

# Spontaneous Closure of a Secundum Atrial Septal Defect

Stephen Y. Wang, B.S.<sup>a</sup>; Terrence D. Welch, M.D.<sup>a</sup>; Aryé Elfenbein, M.D., Ph.D.<sup>b,c</sup>; Aaron V. Kaplan, M.D.<sup>a</sup>

<sup>a</sup>GEISEL SCHOOL OF MEDICINE AT DARTMOUTH, HANOVER, NEW HAMPSHIRE; <sup>b</sup>YALE UNIVERSITY SCHOOL OF MEDICINE, NEW HAVEN, CONNECTICUT; <sup>c</sup>UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, SAN FRANCISCO, CALIFORNIA

**ABSTRACT:** Spontaneous closure of an atrial septal defect (ASD) is well described in pediatric cardiology but may be less familiar to adult internists and cardiologists. We report a moderately sized 6-mm ASD that closed spontaneously without intervention. A literature review found that a smaller defect size and an early age of diagnosis are the most important predictors of closure. Possible mechanisms of a spontaneous ASD closure include adaptive endothelial migration, limited myocardial proliferation, and fibroblast migration with extracellular matrix deposition.

## INTRODUCTION

Atrial septal defect (ASD) is a common congenital disorder with a prevalence of approximately 2 per 1,000 live births.<sup>1,2</sup> There are four types of ASDs: secundum, primum, sinus venosus, and coronary sinus. Secundum ASDs are the most common, making up more than 70% of all ASDs.<sup>2</sup> We present a patient with spontaneous closure of a moderately sized secundum ASD and a small ventricular septal defect (VSD).

## CASE

A newborn girl was noted to have a heart murmur within the first 24 hours of life. Pregnancy, parturition, and two prenatal ultrasounds had been unremarkable. Cardiac auscultation at 3 days of life revealed a grade 3/6, somewhat high-pitched holosystolic murmur at the left lower sternal border radiating throughout the precordium. There was also a systolic murmur over both posterior lung fields. The electrocardiogram was normal except for nonspecific ST- and T-wave changes. A transthoracic echocardiogram (TTE) showed a moderately sized secundum ASD measuring 6 mm in diameter (Figure 1 A, B). There was also a single anterior apical VSD measuring 5 mm. There were no other abnormal findings. Upon physical examination at age 2, the cardiac murmur could no longer be heard.

The patient presented to our institution at age 18 years with a complaint of “heart hurting” beginning 2 to 3 months before evaluation. She described a typical episode consisting of the abrupt onset of precordial pain with her “heart beating crazily.” The episodes were paroxysmal, frequent, and typically lasted between a few seconds and a few minutes. Due to suspected dysrhythmias and a history of ASD, the patient underwent ambulatory heart rhythm monitoring and a TTE. The echocardiogram demonstrated a structurally normal heart with a patent foramen ovale detected by agitated saline. Neither an

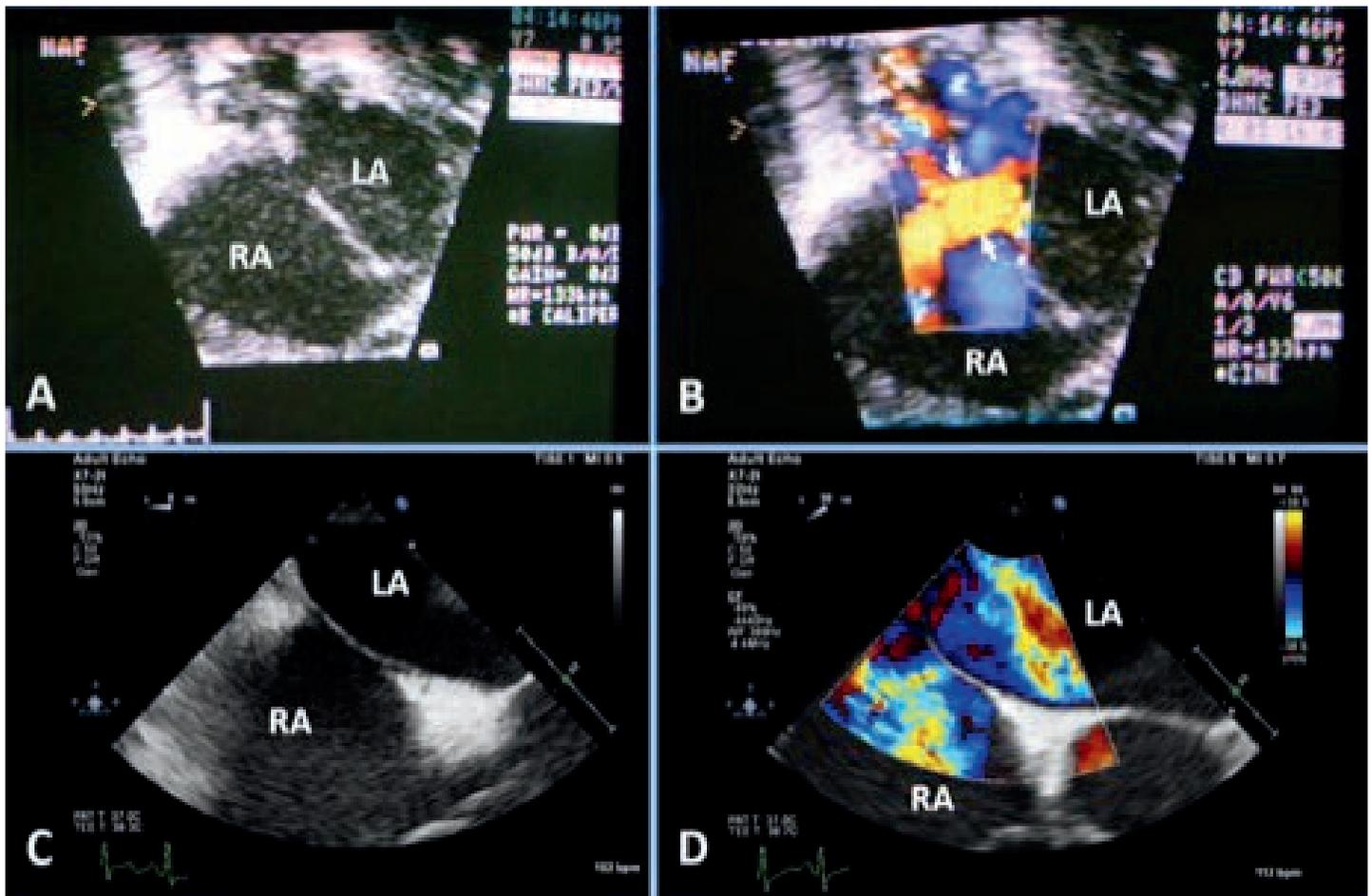
ASD nor a VSD were evident. The ambulatory heart rhythm monitor revealed only rare atrial and ventricular premature contractions corresponding to symptoms.

Due to the less-sensitive nature of TTE, a transesophageal echocardiogram was performed to verify spontaneous and complete closure of the secundum ASD (Figure 1 C, D).

## NATURAL HISTORY

The capacity for tissue growth and closure of an ASD is a well-described phenomenon in the pediatric literature but may be less familiar to adult cardiologists and internists. This case of serial echo-Doppler evaluations provides an unusual opportunity to further support findings in the pediatric literature. The reported rate of spontaneous ASD closure ranges from 4% to 96%, with the variation due to different selection criteria in the study cohorts.<sup>2-14</sup> The most important predictor for spontaneous closure is the size of defect, with smaller defects more likely to close.<sup>2,5,7,9,11</sup> Radzik et al. found that all ASDs < 3 mm in size are expected to close spontaneously if diagnosed within the first 3 months of life.<sup>11</sup> Studies involving ASDs > 3 mm have reported spontaneous closure rates between 4% and 37.5%, whereas many ASDs of moderate diameter (3 mm to 8 mm) may close spontaneously and should be followed.<sup>2,3,5,7,8,11,14</sup> ASDs greater than 8 mm are unlikely to close,<sup>2,5,11,14</sup> although Fiszer et al. reported a case of a very large 10- to 11-mm secundum ASD that closed spontaneously within 1 year.<sup>15</sup>

Spontaneous closure also correlates with age at diagnosis and is more likely to occur when the ASD is detected at an earlier age.<sup>4,7,9,14</sup> For example, more than 80% of ASDs have been reported to close spontaneously in neonates who are diagnosed at a mean age < 1 month.<sup>10,12,13</sup> Consequently, the relatively older age at diagnosis (4.5 years) in the study by McMahon et al. was a likely factor in the extremely low spontaneous closure rate (4%).<sup>8</sup>



**Figure 1.**

Transthoracic echocardiography shortly after birth demonstrates a 6-mm secundum atrial septal defect by 2-dimensional imaging (A, marked by crosshairs). Color Doppler imaging (B) shows left-to-right flow (between arrows) across the defect. Transesophageal echocardiography performed at age 18 demonstrates complete closure of the secundum ASD by 2-dimensional (C) and color Doppler (D) imaging. LA: left atrium; RA: right atrium

Interestingly, there have also been reports of decreases in ASD size without complete closure as well as reports of ASDs that have increased in size over time.<sup>2,3,5,7,8,14</sup> Therefore, the growth and remodeling of the septum over time appears to be a heterogeneous phenomenon that cannot be reliably predicated. Our patient's case involved an ASD measuring 6 mm at 3 days of life. The size and age at diagnosis pointed to a moderate likelihood of spontaneous closure, and the ASD likely closed by the time of the follow-up visit at 2 years of age.

#### POSSIBLE MECHANISMS OF CLOSURE

Although mechanisms of delayed spontaneous closure are not completely understood, recent studies have provided clues for potential contributing underlying processes. One mechanism involves shear stress and blood flow dynamics, which are locally

altered in the setting of an ASD. Such forces are sensed by the endothelium and have been shown to control the subsequent adaptive migration of these cells.<sup>16</sup> Another related process is myocardial proliferation. Although human myocardial division generally does not occur beyond the first few days of neonatal life, limited postnatal regenerative and proliferative capacity has been characterized in various model systems.<sup>17</sup> In addition, cardiomyocytes have recently demonstrated the ability to undergo oriented cell division in postnatal mice<sup>18</sup> and in the context of ventricular morphogenesis of zebrafish trabeculae,<sup>19</sup> likely bearing significant mechanistic overlap with structural cardiac remodeling events such as delayed ASD closure. Finally, the critical role of fibroblast migration and extracellular matrix deposition has been demonstrated in several models of myocardial injury; these processes are also likely to provide part of the structural support required for long-term closure.

## CONCLUSION

ASDs are a common occurrence, and many cases close spontaneously in neonates. Predictors of ASD closure are dependent on defect size and patient age. Routine clinical follow-up with serial echocardiography is the best way to identify those patients who close spontaneously and those who will require closure. Further investigation is needed to understand the mechanisms and heterogeneity of septal growth and remodeling after birth.

### *Conflict of Interest Disclosure:*

The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

### *Keywords:*

cardiology, congenital heart disease, atrial septal defect

## REFERENCES

- van der Linde D, Konings EE, Slager MA, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2011 Nov 15;58(21):2241-7.
- Helgason H, Jonsdottir G. Spontaneous closure of atrial septal defects. *Pediatr Cardiol*. 1999 May-Jun;20(3):195-9.
- Brassard M, Fouron JC, van Doesburg NH, Mercier LA, De Guise P. Outcome of children with atrial septal defect considered too small for surgical closure. *Am J Cardiol*. 1999 Jun 1;83(11):1552-5.
- Cockerham JT, Martin TC, Gutierrez FR, Hartmann AF Jr, Goldring D, Strauss AW. Spontaneous closure of secundum atrial septal defect in infants and young children. *Am J Cardiol*. 1983 Dec 1;52(10):1267-71.
- Demir T, Oztunç F, Eroğlu AG, et al. Outcome for patients with isolated atrial septal defects in the oval fossa diagnosed in infancy. *Cardiol Young*. 2008 Feb;18(1):75-8.
- Garne E. Atrial and ventricular septal defects - epidemiology and spontaneous closure. *J Matern Fetal Neonatal Med*. 2006 May;19(5):271-6.
- Hanslik A, Pospisil U, Salzer-Muhar U, Greber-Platzer S, Male C. Predictors of spontaneous closure of isolated secundum atrial septal defect in children: a longitudinal study. *Pediatrics*. 2006 Oct;118(4):1560-5.
- McMahon CJ, Feltes TF, Fraley JK, et al. Natural history of growth of secundum atrial septal defects and implications for transcatheter closure. *Heart*. 2002 Mar;87(3):256-9.
- Mody MR. Serial hemodynamic observations in secundum atrial septal defect with special reference to spontaneous closure. *Am J Cardiol*. 1973 Dec;32(7):978-81.
- Ozcelik N, Atalay S, Tutar E, Ekici F, Atasay B. The prevalence of interatrial septal openings in newborns and predictive factors for spontaneous closure. *Int J Cardiol*. 2006 Apr 4;108(2):207-11.
- Radzik D, Davignon A, van Doesburg N, Fournier A, Marchand T, Ducharme G. Predictive factors for spontaneous closure of atrial septal defects diagnosed in the first 3 months of life. *J Am Coll Cardiol*. 1993 Sep;22(3):851-3.
- Riggs T, Sharp SE, Batton D, Hussey ME, Weinhouse E. Spontaneous closure of atrial septal defects in premature vs. full-term neonates. *Pediatr Cardiol*. 2000 Mar-Apr;21(2):129-34.
- Fukazawa M, Fukushige J, Ueda K. Atrial septal defects in neonates with reference to spontaneous closure. *Am Heart J*. 1988 Jul;116(1 Pt 1):123-7.
- Azhari N, Shihata MS, Al-Fatani A. Spontaneous closure of atrial septal defects within the oval fossa. *Cardiol Young*. 2004 Apr;14(2):148-55.
- Fischer R, Szkutnik M, Chodór B, Białkowski J. Spontaneous closure of a large atrial septal defect in an infant. *Postępy Kardiologii Interwencyjnej*. 2014;10(4):264-6.
- Baeyens N, Bandyopadhyay C, Coon BG, Yun S, Schwartz MA. Endothelial fluid shear stress sensing in vascular health and disease. *J Clin Invest*. 2016 Mar 1;126(3):821-8.
- Uygun A, Lee RT. Mechanisms of Cardiac Regeneration. *Dev Cell*. 2016 Feb 22;36(4):362-74.
- Ali SR, Hippenmeyer S, Saadat LV, Luo L, Weissman IL, Ardehali R. Existing cardiomyocytes generate cardiomyocytes at a low rate after birth in mice. *Proc Natl Acad Sci U S A*. 2014 Jun 17;111(24):8850-5.
- Han P, Bloomekatz J, Ren J, et al. Coordinating cardiomyocyte interactions to direct ventricular chamber morphogenesis. *Nature*. 2016 Jun 30;534(7609):700-4.