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Covid-19 in an infant with systemic to pulmonary artery shunt dependent functionally univentricular physiology

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Abstract

We report a case of two-month old with a functionally univentricular heart and parallel circulation who presented to the emergency department with Covid-19 and subsequently developed acute respiratory distress syndrome. The course of illness, clinical values, and laboratory markers are characterized in this report.

Introduction

The Covid-19 pandemic has impacted millions of individuals. Symptomatic cases have been documented in both adults and children, although children have been documented to be less likely to be symptomatic and require care in an intensive care unit.

As of today, approximately 150 studies have reported approximately 8,000 pediatric cases of Covid-19. A systematic review published in July synthesized the findings from many of these studies. Indeed, some of the children reported to have Covid-19 have been documented to have cardiac disease, but none with functionally univentricular heart disease and parallel circulation (wherein the ascending aortic saturation and pulmonary artery saturations are equal) have been described yet to our knowledge [1-3]. Two cases of those with functionally univentricular hearts have been described but these patients had already undergone Fontan palliation and no longer had parallel circulation [4, 5].

We report a case of an infant with a functionally univentricular heart and parallel circulation who presented to the emergency department with hypoxemia and was found to have Covid-19.

Case Report

A two-month old African-American female with Ebstein anomaly with pulmonary atresia presented to the emergency department with 24-hour history of hypoxemia and irritability. She was initially born full-term with APGAR scores of 9 and 9 and was placed on intravenous prostaglandin until she underwent Starnes procedure with Blalock-Taussig shunt placement

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early as the first step in staged univentricular palliation. Due to the a very small functional right ventricle secondary to significant displacement of the tricuspid valve this patient was not deemed appropriate for biventricular repair. She had kidney disease improve global outcomes (KDIGO) stage 1 acute kidney injury in the immediate postoperative period and had persistent but improving echogenicity of the renal parenchyma at the time of admission. This child was followed closely in the single ventricle clinic at our institution. The child's mother called the clinic, sharing that the child had been irritable and was desaturating into the low 60's by pulse oximetry compared to her usual pulse oximetry in the low 80s. Mom was asked to place the child on nasal cannula oxygen and bring her into the emergency department.

Upon arrival to the emergency department the child was non-toxic appearing and in no distress. The child was otherwise feeding normally with adequate weight gain and had no other symptoms. She was saturating in the mid 80's with nasal cannula oxygen and would desaturate to the 60's when taken off supplemental oxygen. She otherwise was afebrile, had a normal respiratory rate, normal heart rate, and normal blood pressure. Mom did share that the child had been exposed to her aunt, who lives with the patient, who was found to be Covid-19 positive the day before admission. The mother, aunt, and all other household members were asymptomatic.

An echocardiogram demonstrated a patent Blalock-Taussig Shunt, an adequate and unrestrictive interatrial communication, and normal ventricular function. A rapid Covid-19 test was obtained in the emergency department, as per hospital policy for inpatient admissions,

which was negative. A complete blood count demonstrated a white blood cell count of 5.5 (10^3/mcl), a platelet count of 532 (103/mcl), and a hemoglobin of 14.3 (g/dl). The child was then admitted for observation. An additional Covid-19 test was not pursued at the time due to the lack of respiratory symptoms, fever, and a non-concerning chest x-ray.

Cardiac catheterization was performed to investigate shunt obstruction on the third day of admission as the need for nasal cannula oxygen continued without other symptoms. The child was intubated and mechanically ventilated for the procedure. Cardiac catheterization demonstrated a patent Blalock-Taussig-Thomas shunt and otherwise normal hemodynamics. No source for the hypoxemia was found. Due to some cardiorespiratory instability a more thorough hemodynamic and physiologic evaluation were not felt to be safe at the moment. Thus, information such as pulmonary vein saturations could not be obtained. The child was extubated in the catheterization laboratory but had profound desaturation and respiratory distress and was reintubated prior to leaving the catheterization laboratory.

The child was then admitted to the pediatric intensive care unit after the cardiac catheterization. The child had nasogastric feeds restarted and was placed on sedation upon admission to the pediatric cardiac intensive care unit. Synchronized intermittent mechanical ventilation was accomplished using a pressure responsive volume control mode with pressure support. The tidal volume on admission to the pediatric intensive care unit was 25 mLs, a positive end expiratory pressure of 5 cmH_20, and a pressure support of 10 cmH_20. Peak inspiratory pressures ranged from 20 to 22 cmH_20. The child weighed 3.8 kg. Gas exchange on

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these settings was adequate and the pulse oximetry was 78% with a fraction of inspired oxygen set at 60%. Shortly after admission to the pediatric intensive care unit the child began have desaturations into the 60's of percent. The fraction of inspired oxygen was increased to 65% and inhaled nitric oxide was started at 20ppm. Within a few hours the fraction of inspired oxygen had to be increased to 100% as pulse oximetry was in the high 60's to low 70's, consistently.

Fraction of inspired oxygen and inhaled nitric oxide were slowly weaned on the fourth and fifth days of admission and the radiographs remained unremarkable. Ventilator settings remained the same except for the positive end expiratory pressure which was increased to 7 cmH_20. The child had some intermittent episodes of desaturation which would improve with manual bag ventilation via the endotracheal tube. On the fifth day of admission, a chest radiograph demonstrated ground glass opacities in the right upper and left lower lobes (Figure 1). The child also had a temperature of 38.4 degrees Celsius on the fifth day of admission. A repeat infectious workup was conducted and cefepime and vancomycin were empirically started. Due to documented exposure and increased index of suspicion, a repeat Covid-19 test was obtained this day via nasopharyngeal swab and resulted positive on the seventh day of admission. Vancomycin and cefepime were discontinued at this time and the child was started on remdesivir for 10 days and solumedrol for three days.

The sixth day of admission represents the day during which some of the lowest pulse oximetry saturations were noted, the largest alveolar-arteriolar gradient was present, and the

arteriovenous difference was the greatest. Arteriovenous difference was calculated using the pulse oximetry saturation and the simultaneous renal near infrared spectroscopy value.

On the 10th of admission, the child was successfully extubated to noninvasive pressure control ventilation after seven days of mechanical ventilation. On the 12th day of admission, the child was transitioned to high flow nasal cannula and then on the 14th day of admission was transitioned to nasal cannula.

The child was transferred to the general pediatrics ward on the 19th day of admission. On the 22nd day of admission the child developed a fever and had increase in her inflammatory markers. She was found to have bacteremia. This was treated with antibiotics and after completing an appropriate course of antibiotics it was decided that due to her age that the child could be taken to the operating room for a Glenn procedure. She tolerated the Glenn well and was ultimately discharged home on 1/4 liter nasal cannula and sildenafil.

Echocardiograms during the admission demonstrated preserved left ventricular function. There was no significant liver insufficiency during the admission nor any significant coagulopathy. Multisystem inflammatory syndrome in children was not present. The patient did have stage 1 acute kidney injury per (KDIGO) criteria.

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Pertinent lab values and clinical data from the period of the active coronavirus infection are outlined in Table 1. Key lab values and clinical data are presented graphically in Figure 2 to help demonstrate their values relative to one another at corresponding timepoints.

Discussion

This is the first reported case, to our knowledge, of an infant with functionally univentricular heart disease and parallel circulation with symptomatic Covid-19. Two previous cases of those with functionally univentricular hearts have been reported although these patients had already undergone Fontan and no longer had parallel circulation [4, 5]. There are multiple interesting takeaways from this case.

First, infants with functionally univentricular hearts and parallel circulation can get symptomatic Covid-19. Thus, for such infants who present with respiratory symptoms, including isolated hypoxemia, should be evaluated for Covid-19. Due to lack of significant symptoms and this being our first such patient, we did not do a more high-fidelity Covid-19 test immediately after the rapid test was negative nor pursue a computed tomography scan. A diagnosis of Covid-19 would have also led us to not pursue a cardiac catheterization which was not well tolerated.

Second, this report outlines how a child with such physiology may present. In this case the child presented with hypoxemia, a concerning finding in children who are dependent on a Blalock-Taussig-Thomas shunt. Cardiac catheterization demonstrated a patient shunt, and the child was initially not demonstrating any other findings of a viral illness, thus delaying the diagnosis.

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Hypoxemia in children with parallel circulation may be due to systemic venous desaturation (decreased cardiac output, anemia, increased somatic extraction of oxygen), pulmonary venous desaturation (damaged alveoli, impaired alveolar diffusion, ventilation perfusion mismatch), decreased overall cardiac output (hypovolemia, decreased cardiac function), or impaired pulmonary blood flow. With the ongoing pandemic, one must keep Covid-19 in mind as a part of this differential. Covid-19 in this population may lead to hypoxemia by causing pulmonary venous desaturation by impacting gas exchange in acutely ill lungs and causing systemic venous desaturation by causing anemia.

Third, it is interesting to note that this patient did receive a rapid Covid-19 test in the emergency department that was negative. A repeat Covid-19 test resulted positive only a few days later. While it is possible that the patient was not Covid-19 positive when in the emergency department, it is unlikely that the Covid-19 was hospital acquired. There were no known patients admitted to the hospital at the same time who were Covid-19 positive nor were there any healthcare workers known to be Covid-19 positive at the time. Additionally, the history of exposure to a family member with Covid-19 makes this likely. Thus, one should keep in mind that false negatives may occur and if the index of suspicion is high, a repeat Covid-19 test should be obtained.

Fourth, this case characterizes clinical and laboratory values in a child with parallel circulation and Covid-19. Peak illness, clinically, seemed to occur on the sixth day of admission. At this point the alveolar-arterial gradient peaked at 458, the arteriovenous difference peaked at 48,

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pulse oximetry had its lowest recorded values, and the white blood cell count was at its lowest point. Thus, it appears that these markers may be helpful to follow in these patients. The precise mechanism behind the change in arteriovenous difference is unclear but seems to indicate that at peak illness, systemic oxygen delivery was impaired to a significant degree. During recovery, the arteriovenous difference did decrease into the low 20s.

Fifth, remdesivir and steroid therapy was initiated on the seventh day of admission. Values collected in this report for the seventh day were after several hours of both therapies. It is interesting to note that there was marked improvement in several clinical and laboratory values between the sixth and seventh day of admission. It is feasible that the illness was self-limited and naturally following this trajectory, although it is also possible that these therapies helped alter the trajectory of the illness. It is not possible from these data to make any definitive conclusions. Previous studies have demonstrated that remdesivir and steroids are associated with a decrease in length of admission and mortality in those with Covid-19 [6-8].

Sixth, this case report highlights that infants with parallel circulation who get symptomatic Covid-19 can survive to discharge without systemic ventricular dysfunction.

Conclusion

We report the case of an infant with functionally univentricular heart disease and parallel circulation that was diagnosed with Covid-19 after presenting with hypoxemia. The course of illness, clinical values, and laboratory markers during various periods of illness are

characterized. This child required intubation and mechanical ventilation due to acute respiratory distress syndrome but was discharged home.

Figure and Table legends

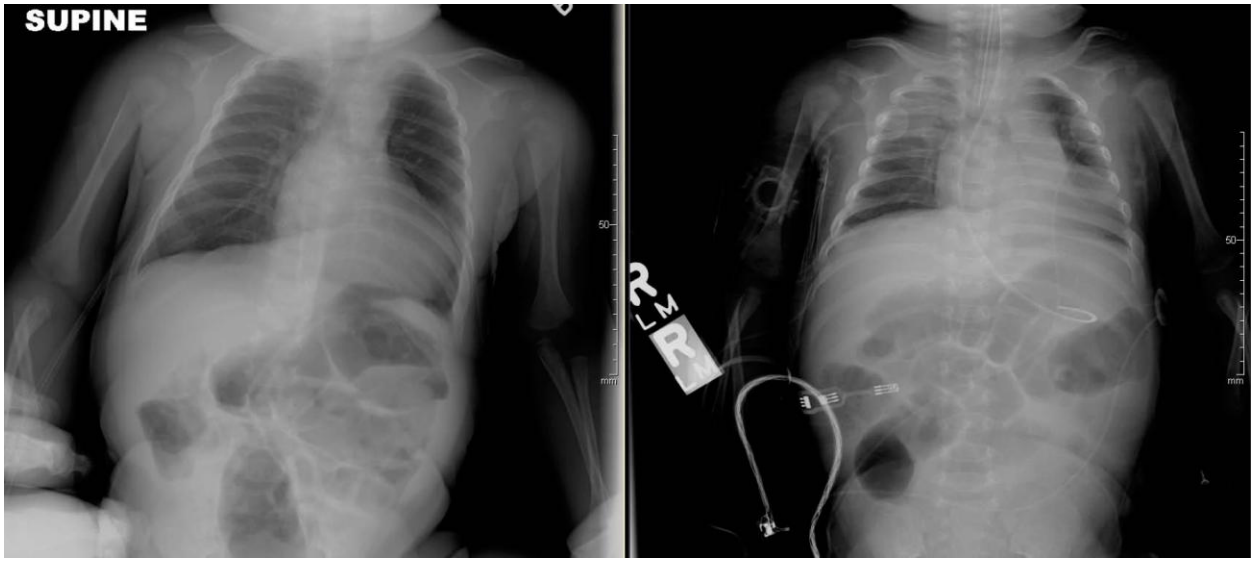

Figure 1. The left panel demonstrates a chest radiograph shortly after admission. No significant pathology is noted. The right panel demonstrates a chest radiograph from the fifth day of admission. Ground-glass opacifications are present in the right upper and left lower lobes.

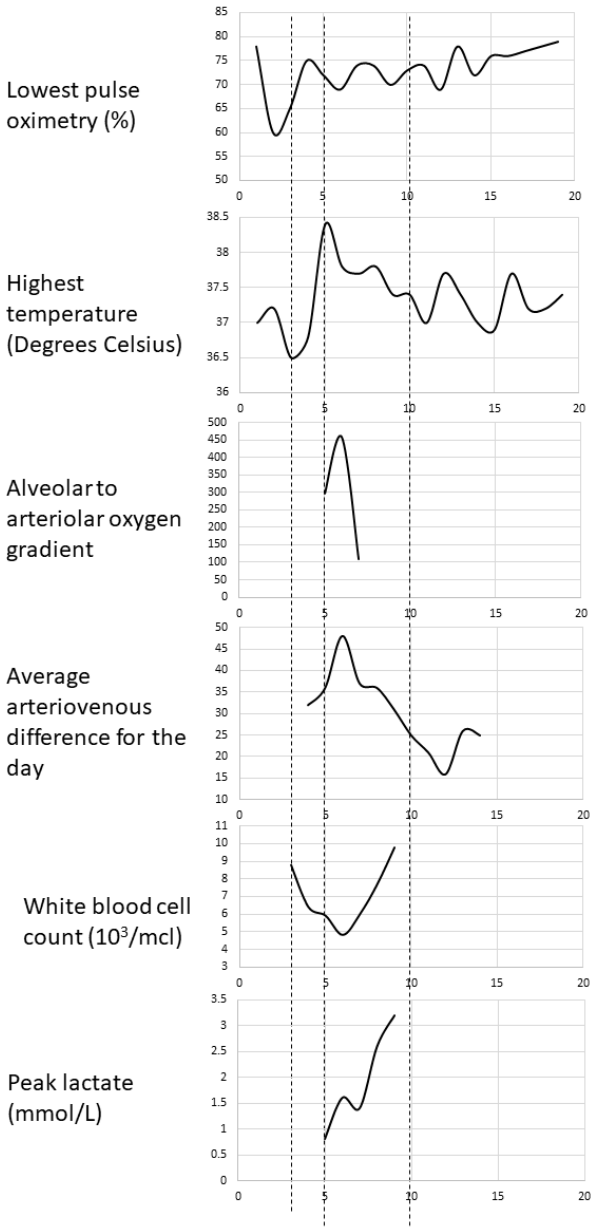

Figure 2. The various panels demonstrate values of clinical parameters and laboratory values during the first 20 days of admission. The day of admission is found on the horizontal axis. Three dashed vertical lines are present. The leftmost dashed line on the third day of admission represents the point at which the cardiac catheterization occurred, the second dashed line on the seventh day of admission represents the time at which the second Covid-19 test resulted positive; the third dashed line on the 10th day of admission represents when extubation occurred.

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Day of admission	Lowest recorded saturation by pulse oximetry (%)	Highest temperature (degrees celsius)	Alveolar-Arteriolar oxygenation gradient (while intubated)	Peak lactate (mmol/L)	Average AVDO2 difference	White blood cell count (x10^3/mcl)	Platelet count (x10^3/mcl)	AST	ALT	Creatinine (mg/dl)	C-reactive protein (mg/dl)	Procalcitonin (ng/ml)	Troponin (ng/ml)
1	78	37											
2	60	37.2											
3	65	36.5	256	2.2		8.8	532	161	46	0.28			
4	75	36.8			32	6.4	316	74	30	0.32			
5	72	38.4	297	0.8	36	5.9	232			0.31			
6	69	37.8	458	1.6	48	4.8	282				1.7	0.07	
7	74	37.7	109	1.4	37			43	17				0.14
8	74	37.8		2.6	36	7.7	329	23	19	0.42		0.05	
9	70	37.4		3.2	31	9.8	406		18	0.26			
10	73	37.4			25			27	19	0.26			
11	74	37			21			38	21	0.29			
12	69	37.7			16			28	20	0.27			
13	78	37.4		1.2	26			25	18	0.32			
14	72	37			25			22	17	0.32			
15	76	36.9						21	19	0.29			
16	76	37.7						26	17	0.36			
17	77	37.2											
18	78	37.2											
19	79	37.4											
20													

AVDO2- arteriovenous oxygen difference, AST- aspartate aminotransferase, ALT- alanine aminotransferase