

## CASE REPORT

# Atrial septal defect can be easily missed in chromosome 18q deletion syndrome

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## Abstract

The frequency of 18q– is estimated to be approximately 1/40 000 live births and is more commonly associated with certain clinical features including short stature, intellectual disability and malformations of many major organ systems. Congenital cardiac abnormalities are present in 24–36% of cases and screening can prove difficult. A 28-year-old Caucasian female with a history of long arm chromosome 18q deletion was evaluated for persistent dyspnea and decreased activity level. Multiple hospitalizations failed to identify the etiology of her symptoms. Initial transthoracic echocardiogram failed to show any underlying cardiac etiology of her symptoms. Multiple recurrent hospitalizations with the same chief complaint. A transesophageal echo (TEE) showed large secundum atrial septal defect (ASD). Successful surgical closure of her large secundum ASD provided significant symptoms relief. The threshold of obtaining TEE should be low in patients with 18q– which permits early recognition and treatment of underlying structural heart disease.

## INTRODUCTION

Chromosomal 18 long arm deletion or (18q–) syndromes were first described in 1964 [1]. Since the advent of more refined techniques in the field of molecular genetics, it has been observed that 18q– is actually made up of a vast array of chromosomal microdeletions, involving many different locations of the chromosome, and displaying a wide variety of clinical phenotypes [2, 3]. The frequency of 18q– is estimated to be ~1/40 000 live births and is more commonly associated with certain clinical features including short stature, intellectual disability, congenital aural atresia, abnormalities of the feet, as well as malformations of many major organ systems [4].

Congenital cardiac abnormalities are present in 24–36% of cases, and can include a range of malformations, including

Ebstein anomaly, Wolff-Parkinson-White, as well as other valvular and septal defects [5]. The most commonly described malformations are pulmonary valve anomalies and atrial septal defects. Given the relative frequency of congenital cardiac malformations in these patients, it is important to carefully evaluate with physical exam, ECG and echocardiography. However, screening can prove difficult, with cardiac symptoms may be overlooked given that patients are developmentally delayed; and it has been previously demonstrated that prenatal ultrasound can possibly give undue reassurance, by revealing no abnormalities [6].

## OUR CASE

A 28-year-old Caucasian female with a history of long arm chromosome 18q deletion was evaluated for persistent dyspnea

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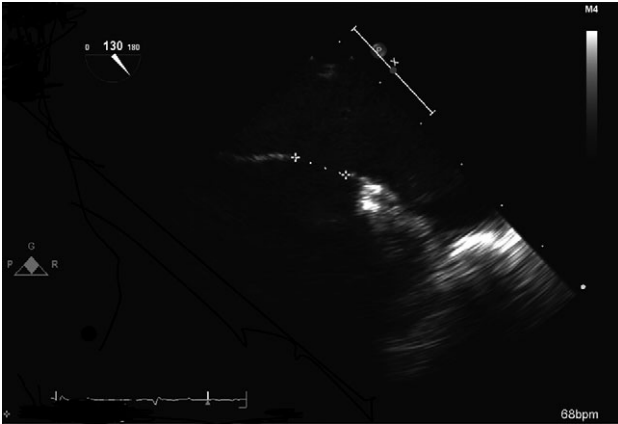


Figure 1: (2D) Transesophageal echocardiogram showing ostium secundum ASD, note the ASD borders between the two small (+) marks

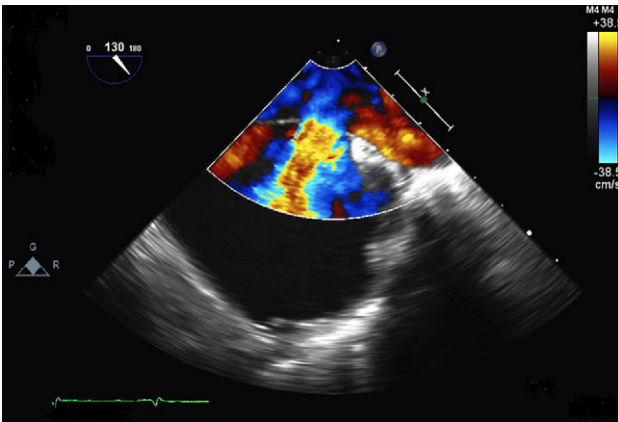


Figure 2: (2D) Transesophageal echocardiogram doppler showing left to right shunt across ASD. The blue jet indicates the flow direction from the left to right

and decrease activity level. Multiple hospitalizations failed to identify the etiology of her symptoms. Initial transthoracic echocardiogram (TTE) showed normal left ventricle (LV) size and function with estimated ejection fraction (EF) of 60%. Right ventricle (RV) was moderately enlarged with normal RV function. Right atrium (RA) was moderately enlarged, and there was moderate tricuspid regurgitation (TR).

Multiple recurrent hospitalizations with the same chief complaint and repeated TTE showed the same findings. The patient was then referred to a cardiologist for further evaluation and transesophageal echocardiogram (TEE) was ordered which showed severely enlarged RA and a large secundum atrial septal defect (ASD) that appears to be sigmoid shaped. The longitudinal diameter of this defect was 1.4 cm, the maximum width was 1.71 cm, the maximum width across the body of the ASD was 1.04 cm, there was a large left-to-right shunt by Doppler examination, and the overall area of the ASD was 1.25 cm<sup>2</sup>.

Initial attempt with transcatheter closure was not successful, and intraoperative findings included TEE and sizing balloon of the atrial septal defect demonstrated larger size than initially seen on TEE with measurement of up to 28 mm during balloon inflation with stoppage of flow, and this was felt to be too large to accommodate the transcatheter septal occluder and therefore anatomy was not suitable to proceed with transcatheter closure.

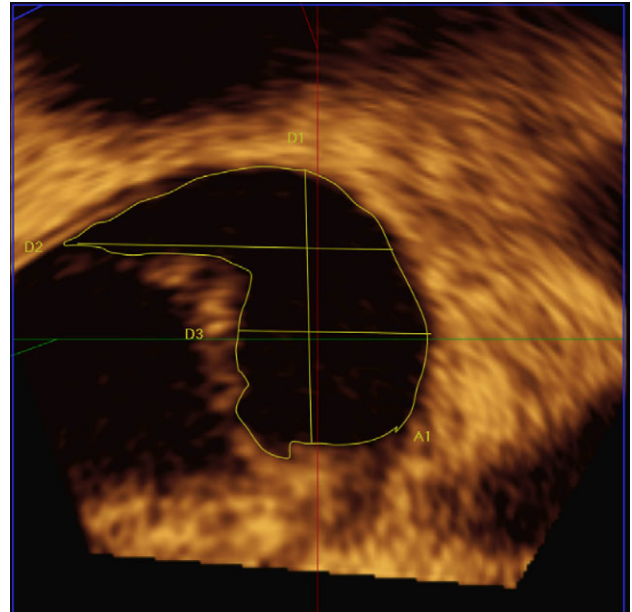


Figure 3: (3D) Transesophageal echocardiogram showing L-shaped ASD, note the letters D1, D2, D3 and A1 define the ASD borders

The patient then underwent a successful surgical closure of her large secundum ASD high near SVC with no residual shunt. The patient recovered completely after the surgery and her activity level was back to normal (Figs 1–3).

## DISCUSSION

Chromosome 18 deletion has been associated with congenital heart disease, common cardiac abnormalities related to chromosome 18q– are atrial septal defect, ventricular septal defect, pulmonary stenosis, total anomalous pulmonary venous return and anomalies coronary artery [4].

Symptomatic ostium secundum ASD tend to be more common in adults who are more prone to develop chronic right atrial dilatation resulting in atrial flutter and fibrillation, aside from respiratory distress, which demonstrates the importance of early detection and treatment [7]. ASD closure had shown benefit in the setting of symptoms or left to right shunt [8].

TEE has been proven to be more superior than TTE in detecting intracardiac shunts, and that's attributed to the ability of the TEE to better visualize the interatrial septum [9].

Jannine *et al.* [4] reported the association between chromosome 18q– and ASD, although there was no specification of the ASD type and symptoms. Transcatheter approach using Amplatzer device serves as a safe and effective treatment for ASD closure with mean ASD diameter 19.5 ± 5.5 mm [10]. Our case represents a symptomatic ostium secundum ASD that was not detected in multiple TEE, which led to continuous patient's suffering and recurrent hospitalizations. TEE was the diagnostic method of choice to diagnose the underlying disease for the symptoms of our patient.

The L-shaped ASD and the large size made the surgical options as the treatment of choice as comparison with the percutaneous transseptal approach.

## CONCLUSION

The threshold of obtaining TEE should be low in patients with 18q– which permits early recognition and treatment of

underlying structural heart disease. The known association between chromosome 18q deletion and ASD justify the early use of TEE in the diagnostic work up of the patients' symptoms.

### CONFLICT OF INTEREST STATEMENT

None declared.

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No funding was received to publish this case report.

### ETHICAL APPROVAL

IRB approval was given by IRB Review Committee of United Health Services Hospitals UHSH.

### REFERENCES

1. De Grouchy J, Royer P, Salmon C, Lamy M. Deletion partielle du bras longs du chromosome 18. *Path Biol (Paris)* 1964;12:579–82.
2. Feenstra I, Vissers LE, Orsel M, van Kessel AG, Brunner HG, Veltman JA, et al. Genotype-phenotype mapping of chromosome 18q deletions by high-resolution array CGH: an update of the phenotypic map. *Am J Med Genet* 2007;143A:1858–67.
3. Cody JD, Hasi M, Soileau B, Heard Patricia, Erika Carter, Courtney Sebold, et al. Establishing a reference group for distal 18q-: clinical description and molecular basis. *Hum Genet* 2014;133:199–209.
4. Cody JD, Ghidoni PD, DuPont BR, Hale DE, Hilsenbeck SG, Stratton RF, et al. Congenital anomalies and anthropometry of 42 individuals with deletions of chromosome 18q. *Am J Med Genet* 1999;85:455–62.
5. Van Trier DC, Feenstra I, Bot P, de Leeuw N, Draaisma JM. Cardiac anomalies in individuals with the 18q deletion syndrome; report of a child with Ebstein anomaly and review of the literature. *Eur J Med Genet* 2013;56:426–31.
6. Shen O, Yagel S. Prenatal sonographic findings in chromosome 18q deletion syndrome. *Ultrasound Obstet Gynecol* 2010;36:201.
7. Kuijpers JM, Mulder BJM, Bouma BJ. Secundum atrial septal defect in adults: a practical review and recent developments. *Neth Heart J* 2015;23:205–11.
8. Gatzoulis MA, Redington AN, Somerville J, Shore DF. Should atrial septal defect in adults be close? *Ann Thorac Surg* 1996;61:657–9.
9. De Bruijn SF, Agema WR, Lammers GJ, van der Wall EE, Wolterbeek R, Holman ER, et al. Transesophageal echocardiography is superior to transthoracic echocardiography in management of patients of any age with transient ischemic attack or stroke. *Stroke* 2016;37:2531–4.
10. Behjati M, Mirhosseini SJ, Hosseini SH, Rajaei S. Transcatheter closure of atrial septal defect with amplatzer device in children and adolescents: short and midterm results; an Iranian experience. *Iran J Ped* 2011;21:166–72.