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Berry syndrome: a rare cardiac malformation with extra-cardiac findings

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Dear Editor,

Berry syndrome is a rare combination of congenital cardiac malformations characterized by four abnormal features; namely, an aortopulmonary window (APW), aortic origin of the right pulmonary artery, hypoplasia or interruption of the aortic arch, with an intact ventricular septum. The disease was first reported by Berry in 1982, who estimated the incidence within the population with congenital cardiac malformations to be 0.046% (Berry et al., 1982). Until recently, there has been a paucity of literature addressing patients with Berry syndrome <60 publications (Hu et al., 2017). With the development of ultrasonography, transthoracic echocardiography (TTE) serves as a noninvasive method to diagnose congenital cardiac defects, by providing important information regarding the anatomic, functional, and hemodynamic performance of the cardiovascular system. In this case series, we present our analysis of echocardiographic findings in a group of patients diagnosed with Berry syndrome. We aimed to determine whether TTE can serve as the primary method to diagnose Berry syndrome, while providing a safer and less invasive modality.

Twelve patients with Berry syndrome underwent TTE and were initially diagnosed using echocardiography. Diagnosis was confirmed with computed tomography angiography (CTA) in all patients, of whom four were additionally diagnosed surgically. The age of patients ranged from 1 day to 18 years. We found four patients >3 years of age. All the patients who presented with this complex anomaly were often critically ill. Clinical manifestations included cyanosis, dyspnea, murmur, acute respiratory distress syndrome and heart failure. The physical examination included tachycardia, tachypnea, bilateral lower extremities hypotension, cyanosis of lips, cardiac murmur and the lower blood oxygen saturation. In addition, we found extra-cardiac abnormalities in a 4-year-old girl with respiratory distress caused by congenital lobar emphysema, as well as in a 6-year-old boy with a surgical history for hypospadias correction.

All the patients were diagnosed using TTE, which showed an interrupted aortic arch (IAA) or coarctation of the aorto (COA) in the suprasternal long-axis view (Figure 1A and B); a right pulmonary artery arising from the ascending aorta, an

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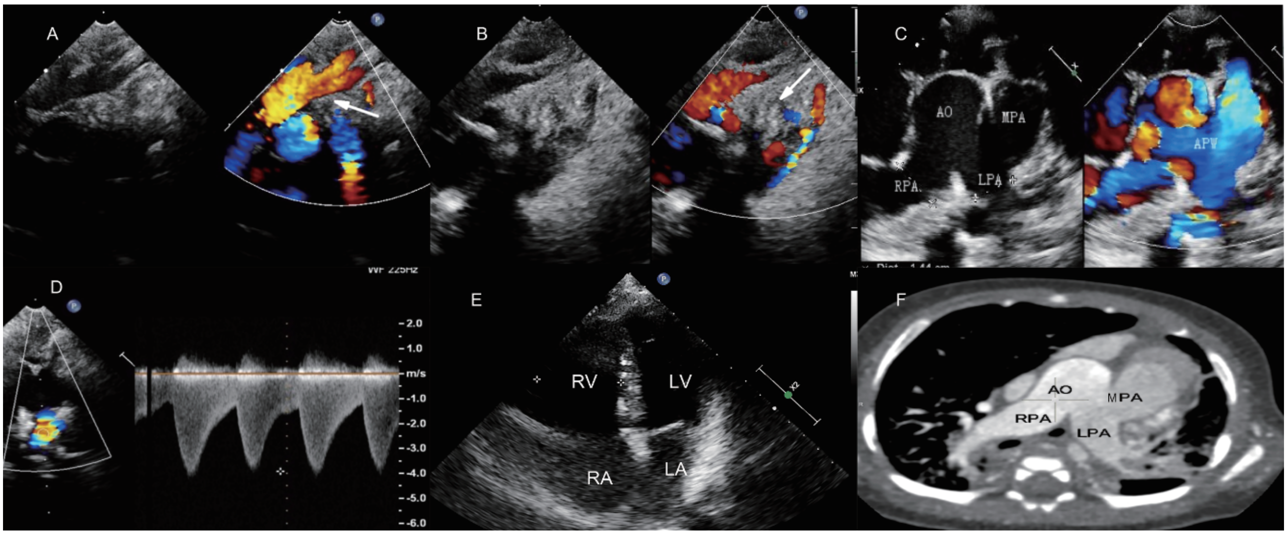

Figure 1 Imaging features of Berry syndrome. A and B, Suprasternal long-axis view showing IAA types A and B (arrow). C, Parasternal short-axis demonstrating the butterfly sign. D, PDA. E, Apical view showing an intact ventricular septum. F, CTA image showing the butterfly sign. AO, aorta; MPA, main pulmonary artery; LPA, left pulmonary artery; RPA, right pulmonary artery; APW, aorta pulmonary window; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

APW and patent ductus arteriosus (PDA) in the parasternal short-axis view (Figure 1C and D); and intact ventricular septum in the apical view (Figure 1E). The CTA image showed the right pulmonary artery arising from the ascending aorta and an APW (Figure 1F).

Berry syndrome was first described in 1982. The four features derived from a similar embryological origin consisting of associated cardiovascular malformations. TTE should be the first-line diagnostic tool for Berry syndrome. CTA and magnetic resonance imaging (MRI) have been secondary imaging tools to ascertain additional information on patients with Berry syndrome. TTE has a series of routine views and a distinctive sign, the most important of which is the "butterfly sign". In the parasternal short-axis view, we observed the "butterfly sign", which comprises of the pulmonary trunk and left pulmonary artery on one side, and the aorta and right pulmonary artery on the other side. An APW is located between the two parts. We can also observe this sign on CTA. A large type II APW was the most common feature in all the patients, detected on the parasternal view. In a prior study, type A IAA and COA were reported, but type B IAA cases were rare. However, in this study, type B cases could be reviewed.

TTE could detect the hemodynamics changes in Berry syndrome. Due to the increased blood flow in the pulmonary artery, pulmonary hypertension is a major complication of Berry syndrome. The onset of pulmonary hypertension can be evaluated based on the shunt direction of APW. Five patients in our research had a right-to-left shunt and four had a bidirectional shunt. We estimated the severity of hypertension by using echocardiography to make a preliminary judgment. As for patients with IAA, a closed ductus arteriosus or a narrow duct predicted poorer prognosis. Berry syndrome, with ductal dependent systemic circulation, should be treated with prostaglandin E2 to maintain an open ductus arteriosus until further surgery (Fong et al., 2006). However, some patients who do not undergo surgery may achieve a long-term survival. In our patient population, two patients had a thick PDA between 8–15 mm and one patient had collateral vascularity, which became the vital blood supply to the lower part of the body. The 4-year-old girl had a slight COA, so the perfusion was sufficient. The oldest Berry syndrome patient published prior to this study was a 12-year-old male, who had a thick PDA (Yang et al., 2008). Therefore, the evaluation of the severity of aortic arch dysplasia, shunt flow of the ductus arteriosus and the collateral vascularity provided very important information for the patient's prognosis.

Although CTA and MRI allow for easy visualization of abnormalities in arteries (Mannelli et al., 2011), their main disadvantages include radiation exposure, high cost, and inability to assess blood flow. TTE has the advantage of hemodynamics assessment, safe approach, and repeatability. Our experience indicated that TTE can provide adequate diagnostic information for most patients, as all relevant preoperative information regarding anatomy and hemodynamic data can be obtained. In our 12 patients, a definitive diagnosis was made with TTE. The four patients who had an early diagnosis underwent successful surgical correction. The four abnormal features of Berry syndrome were so characteristic that misdiagnosis was unlikely when TTE was used, even in the case of neonates.

In conclusion, we indicate that TTE is an important technique in the initial evaluation of complex congenital heart disease. Compared to CTA, TTE is a safer and less invasive method to diagnose Berry syndrome, while also providing structural and hemodynamic details to assess and plan for surgery. Patients with extra-cardiac manifestation indicate that we should pay more attention to genetic evaluation before surgery. All the clinical data have been deposited into the rare disease database, eRAM, at http://www.pediascape.org/eram/.

Compliance and ethics *The author(s) declare that they have no conflict of interest.*

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