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ORIGINAL ARTICLE

Outcome of Aneurysmal Septum Primum with Non-restrictive Foramen Ovale in Fetuses with Structurally Normal Hearts: A Tertiary Center Experience

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Abstract The aim of this analysis was to study the postnatal short-term outcome of cases with aneurysmal septum primum (ASP) and non-restrictive foramen ovale in otherwise structurally normal hearts. This is a retrospective review of fetuses with ASP referred between 2016 and 2018 to the University Hospital of Cerrahpasa, Department of Fetal Cardiology for cardiac scanning. Prenatal and postnatal clinical features and outcomes for each case were ascertained from the departmental database and from individual clinical hospital records. We presented twenty-four cases which also had postnatal echocardiographic examination in our hospital. At the time of diagnosis of ASP, the mean maternal age was 31.1 ± 5.7 years, the mean gestational age was 28.9 ± 5.9 weeks, the mean birth week was 37.4 ± 3.1 weeks, and the mean birth weight was 2940.8 ± 736.6 g. The postnatal first 3 months prevalences of atrial septal aneurysm, patent foramen ovale and, secundum atrial septal defect (ASD) were 12.5%, 12.5%, 20.8% among fetuses with ASP, respectively. ASP may persist after birth and may increase the frequency of secundum ASD. These data suggest that fetuses with ASP should be followed by a pediatric cardiologist in postnatal life.

Keywords Aneurysmal septum primum · Atrial septal aneurysm · Fetal echocardiography · Foramen ovale · Postnatal outcome

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Introduction

The foramen ovale is an important distributor of blood during fetal life, supplying the left atrium with one-third of the combined cardiac output during mid-gestation and one-fifth during the third trimester [1]. At 4 weeks in an embryo, the primordial single atrium divides into right and left sides by formation and fusion of two septa: the septum primum and septum secundum. The septum secundum gradually grows and overlaps part of the foramen secundum, forming an incomplete septal partition as an oval-shaped window. It is this window that becomes the foramen ovale. As oxygenated blood in utero flows from the inferior vena cava and enters the right atrium, it crosses the patent foramen ovale and becomes the systemic circulation. Most blood flow from the superior vena cava is routed through the tricuspid valve and enters the right ventricle. At birth, right heart pressure and pulmonary vascular resistance drop as pulmonary arterioles open in reaction to oxygen filling the alveolus. Left atrial pressure may also rise as the amount of blood returning from the lungs increases. Either or both of these mechanisms may cause flap closure against the septum secundum [2].

Aneurysmal septum primum (ASP) may develop secondary to interatrial pressure difference or may be the result of a primary malformation involving the fossa ovalis region or the entire septum [3]. Persistency of ASP in postnatal life is associated with patent foramen ovale (PFO) [4]. Atrial septal aneurysm and PFO, especially if they are together, emerged as a predictor of increased risk for recurrent cryptogenic stroke in some reports [5–9].

This study aims to present the postnatal short-term outcome of cases with non-restrictive ASP in otherwise structurally normal hearts.

Materials and Methods

This is a retrospective review of fetuses with non-restrictive aneurysmal foramen ovale referred between 2016 and 2018 to the University Hospital of Cerrahpasa, Department of Fetal Cardiology for cardiac scanning with any reason. Ethics Committee approval was not necessary because the review was retrospective. All fetal and postnatal cardiac examinations were performed by a single operator (F.O). The equipment used was a commercially available echocardiography device (Philips iE33, Philips Medical Systems, Andover MA, USA) equipped with a broadband X5-1S MHz transducer. Postnatal cardiac examinations were performed within the first 3 months after birth.

Cases were included with ASP if the flow across the foramen ovale was unrestrictive with a triphasic Doppler pattern. The position of the atrial septum was estimated with atrial septal excursion (ASE) index. In the apical four-chamber view, the maximum extent of bowing of the atrial septum towards the left atrial free wall was measured and divided by the diameter of the left atrium, measured from the base of the atrial septum to the free wall of the left atrium (Figs. 1, 2). An ASP was defined as an ASE index equal to or greater than 0.55 [10, 11]. Cases with complex congenital heart defects and chromosomal abnormalities were excluded. Prenatal and postnatal clinical features and outcomes for each case were ascertained from the departmental database and from individual clinical hospital records. A secundum ASD was differentiated from PFO in postnatal echocardiographic studies with these measurement criteria: size and appearance of the defect, presence or absence of a flap of septal tissue, and presence/absence/amount of blood shunting across through the opening [12].

Data are presented as frequencies, mean ± SD or median and range as appropriate.

Results

During the study period, 1563 fetuses were referred for cardiac scans. No structural heart defects were found in 542 of these evaluations. Thirty-nine had an ASP with non-restrictive foramen ovale with a structurally normal heart, giving a prevalence of 7.2% among this selected cohort. We presented twenty-four cases which also had postnatal echocardiographic examination in our hospital. At the time of diagnosis of ASP, the mean maternal age was 31.1 ± 5.7 years (range 21–47), the mean gestational age was 28.9 ± 5.9 weeks (range 20–38), the mean birth week was 37.4 ± 3.1 weeks (range 29–41), and the mean birth weight was 2940.8 ± 736.6 g (range 1100–4000). In the first 3 months of postnatal life, the prevalence of atrial septal aneurysm, patent foramen ovale (PFO) and, secundum atrial septal defect (ASD) were 12.5%, 12.5%, 20.8% among fetuses with ASP, respectively.

There was an unexplained intrauterine demise at 32 weeks. The characteristics of all cases are listed in Table 1.

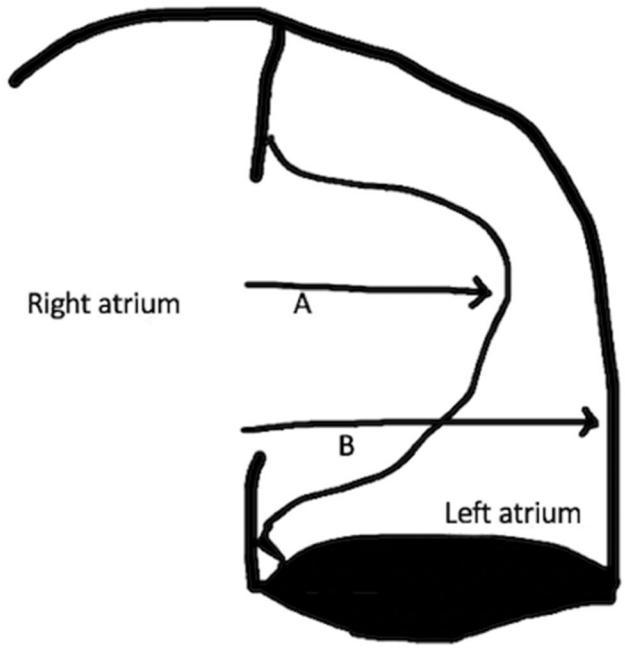

Fig. 1 Diagram depicting measurements for determination of atrial septal excursion index

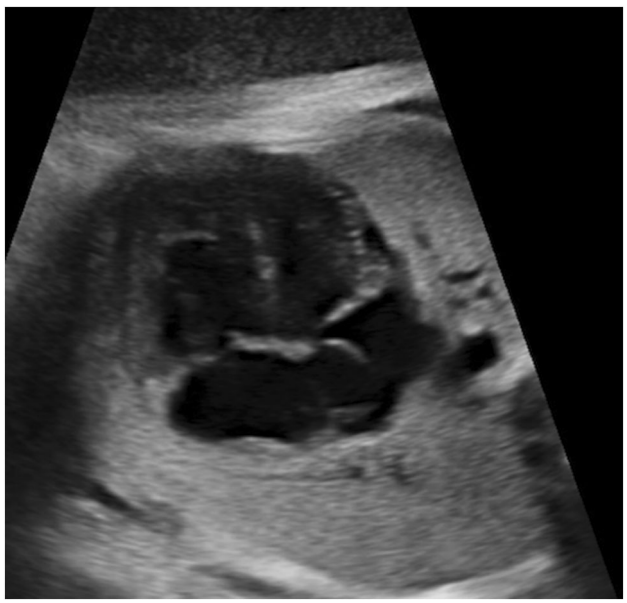

Fig. 2 An aneurysmatic foramen ovale projecting into the left atrium during atrial diastole

Discussion

Reports that investigate atrial septum in intrauterine life, have increased recently. To our knowledge, this is the first study that demonstrates outcomes of ASP with non-restrictive foramen ovale in fetuses with structurally normal hearts.

The pathogenesis of an ASP is uncertain, although abnormal atrial pressure causing deformation and weakness of the septum primum and an underlying cardiac connective tissue disorder deforming both the atrial septum and atrioventricular valves have been reported as potential causes [13, 14]. Tague et al. [15] reported that aneurysms of the septum primum were more frequently noted after 34 weeks (37.5% versus 80%). They propose that this finding in the absence of any other systemic findings is benign and represents changes in the in utero physiologic mechanisms that occur late in pregnancy. In a recent study of 1072 newborns, the prevalence of atrial septal aneurysm was reported to be 11.1% in preterm neonates and 7.1% in full-term neonates [16]. Bassareo et al. recently reported a statistically significant difference between the prevalence of atrial septal aneurysm in young adults born preterm with extremely low birthweight in comparison with healthy controls born at term. They also reported a significant association between atrial septal aneurysm and the presence of both respiratory distress at birth and patency of the ductus arteriosus [17].

The prevalence of ASP is 7.2% in our study group that includes second and third trimester pregnant women. The aneurysmal state of atrial septum regressed spontaneously

Table 1 The clinical characteristics of the cases

Case no.	Referral reason	Postnatal echocardiography	Outcome
1	Suspicion of ASD	Patent ductus arteriosus Patent foramen ovale	Alive
3	ASP	Normal	Alive
4	ASP	Normal	Alive
6	ASP	Normal	Alive
8	ASP	Normal	Alive
13	ASP	ASA	Alive
14	ASP	Patent ductus arteriosus Patent foramen ovale	Alive, closed spontaneously
15	ASP	Normal	Alive
16	VSD history in sister	Normal	Alive
17	Suspicion of VSD	Secundum ASD, rhabdomyoma diagnosis of rhabdomyoma is not definitely, yet	Alive
18	Maternal age	Normal	Alive
20	ASP	Normal	Alive
21	HIF in right ventricle	Secundum ASD, ASA	Alive
25	Suspicion of VSD	Normal	Alive
26	Maternal age, DM Type 2	Secundum ASD	Alive, closed spontaneously
27	Suspicion of VSD	Normal	Alive
28	ASP	Secundum ASD	Alive, Follow-up
30	Suspicion of ASD	ASA, Patent foramen ovale	Alive, Follow-up
31	Suspicion of VSD	Normal	Alive
32	Suspicion of VSD	Normal	Alive
33	Arrhythmia	Normal	Alive
34	Suspicion of VSD	Normal	Alive
36	Suspicion of hypoplasia of aorta	Secundum ASD	Alive, Follow-up
37	Maternal SLE	Normal	Alive

ASD atrial septal defect, *ASP* aneurysmatic septum primum, *VSD* ventricular septal defect, *ASA* atrial septal aneurysm, *HIF* hyperechogenic intracardiac focus, *SLE* systemic lupus erythematosus

within the first 3 months of postnatal life in 87.5% of cases. However, the persistence of ASA may be associated with some morbidities. Atrial septal defects, account for the second most common congenital heart malformation and, have a worldwide prevalence of 1.65 per 1000 live births [18]. Ostermayer et al. [19] in their retrospective study reported that 9.2% of transcatheter secundum atrial septal defect closure cases were associated with an atrial septal aneurysm. In our results, we found that secundum ASD in 20.8% of fetuses with ASP. This high rate may be secondary to retraction of the aneurysmal valve and/or to atrial dilatation causing stretching of the muscular rim which causes the flap valve to bow into the atrial chambers, decreasing the overlap.

Carerj et al. evaluated the prevalence of atrial septal aneurysm in patients with migraine. They found that the prevalence of isolated atrial septal aneurysm was higher in patients with migraine with aura (28.5%) than in patients with migraine without aura (3.6%) ($P < .005$) or in control subjects (1.9%) [20]. Some fetuses with aneurysmal septum primum can develop a restrictive foramen ovale in intrauterine life. Uzun et al. analyzed the clinical outcomes of all fetuses with restrictive foramen ovale. Restrictive foramen ovale was identified in 23 of 1682 (1.4%) fetuses with no congenital heart disease. They reported that 91% of the cases were with hypermobile or redundant primum atrial septum [21].

There are some reports that emphasize an association between PFO and cryptogenic stroke (OR 2.9) especially in young adults (< 55 years of age), which in some studies was higher among patients with an associated atrial septal aneurysm > 10 mm or a large right-to-left shunt [6]. Di Tullio et al. [22] sought to assess the risk of ischemic stroke from a PFO in a multiethnic prospective cohort; their results showed that PFO was not found to be significantly associated with stroke and that the coexistence of PFO and atrial septal aneurysm did not increase the stroke risk but isolated atrial septal aneurysm was associated with elevated stroke incidence.

The main limitations of this study are that it is retrospective and it has a small sample size with a short follow up period. Given the study design, no postnatal long-term echocardiographic data were available. Prospective studies on an unselected cohort would be required to confirm the true incidence and postnatal long-term outcomes of ASP.

Conclusion

Aneurysmal septum primum in fetal life may persist and show an increase in the frequency of secundum ASD after birth. The cases who are diagnosed in fetal life should be followed by a pediatric cardiologist in postnatal life.

Author Contributions All authors contributed to the study conception and design. Conceptualization: AO and FO methodology; AO, FO, and RM material preparation, data collection and analysis; AO, RD, EAD, RM, and FO the first draft of the manuscript was written by AO and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This retrospective study is in accordance with the ethical standards of the institution and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Research Involving with Humans and Animals Rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent The need for informed consent was waived by the IRB.

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