

# Eisenmenger Syndrome: Closing the Hole (RCD code: IV-2B.1)

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## Abstract

Eisenmenger syndrome represents the extreme manifestation of pulmonary arterial hypertension associated with congenital heart defects (CHD). Adults with CHD represent an increasing population which will require management in the long term. We present a case of a 38 year old female who presented with progressive dyspnea along with cyanosis at rest. Echocardiography showed a dilated right ventricle and an ostium secundum ASD with bidirectional shunting. Catheterization revealed severe pulmonary hypertension and evidence of partial anomalous pulmonary venous return. Warden procedure for PAPVR repair was performed along with a fenestrated pericardial ASD patch to close the shunt. A Maze Cox III procedure was also performed to treat the atrial fibrillation. Both procedures were performed successfully with significant improvement in patient's clinical status. This article provides details regarding etiology, pathogenesis, clinical features, and diagnostic evaluation of Eisenmenger syndrome. It covers recent guidelines for screening and therapy as well as information regarding innovations in social and healthcare. JRCD 2014; 1 (6): 33–35

**Key words:** Eisenmenger; atrial septal defect; congenital heart disease; pulmonary hypertension

## Case presentation

A 38 year white female presented with a six week history of progressive dyspnea classified as New York Heart Association (NHYA) Class III. Her past medical history is notable for 4 pregnancies. She denied chest pain, lightheadness, syncope, or palpitations. Upon arrival, her blood pressure was 122/72 mm Hg. Heart rate was 102 beats per minute and regular with a respiratory rate of 28 breaths per minute. Physical examination revealed central cyanosis with clubbing of fingers. +1 pitting bilateral lower extremity edema was also noted. On cardiac auscultation, a Grade 2 blowing systolic murmur was heard in the pulmonic area and lung fields were clear. In arterial blood gas analysis, her arterial oxygen tension was 66 mmHg (saturation 89%) breathing room air, improving to 91 mmHg (saturation 94%) on 15 l/min oxygen therapy.

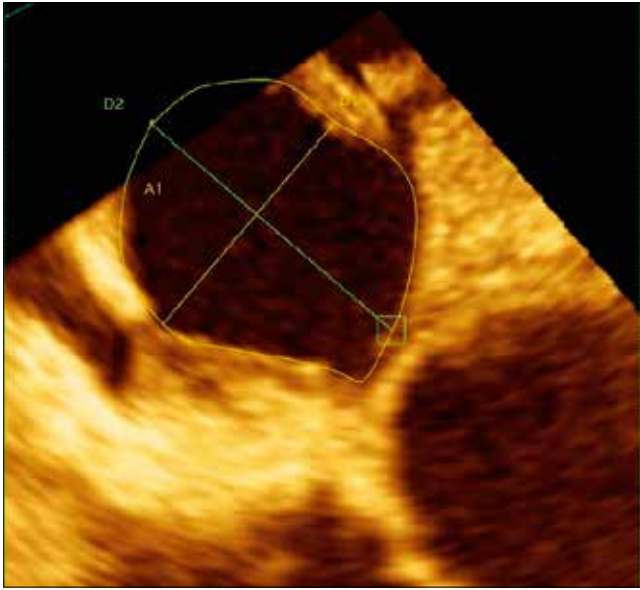
Blood tests showed Hb 16.3(Hct 47.9%) but otherwise complete blood count, coagulation, and biochemistry were within normal limits. Resting electrocardiogram (ECG) showed sinus rhythm at 99 beats per minute with right axis deviation and right ventricular hypertrophy. Chest radiography revealed enlarged prominent central pulmonary arteries. Chest computed tomography did not

reveal evidence of interstitial lung disease or pulmonary embolus. While hospitalized, episodes of atrial fibrillation were caught on monitor strips giving a new diagnosis of paroxysmal atrial fibrillation. A transesophageal echocardiogram showed a large ostium secundum atrial septal defect (ASD) (23 mm) (Figure 1) with bidirectional shunting (Figure 2) and evidence of right cardiac chamber enlargement (Figure 3). Systolic pulmonary artery pressure of 79 mm Hg and right ventricular systolic pressure (RVSP) of 84 mm Hg were noted. Tricuspid annular plane systolic excursion (TAPSE) was calculated to determine at a value of 12 mm indicative of right ventricular dysfunction. Pediatric cardiology was consulted on the case to evaluate operability status for which the patient underwent cardiac catheterization. There was significant desaturation in the pulmonary artery (70%), and aorta (79%). There was evidence of severe pulmonary hypertension (88/37) with a calculated pulmonary vascular resistance of 25.1 Wood units and Qp (pulmonary blood flow):Qs (systemic blood flow) at 0.55. On administration of oxygen and 80 parts per million nitric oxide, Qp:Qs increased to 0.94 and pulmonary vascular resistance dropped to 9.3 Wood units. Of note was a partial anomalous pulmonary venous return with the right upper pulmonary vein draining into the superior vena cava.

Conflict of interest: none declared.

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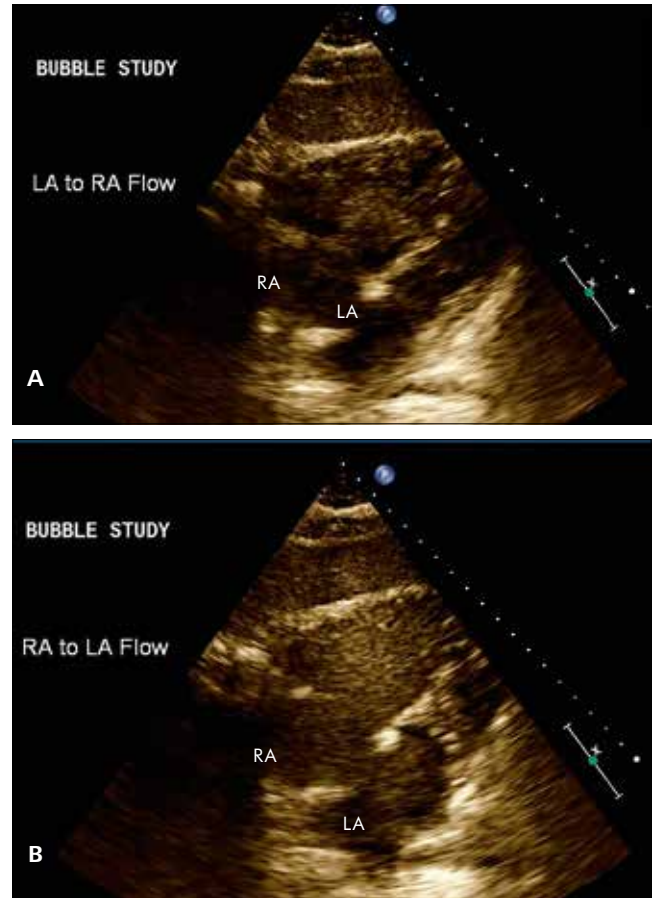


**Figure 1.** Transesophageal echocardiogram. Large atrial septal defect secundum (23 mm)

## Literature review

Adults with congenital heart defects (CHD) represent a growing population subset due to continuing medical and surgical advances in pediatric cardiology. It is estimated that 5–10% of CHD patients will develop pulmonary arterial hypertension (PAH) [1]. Eisenmenger syndrome (ES), defined as pulmonary hypertension at the systemic level due to high pulmonary vascular resistance index ( $>10$  WU  $m^2$  or  $800$  dyne/s/cm $^5$ ) with bidirectional or reversal of shunt (RL) [2]- represents the extreme manifestation of PAH in patients with CHD. Patients with ES have the highest rates of mortality and poorer quality of life among the PAH-CHD population subset. The incidence of CHD is estimated at 8 per 1000 live births [3]. PAH in CHD patients is thought to develop secondary to increased pulmonary arterial flow due to presence of a left-to-right shunt. The shunt increases pressure in the pulmonary arteries leading to abnormal shear stress, circumferential wall stretch and endothelial dysfunction. The loss of function of the endothelial barrier causes altered expression of vasodilators (nitric oxide, prostacyclin, endothelin-1) resulting in vasoconstriction, leading to increased pulmonary vascular resistance and ultimately remodeling of the pulmonary vasculature [4]. ES develops in 10% of patients with unrepaired large ASDs and in 80% of patients with large unrepaired ventricular septal defects (VSD) or patent ductus arteriosus (PDA). 90% of patients with ASD present during adulthood compared with 80% of VSD or PDA cases which present during infancy [5]. It is of significance to note that the mean age of death is  $37.5 \pm 4.5$  years in patients with an uncorrected ASD

The dynamics of CHD have changed drastically over the years. Due to the advances in pediatric cardiology, greater than 85% of infants can be expected to reach adulthood, compared to less than 15% survival rate into adulthood before the 1970s [6]. Pregnancy



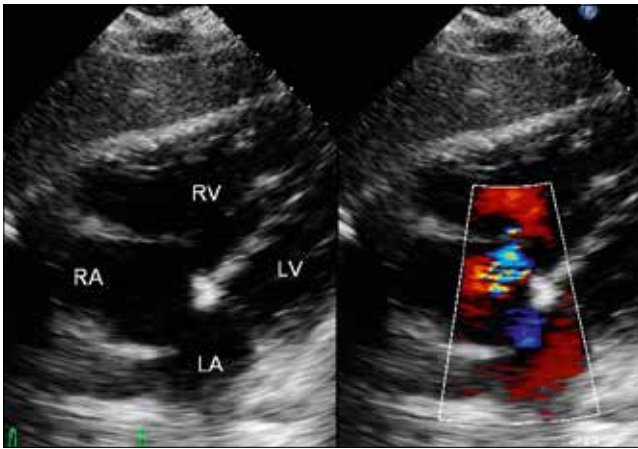
**Figure 2.** Transesophageal echocardiogram. Bubble study showing bidirectional flow across atrial septal defect. A. Flow from LA to RA. B. Flow from RA to LA. RA – right atrium, LA – left atrium

is contraindicated in females with PAH due to rates of maternal mortality as high as 30–56% [7].

ES is the only type of PAH where its development is preventable by closure of underlying defect. Once developed though, closure of present defect is contraindicated. The most crucial factor in determining late outcome is the age at which repair is carried out. Most children operated upon by 9 months of age have a normal pulmonary vascular resistance one year after repair. After 2 years of age resistance may fall, but not to a normal level [8]. The exact level of PVRI that precludes safe closure of a defect is controversial and varies with each lesion. Steele and colleagues [9] suggests surgical treatment can be advised and tied to improved outcomes with pulmonary vascular resistance of less than 15 Wood units.

Pulmonary vasoreactivity has been shown to have prognostic value for adult patients with Eisenmenger physiology with positive responders defined a reduction of pulmonary artery pressure and pulmonary vascular resistance of  $> 20\%$  [10]. The only curative option for end-stage disease being lung transplantation with repair of the cardiac defect or combined heart-lung transplantation is reserved for recalcitrant cases due to significant morbidity and mortality.

3 classes of pulmonary vasodilators targeting one of three key pathological pathways in PAH: the prostacyclin, endothelin, and



**Figure 3.** Transesophageal echocardiogram. Four chamber view. Large atrial septal defect secundum with bidirectional shunting. Enlargement of the right atrium and right ventricle. RA – right atrium, RV – right ventricle, LA – left atrium, LV – left ventricle

nitric oxide pathways have emerged as advanced therapy (AT) for PAH: (1) prostanoids, (2) endothelin receptor antagonists, and (3) phosphodiesterase-5 inhibitor. Treatment with advanced therapies (predominantly bosentan) was associated with a significantly lower rate of cumulative mortality over 7 yrs versus no therapy [11]. Combination therapy is recommended for patients in WHO (World Health Organization) functional class IV or patients who remain in WHO functional class III despite PAH monotherapy treatment [12]. The development of PAH, and particularly Eisenmenger's syndrome, in patients with CHD is associated with increased morbidity and mortality. Pulmonary vascular disease secondary to congenital heart disease is a preventable illness. The best therapy for PAH-CHD still remains prevention via repair of the defect.

## Patient management and follow up

Patient was treated with anticoagulant therapy with low dose molecular heparin and supportive management with diuretics and digitalis for the right heart failure as well as beta blocker therapy. A consult was placed with pediatric cardiothoracic surgery. After reviewing the case it was recommended patient undergo operative repair of the ASD. It is important to note that even though based on current guidelines [13] this patient is contraindicated to undergoing repair of the atrial septal defect secondary to development of ES, based on the positive vasoreactivity testing with drastic improvement of resistance index along with the patient being severely symptomatic, it was decided to not undergo the “treat-and-repair” approach and rather that surgical repair along with post-operative therapy with pulmonary vasodilators would be the best option for this patient. This would allow marked improvement in symptoms followed by continued re-modeling of the pulmonary vasculature. Patient underwent Warden procedure for repair of the anomalous pulmonary vein with a fenestrated pericardial ASD patch to close the ASD. It was also decided to have the patient undergo a Cox Maze III procedure for surgical cure of atrial fibrillation. Surgery was uneventful with pulmonary artery pressure post-operative-

ly of 63/35 with drastic improvement in oxygenation saturation (SpO<sub>2</sub>) ranging from 90–95% compared to pre-operative saturations ranging from 84–89% on room air. Echocardiographic imaging were routinely done post-operatively to monitor RVSP and systolic cardiac function. RVSP improved greatly following surgery with pressures as low as 43 mm Hg and TAPSE at 13 on post-op day # 9. Patient was discharged post op day # 12 on advanced combination therapy of ambrisentan and tadalafil and in good hemodynamic condition with oxygen saturations > 92% room air. Surgical intervention and vasodilator therapy started immediately after the operation improved the NYHA functional status of the patient with NYHA Class II functional status upon one month followup.

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