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CASE REPORT

ADVANCED

CLINICAL CASE

2 Cases of Spontaneous Coronary Artery Dissection in Neonates

Sunakshi Bassi, MD, MHS,[a] Addison Gearhart, MD,[a,b] Stephen P. Sanders, MD,[a,c] Chrystalle Katte Carreon, MD,[c,d] Brian Quinn, MD,[a,b] Christina VanderPluym, MD,[a,b] Rebecca S. Beroukhim, MD[a,b]

ABSTRACT

Spontaneous coronary artery dissection in infants is a rare phenomenon. We present 2 neonates with severe ventricular dysfunction due to coronary artery dissection. Neither patient had evidence of extracardiac fibromuscular dysplasia or other comorbidities that would explain the presentation. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2023;6:101704) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

CASE 1

PRESENTATION. A term female infant, born to a 29-year-old G1P0 mother, presented with cyanosis 12 hours after an uncomplicated delivery. The mother had been adequately treated with levothyroxine for hypothyroidism. Prenatal imaging, maternal cell-free DNA testing, and pregnancy history were unremarkable. The infant was resuscitated with intubation and prostaglandin and epinephrine infusions, and transferred to our center.

LEARNING OBJECTIVES

- To understand that neonatal SCAD is a rare entity associated with significant morbidity and mortality.
- To form a differential diagnosis for ventricular failure in neonates, particularly in those with a pattern of ventricular dominance, and to consider SCAD as a diagnostic possibility.

INVESTIGATIONS AND MANAGEMENT. Echocardiography demonstrated severe right ventricular (RV) systolic dysfunction, absent flow through the pulmonary valve, and exclusive right-to-left shunting across the foramen ovale with preserved left ventricular function (Video 1). Her venous blood gas was notable for profound metabolic acidosis (pH 7.07, CO_2 35 mm Hg, and lactate >12.5 mmol/L [normal: 0.5-2.2 mmol/L]).

She developed an unstable ventricular tachycardia, which progressed to asystolic cardiac arrest prompting extracorporeal membrane oxygenation (ECMO) support. Cardiac catheterization revealed proximal/middle right coronary artery (RCA) stenosis with a linear filling defect and false lumen consistent with a type 1 coronary dissection at the origin of the anterior marginal branch (Video 2). The RCA was hypodominant with a small thready left coronary artery (LCA). Notably, there was preserved coronary blood flow distal to the lesion.

Whole-exome sequencing revealed a heterozygous, maternally inherited variant of uncertain significance

From the [a]Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA; [b]Department of Cardiology, Boston Children's Hospital, Boston, Massachusetts, USA; [c]Cardiac Registry, Departments of Cardiology, Pathology, and Cardiac Surgery, Boston Children's Hospital, Boston, Massachusetts, USA; and the [d]Department of Pathology, Boston Children's Hospital and Harvard Medical School, Boston Children's Hospital, Boston, Massachusetts, USA.

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ABBREVIATIONS AND ACRONYMS

ACTN2 = alpha-actinin 2

ECMO = extracorporeal membrane oxygenation

FMD = fibromuscular dysplasia

LAD = left anterior descending artery

LCA = left coronary artery

LV = left ventricular

MCA = middle cerebral artery

PCA = posterior cerebral artery

RCA = right coronary artery

RV = right ventricular

SCAD = spontaneous coronary artery dissection

SVT = supraventricular tachycardia

in the alpha-actinin 2 gene (*ACTN2*). After the variant was discovered to be maternally inherited, the patient's mother underwent a cardiac workup, with normal echocardiography. The patient's father did not harbor the variant.

FOLLOW-UP. The patient was decannulated from ECMO at 8 days and discharged at 6 weeks with fully recovered RV systolic function. Repeated catheterization at 6 months showed a persistent dissection of the mid-RCA with robust flow into the distal branches (Video 3). According to cardiac magnetic resonance imaging, the inferior and inferoseptal walls of the LV from base to apex were hypokinetic, with corresponding subendocardial and transmural late gadolinium enhancement, and borderline depressed LV function (ejection fraction 53%) (Video 4). The RV systolic function had normalized with no regional wall motion abnormalities. At 10 months, the patient was clinically well with normal growth and development.

CASE 2

HISTORY OF PRESENTATION. A newborn girl, born to a 36-year-old G4P3 mother, with a late prenatal diagnosis of fetal supraventricular tachycardia (SVT) was emergency delivered via cesarean section at 36 weeks of gestation owing to fetal decelerations. She emerged limp, apneic, and bradycardic, and received 18 minutes of cardiopulmonary resuscitation. Echocardiography demonstrated normal anatomy with severe biventricular dysfunction (Video 5) and a small pericardial effusion. She developed recurrent SVT requiring direct-current cardioversion and procainamide infusion. Because of worsening metabolic acidosis (lactate 14.4 mmol/L) and ventricular dysfunction, she was cannulated to ECMO at 10 hours of life and transferred to our center. Maternal history and prenatal laboratory tests were unremarkable, including negative noninvasive prenatal testing. The patient's siblings were healthy.

INVESTIGATIONS AND MANAGEMENT. The patient underwent balloon atrial septostomy to decompress the left atrium while on ECMO. Coronary angiography revealed a filling defect consistent with a type 1 LCA dissection, extending partially into the left circumflex artery and farther into the left anterior descending artery (LAD) with good distal flow (Video 6). Her 12-day ECMO course was complicated by left middle cerebral artery (MCA) and posterior cerebral artery (PCA) strokes. On subsequent catheterization, the filling defect improved (Video 7) but ventricular function worsened, leading to placement of an LV assist device.

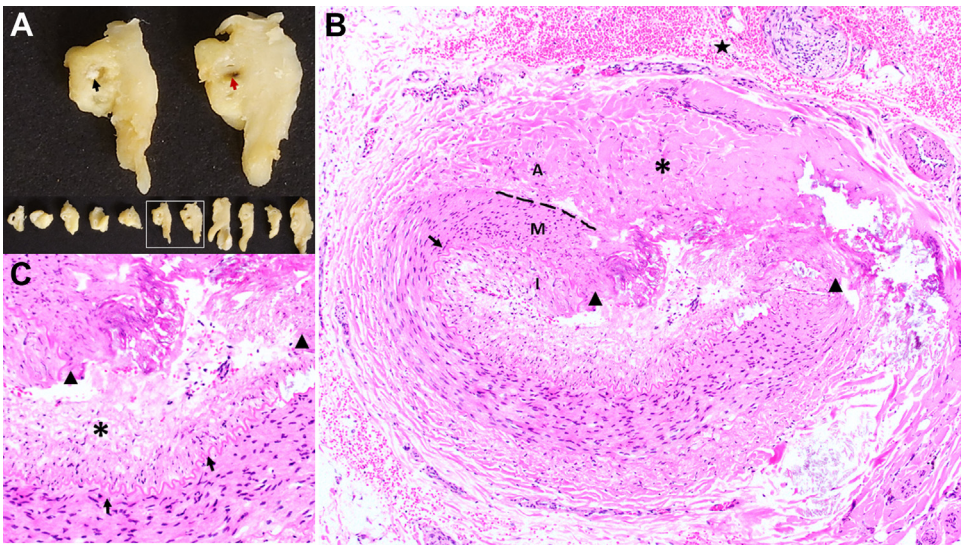
FOLLOW-UP. At 4 months of age, she underwent orthotopic heart transplantation. The proximal LAD sections from the explanted heart showed intimal hyperplasia with disruption of the internal elastic lamina and tunica media. There was prominent adventitial and medial fibrosis in what appeared to be the site of dissection (**Figure 1**). Rapid whole-exome sequencing was negative. Now at 4 years of age, she has mild language and cognitive delay, and she is ambulatory despite right-side hemiparesis and hypertonia.

DISCUSSION

We describe 2 cases of spontaneous coronary artery dissection (SCAD) in neonates. Most cases of coronary artery occlusion reported in the literature have involved the LCA, as in our second case. There are also a few reports that describe isolated RV failure in neonates, as in our first case.[1] Only 1 case of a 5-day old infant with critical aortic stenosis showed RCA occlusion at the mid-segment, likely secondary to in situ thrombus formation in the setting of low cardiac output or atrial arrhythmia.[2] Another case of RV ischemia occurred in a neonate with intermittent occlusion of the RCA by an echogenic mass of unknown etiology.[3] Unlike our cases, those reports described patients with congenital heart disease as the etiology for coronary artery occlusion, rather than dissection. The etiology of ventricular dysfunction in our patients is likely multifactorial: myocardial ischemia from coronary hypoperfusion, unstable arrhythmia (ventricular tachycardia in case 1 and SVT in case 2), and marked associated metabolic acidosis.

The cause of SCAD in our patients remains uncertain. SCAD in adults is often associated with fibromuscular dysplasia (FMD), commonly affecting the renal, cerebral, and carotid arteries.[4] There have been 2 reports of infants with autopsy-confirmed FMD of the coronary arteries. The first was a 1-day-old with LV dysfunction who was found to have concentric collagen accumulation in the media and adventitial layers of the LAD.[5] The second was a 5-month-old in whom both coronary arteries were cord-like and showed luminal narrowing with diffuse thickening through the smooth muscle layer.[6] A 2-day-old infant with tetralogy of Fallot was found to have coronary artery FMD, with the classic "string of beads" appearance, but without histologic confirmation.[7]

FIGURE 1 **Left Anterior Descending Artery (LAD) Pathology**



(A) Macroscopic sections of proximal to mid-LAD (left to right). Left zoomed section demonstrates a focal white fibrous solid area without visible vascular lumen **(black arrow)** and a faint brown area of adjacent hemorrhage. Right zoomed section demonstrates perivascular hemorrhage, represented by a dark brown area underneath the slit-like coronary artery within the epicardial fat **(red arrow)**. **(B)** LAD shows 3 distinct layers: adventitia (A), media (M), and intima (I). Intimal hyperplasia with disruption of internal elastic lamina (**black arrow** points to intact elastic lamina; if traced circumferentially, the disrupted region is between the 2 **triangles**) and tunica media, and prominent adventitial and medial fibrosis **(asterisk)** at the site of injury/dissection, with resultant narrowing of the lumen, are shown. Perivascular hemorrhage **(star)** corresponds to area of hemorrhage in **A**, as the patient was taking aspirin and bivalirudin at time of transplantation. Between the adventitial and medial layers, a plane of separation **(dashed line)** is seen focally with a much larger gap and disruption toward the right side. **(C)** Close-up view of disrupted internal elastic lamina (**arrows** mark intact region; **triangles** mark area of disrupted region) and thickened fibrointima **(asterisk)**.

In our first case, the patient did not have involvement of the renal or cerebral vessels to suggest FMD. Coronary biopsies were not collected for definitive assessment, but the overall appearance in angiography was inconsistent. In case 2, the observed intimal hyperplasia and medial fibrosis suggested FMD, but the patient has had no other evidence of vascular involvement. Cerebral angiography after the MCA/PCA strokes showed no evidence of dissection. To date, there is no evidence of an association between fetal SVT and SCAD, making it less likely that these two events were related. It remains unclear whether the pathologic changes observed in **Figure 1** preceded or followed the dissection.

Interestingly, in the midst of significant diagnostic workup in case 1, a heterozygous mutation of uncertain clinical significance was identified in the *ACTN2* gene. *ACTN2* encodes a protein found only in cardiac muscle.[8] Mutations in *ACTN2* have been associated with a wide variety of phenotypes, including hypertrophic cardiomyopathy, dilated cardiomyopathy, and arrhythmogenic cardiomyopathy.[9] Thus far, no *ACTN2* mutations have been identified in association with SCAD or isolated RV failure.

The persistent dissection at 6 months could be related to the *ACTN2* mutation; however, there is no known association between *ACTN2* mutations and poor wound healing. While there is little information on the expected course and recovery of this disease in neonates, adult studies have shown that hypertension is a risk factor for dissection extension or recurrent SCAD.[10] Our patient, however, had well controlled blood pressures throughout her course. Although her lesion had improved over 6 months, it had not healed within the expected 35 days, as is typically seen in adults. It is unclear why her dissection continues to persist despite adequate mitigation of exacerbating factors such as hypertension.

CONCLUSIONS

SCAD in the neonate is a rare entity associated with significant morbidity and mortality if undetected. We describe 2 cases without convincing evidence of FMD

or other identifiable etiology. In both cases, catheter angiography identified the diagnosis.

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ADDRESS FOR CORRESPONDENCE: Dr Sunakshi Bassi, Department of Pediatrics, Boston Children's Hospital, 300 Longwood Avenue, Boston, Massachusetts 02115, USA. E-mail: sunakshi.bassi@childrens.harvard.edu. Twitter: @addisongearhart.

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KEY WORDS coronary artery, heart failure, spontaneous coronary artery dissection

APPENDIX For supplemental videos, please see the online version of this paper.