A Novel Treatment for Malignant Cough Syncope

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Abstract
Cough Syncope, a form of Neurocardiogenic Syncope, occurs immediately after coughing due to to arterial baroreflex-mediated vasodilatation. Cough syncope has been classically described in patients with obstructive pulmonary diseases. Pulmonary Vascular Diseases, though rare, also present with cough syncope. Malignant Syncope is defined as recurrent syncope with minimal warning, and often associated with self-injury. Here we describe how we managed a case of a young male presenting with recurrent attacks of Malignant Cough syncope.

Introduction
Cough Syncope, a form of Neurocardiogenic Syncope, occurs immediately after coughing. During cough, there is an increase in thoracic and abdominal pressure which is transmitted via the great veins to the cranial cavity, causing an acute pressure increase in the skull due to a Valsalva like manoeuvre. Also, abrupt very high intra-thoracic pressure decreases venous blood return causing fall in cardiac output. In addition, this causes hypotension leading to arterial baroreflex-mediated vasodilatation. The combination of increased venous pressure in the skull and the lowered arterial pressure results in a perfusion stand-still in the brain or even backflow in the brain. Cough syncope has been classically described in patients with obstructive pulmonary diseases and in males. Pulmonary Vascular Diseases, though rare, also present with cough syncope. Malignant Syncope is defined as recurrent syncope with minimal warning, and often associated with self-injury, when conventional investigations fail to reveal a cause but prolonged head-up tilt testing without drug challenge precipitates the patient’s symptoms. The term malignant is chosen to distinguish this form of vasovagal syncope from that seen commonly in young people, where there is a significant duration of prodrome. Here we describe how we managed a case of a young male presenting with recurrent attacks of Malignant Cough syncope.

Case Report
30 year old, Male, Truck driver, resident of Mumbai, presented in 2013 with history of acute onset progressive dyspnea on exertion (NYHA Class II-III) of 3 years duration. He had history of recurrent cough syncope of one year duration. He developed bilateral pedal oedema over the last 6 months and had dull aching pain in the right hypochondrium in the last 3 months. His clinical evaluation revealed tachycardia with a low volume pulse, cyanosis, bilateral pitting pedal oedema, raised jugular venous pressure (prominent v waves) and moderate tender hepatomegaly. Cardiovascular examination revealed a RV type of an apex with Grade II parasternal heave and palpable 2nd heart sound in the left 2nd intercostal space. A Grade III/VI pansystolic murmur was audible at the left lower sternal border in left lateral position and at the end of the expiration and was accentuated with passive leg raising and deep inspiration (Carvallo’s Sign), suggestive of Tricusped Regurgitation. On initial evaluation, his electrocardiogram showed Right Axis Deviation (+130°), Right Ventricular Hypertrophy and Right Atrial Enlargement while chest radiograph features of cardiomegaly, right atrial dilatation, Dilated MPA, RPA and LPA with peripheral Pulmonary Arterial Pruning but no features of Pulmonary Venous Congestion. An initial screening transthorasic echocardiography revealed a dilated RA and RV, small sized LA and LV with bulging of IVS into LV; Severe RV Dysfunction with a normal LV systolic Function; Severe (Grade III/III) Tricuspid Regurgitation with severe Pulmonary Artery Hypertension (PASP=80+15 mmHg); small pericardial effusion over the RV free wall (no evidence of Cardiac Tamponade) with a partial inspiratory collapse of the IVC (IVC diameter-20 mm). The IAS and IVS were intact and there was no evidence of ASD/VSD/PDA (confirmed with TEE and saline contrast studies). There was no evidence of Pulmonary Thromboembolism on CT Pulmonary Angiography and Lung Ventilation/Perfusion studies or any Lung Parenchymal involvement on HRCT Chest. His workup for Connective Tissue Disease (ANA, anti DsDNA, candp ANCA, RA factor and CRP) was negative. He was advised Right Heart Cath study but was deferred as he was unwilling. He was managed as a case of Idiopathic Pulmonary Artery Hypertension with progressively increasing doses of sildenafil and followed up monthly for 9 months. However, he had no significant improvement with sildenafil and he continued to remain in NYHA Class III with persistent cough syncope. He was started on Ambrisentan 5 mg OD and home based Oxygen Therapy and followed up for another 4 months. Subsequently, he developed reduced frequency of cough syncope but had worsening of dyspnea, pedal oedema and right hypochondrial pain. Diuretics could not be used in adequate doses as had severe postural hypotension.

In view of persistent symptoms, he underwent Balloon Atrial Septostomy in November 2013 with 10mm Balloon. LA saturation reduced from 96% to 79% post procedure with no change in PA pressure. He had Significant symptomatic improvement after 8 days of the procedure with no Syncopal episodes. His post procedure 2D ECHO showed a Patent Atrial Septostomy with Right to Left shunt.

However, the patient reported after 1 month with deterioration in effort tolerance. His arterial saturation was 96%. A repeat 2D echocardiography showed no shunt across atrial septum.
Improvement following balloon septostomy encouraged us to offer Atrial Septal Stenting to this patient. Since a manufactured atrial septal stent of appropriate size was not available in India and importing the stent was not financially feasible, we improvised the atrial septal stent using available hardware. A 40 X 20 mm Tyshak Balloon was modified by creating a ‘waist’ in the centre by tying a ligature in the centre. The ligature was kept a little loose and was prevented from movement on the balloon by firmly securing the front and rear ends of the ligature to the appropriate ends of the balloon. A 30 X 16-22 mm Cordis stent was hand crimped on this balloon (Figures 1-4).

He underwent a repeat balloon atrial septostomy with a 10 X 20 mm balloon and the stent was delivered via a 14 F long sheath and was deployed across the atrial septum. The patient tolerated the procedure. He was subjected to a 6 minute Hall Walk test which has been depicted below. He had significant symptomatic improvement post stenting with a worsening of cyanosis. The Hemodynamic Parameters have been depicted in Table 1. He has been on OPD follow up and was able to perform his activities of daily living as on July 2016. He has been advised a diagnostic cath study to assess the stent status, but is unwilling at present.

**Discussion**

Pulmonary vascular bed has a surface area of about 50-70 m² at rest, with almost 2/3rds of it being kept in reserve, available for recruitment. Under normal situations, it is a high flow, low pressure, and low resistance system which can accommodate marked increase in cardiac output without any significant increase in pressure. However, in conditions with an abnormal pulmonary vasculature, pressure rise can approach up to and even beyond, systemic levels. Pulmonary arterial hypertension (PAH) has been first described in 1891 in case reports. The term “primary pulmonary hypertension” was first used in 1951 to describe the clinical features and hemodynamics of 39 patients who had causeless PAH.

Symptoms in advanced cases of IPAH with heart failure are essentially due to low cardiac output. Inability of the right heart to pump against the excessively increased pulmonary vascular resistance in the long term causes the right heart to fail resulting in reduced right heart output into the pulmonary circulation resulting in the poor filling of the left ventricle. Also, intractable systemic venous congestion which is invariably present in these subjects also has significant symptoms which need relief.

Prior to specific therapies for pulmonary hypertension (PH), idiopathic pulmonary arterial hypertension (IPAH) was universally fatal with a median survival of 2.8 years. Until recently, medical therapies were mostly ineffective in improving symptoms or survival. Over the last decade, various therapies have become available; however they are very expensive and at best have minimal effect on long term survival. Curative therapies like Heart Lung transplantation are rarely feasible. Hence, as of now the aim of treatment in most patients of IPAH is to provide palliation. In a resource poor country like ours, cost of treatment is also a major hurdle in implementation of therapies.

Specific Pulmonary vasodilators like calcium channel blockers, alpha adrenergic blockers, PDE-5 inhibitors, endothelin receptor blockers and prostanoids become ineffective in endstage disease. There are very few practical options for these patients.

Establishing a right to left shunt by an atrial septostomy or central aortopulmonary shunts are a few ways of improving left sided filling in IPAH patients.

Here we present a case of endstage IPAH with severe congestive failure and low systemic output who presented with malignant cough syncope and severe restriction of physical activities who improved dramatically for a short while conventional balloon atrial septostomy. Unfortunately, within a month’s time, he had a recurrence of congestive failure and low output symptoms which were confirmed to be due to closure of interatrial communication which was confirmed on echocardiography.

We were encouraged to re-establish the interatrial communication using a more durable and long lasting mechanical solution at an affordable price using readily available hardware.

**Conclusion**

Atrial Septostomy is an established and an easy procedure for palliation in IPH. Improvement in dyspnoea occurs by ~ 1 NYHA class. Atrial Septal stenting is an alternative to Septostomy with added advantage of assured patency. Atrial Septal stents are not readily available in India and importing these stents is not cost effective. Atrial

**Table 1: Hemodynamics**

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<th>Before stenting</th>
<th>After stenting</th>
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<tr>
<td>RA pressure (mmHg)</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>LA pressure (mmHg)</td>
<td>10</td>
<td>15</td>
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<tr>
<td>RA saturation (%)</td>
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<td>75</td>
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<tr>
<td>LA saturation (%)</td>
<td>96</td>
<td>80</td>
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<tr>
<td>RV O2 saturation (%)</td>
<td>55</td>
<td>75</td>
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<td>RV pressure (Peak) mmHg</td>
<td>110</td>
<td>100</td>
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<tr>
<td>Aortic pressure (mmHg)</td>
<td>90</td>
<td>100</td>
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septal stenting done by our method using readily available hardware is as effective and more economical as the imported stents. However, Atrial Septal stenting only improves the symptoms but not the survival. Closure of Septostomy is a frequent problem. There are Anecdotal reports of improved survival.

References


