can cause severe hemolysis, whereas significant leaks may cause no hemolysis. Smolka et al. [13] analyzed 116 patients with transcatheter PVL closure, and, concluded that the procedure could effectively diminish hemolysis if at least a 90% reduction in the cross-sectional area of PVLs was achieved. They also reported that the effect was sustained in a 6-month follow-up period. The incomplete closure of PVLs may increase the magnitude of hemolysis. New hemolysis which requiring blood transfusions occurred in 1% to 2% of patients undergoing percutaneous PVLs closure in 2 large registries in the United Kingdom and the United States, likely due to the incomplete obliteration of the PVLs. Higher profile devices (ventricular septal occluders) are associated with more hemolysis, more frequently than are the lower profile Amplatzer vascular plugs [14]. In our study, among 13 cases of PVLs closure within 2 years, we detected 1 case of post procedural severe hemolysis.

The optimal treatment strategies for clinical hemolysis following device closure are determined based on the degree of hemolysis, the magnitude of hemoglobin drop, the duration of gross hematuria, the number of packed RBCs units needed for transfusion, the degree of elevation in creatinine and bilirubin levels and clinical symptoms. Almost always, severe hemolysis is self-limiting and its symptoms and signs may be resolved with the conservative approach within 5-7days. Medical therapies include: massive hydration, beta-blockers (to reduce the shear stress), iron supplementation, blood transfusion, pentoxifylline (to improve blood viscosity and erythrocyte deformability) and, corticosteroids. The roles of these medications in the treatment of these patients are not clear; they may simply have a placebo effect and hemolysis might resolve spontaneously within several days, with a reduction in the residual shunts and the thrombosis of the device mesh.

Nevertheless, in patients with refractory hemolysis, invasive approaches should be considered if 2 weeks of full medical therapy fails to resolve continuing elevation in renal function markers (which might require hemodialysis) and bilirubin levels, ongoing hemoglobin drops, persistent hematuria, and recurrent blood transfusions.

In patients with progressive and refractory hemolysis, the threshold for invasive strategies is lower. Obviously, the best approach is to employ the interventional transcatheter procedure and to close the residual shunt with another device such as coils with the aim of eliminating the residual shunt or removing the device. Surgical device removal should be the last resort. There are scant case reports of severe hemolysis leading to surgical device removal. One of these reports was on a patient with a post traumatic-VSD, which was closed with an ASD device, and an-other one was on a patient with postoperative VSD repair with residual shunts from pervious patch-plasty, who had refractory hemolysis after transcatheter device closure. (Both of these patients were scheduled for surgical device extraction).

CONCLUSION

Recent experience, in the field of TCC have ushered in lower post-procedural complication rates, even in very complex cases. Clinical hemolysis following device closure is a rare, albeit life threatening, complication whose optimal management still requires further data. The selection of the appropriate device to minimize residual shunts and the use of lower-profile devices appear to be significant preventive strategies. In our study, patients with conservative management had improved clinical hemolysis and stop drop in hemoglobin, during the first week after the procedure (ranged 3-7 days). Additionally, all of them had completely stopped hemolysis within 2 weeks (ranged 5-11 days).

The rationale for our approach is that, in cases of self-limiting hemolysis, patients almost always, respond dramatically insofar as they experience no more drops in the hemoglobin level and show improvements in lab data (e.g., creatinine and bilirubin levels) and hemolysis signs. Still, in case of continuing hemolysis, patients experience persistent hematuria, continuous hemoglobin drops, constant elevations in the levels of creatinine and bilirubin, as a result, need early invasive interventions (either transcatheter or surgical).

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