COVID-19 pneumonia, pulmonary hypertension, and a patent ductus arteriosus:

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**Background:** Severe Novel Coronavirus Disease 2019 (COVID-19) infection in neonates is possible but reports are scarce. Ultrasound has been reported useful for triaging, diagnosing, and monitoring of patients with COVID-19.

**BW & Birth GA:**

A 3,140-g male infant was born at 40.3 weeks’ gestation to a 20-year-old gravida woman with history of type 1 diabetes mellitus in control with insulin. The pregnancy had irregular follow up with normal second and third trimester fetal ultrasound. On the day of delivery during labor fetal heart rate late decelerations to 60 beats per min were noted so an emergent cesarean section was planned.

**Birth History:**

During resuscitation, no late cord clamping was performed, and supplemental oxygen was needed. Apgar scores were 8-9 at 1 and 5 minutes. Oxygen was stopped at minute 16. Silverman Andersen score was one with discrete nasal flaring. No skin-to-skin contact was performed (mother with general anesthesia).

**Medical History:**

After transition, desaturation occurred so oxygen hood with 30% FiO₂ was applied. Respiratory distress progressed and required high flow nasal cannula on day 2, CPAP on day 3 and was intubated on day 4 secondary to CPAP failure (Silverman Andresen score of 4, FiO₂ ≥ 40%, hypoxemia and hypercapnia) with AC(VG) (5.8ml/kg), 30% FiO₂. Real time RT-PCR (RT-PCR) from respiratory tract swabs for SARS COV 2 (sampled on day 3) were positive for the baby and both parents. Posterior analysis of the placenta showed chronic fetal vascular under perfusion and inflammation. RT-PCR determination by disruption of the tissue through mechanical lysis was carried out and positive amplification of viral E gene was found (ct 30).

An echocardiogram by Pediatric Cardiology was performed finding moderate to severe pulmonary hypertension with right ventricular dilatation. Mild tricuspid and mitral regurgitation were noted. A 6 mm bidirectional patent ductus arteriosus (PDA) was noted with a caution note to evaluate the aortic arch once the PDA closes. The baby was transferred to a COVID-19 third level referral hospital.

**X ray Findings**

On chest radiography important cardiomegaly and bilateral ground-glass opacities were noted.

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**Key physiological insight/learning points:**

Ventilation with supplemental oxygen is the foundation of management in newborns with pulmonary hypertension. LUS helps assessing pulmonary status and guide management.

Aortic arch appraisal in the presence of a large PDA is difficult and some indices like the carotid-subclavian index are useful.

Although normally a PDA in the context of pulmonary hypertension closes on its own in some inflammatory states the closing mechanisms might fail leaving a patent (and then prolonged) ductus arteriosus.
Relevant Labs:

Admission laboratory exams showed lymphocytic predominance with mild thrombocytopenia with normal coagulation times (Table 1).

Table 1.

<table>
<thead>
<tr>
<th>Examination</th>
<th>Result</th>
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<tbody>
<tr>
<td>WBC (x10^9/L)</td>
<td>11.3</td>
</tr>
<tr>
<td>L% (%)</td>
<td>51</td>
</tr>
<tr>
<td>PLT (x10^9/L)</td>
<td>105</td>
</tr>
<tr>
<td>Hb (g/L)</td>
<td>160</td>
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<tr>
<td>CRP (mg/L)</td>
<td>&lt;0.5</td>
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<tr>
<td>ALT (U/L)</td>
<td>17</td>
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<tr>
<td>AST (U/L)</td>
<td>49</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>1.42</td>
</tr>
<tr>
<td>sCr (µmol/L)</td>
<td>36</td>
</tr>
<tr>
<td>CK-MB (U/L)</td>
<td>80</td>
</tr>
<tr>
<td>PT (s)</td>
<td>12.1</td>
</tr>
<tr>
<td>APTT (s)</td>
<td>21</td>
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</tbody>
</table>

| WBC, white blood cell; L%, percentage of Lymphocyte; PLT, Platelet count; Hb, hemoglobin; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea Nitrogen; sCr, serum creatinine; CK-MB, creatine kinase-MB; PT, prothrombin time; APTT, activated partial thromboplastin time. |

Important vitals

Heart rate 160, Blood pressure: right arm 64/42, right leg 49/35, left arm 52/36, left leg 50/35.

Hemodynamic Consultation:

Upon arrival (day 5) portable LUS (Konted™, Beijing China, Linear 10.0MHz) showed an irregular pleural line (shred sign), multiple confluent B-lines and bilateral ≥ 0.5 cm consolidations (Figure 1). Prone positioning and increased PEEP 6-8 allowed FiO2 to be lowered from 45 to 28%. As oxygen was weaned after respiratory maneuvers, and no blood pressure gradient was found, echocardiography was postponed. On day 9 of life the neonatal intensive care unit ultrasound equipment (Vivid™ E90, GE Medical Systems, Milwaukee, WI, USA) was prepared according to the Canadian Association of Emergency Physicians¹ and Pediatric cardiology confirmed a normal aortic arch with a carotid-subclavian index of 2.3².

Targeted Neonatal Echocardiography (TnE) reported mild to moderate pulmonary hypertension (Flat septum on systole, pulmonary vascular resistance index of 3.4) with a 2.3 mm restrictive left to right PDA with normal RV function (TAPSE 10.4 mm, fractional area change of 48% and right ventricular output of 201 ml/kg/min) though with dilation. LV was dilated as well (LA/Ao 2.4 and right ventricular end diastolic dimension Z-score of 3.3) with normal function (Simpsons biplane of 57% and left ventricular output of 249 ml/kg/min). Portable LUS showed improvement without big consolidations detectable, still irregular pleural line and less confluent B-lines. Cranial Ultrasound was normal.

Follow up:

The infant was kept in an incubator, no antibiotics were used. Blood cultures were negative. Mechanical ventilation occurred for 6 days, then 3 days of CPAP and 3 days of supplemental oxygen. Biventricular dilatation was managed with diuretics. At day 20, TnE examination reported a 1.9 mm non hemodynamically significant restrictive PDA with improvement of biventricular dilatation and a normal LUS (Figure 2). Baby was discharged at day 26 to an uninfected family member younger than 60 years without co-morbidities.

The baby was lost on follow up during the first two peaks of the pandemic. At one year of age the baby appeared on follow up clinic with moderate malnutrition, a medium pitched high-grade continuous murmur at the pulmonic...
position, cardiomegaly on chest radiography and history of frequent upper airway infections and cough. Cardiology confirmed a patent ductus arteriosus and programed the child for device closure (Figure 3).

Figure 1. Radiologic and ultrasonographic findings on admission. A. 6 mm PDA; B. Pulsed doppler showing bidirectional, right to left on systole flow; C. Right ventricular dilatation; D. Flat interventricular septum on systole; E. (longitudinal view) – F. (transverse view); Posterior right LUS scan showing shred sign and subpleural consolidation (thick arrows); G. Chest radiography with cardiomegaly and ground-glass opacities; H. (longitudinal view) – I. (transverse view): Posterior left LUS scan showing shred sign, subpleural consolidation and confluent B-lines (thin arrows).

Figure 2. Radiologic and ultrasonographic findings prior to discharge. A. 1.9 mm PDA; B. Continuous doppler showing left to right restrictive left to right flow; C. Improvement of biventricular dilatation; D. Round interventricular septum on systole; E. (longitudinal view) normal LUS; F. carotid-subclavian index (b/a) of 2.3G. (transverse view): normal LUS.

Figure 3. Chest radiography at one year of age with cardiomegaly and venocapillary congestion.

Discussion

Case reports or comparative studies on SARS-CoV-2 neonatal infection are limited. In our case, the baby had respiratory distress shortly after birth and RT PCR was positive on day 3 with both asymptomatic parents being positive as well. Zeng and colleagues reported the outcome of 3 neonates born to mothers with COVID-19 finding despite implementing strict infection control measures 3 neonates (9%) presented with early onset SARS-CoV-2 infection. Transplacental transmission is feasible as virions invading syncytiotrophoblast in placental villi have been documented by electron microscopy. Additionally, Vivanti and colleagues demonstrated a case of transplacental transmission of SARS-CoV-2 from a pregnant woman affected during late pregnancy with her offspring being positive and showing gliosis of the deep white periventricular and subcortical matter. According to the classification system and case definition proposed by Shah and colleagues this case was possibly acquired either intrapartum or vertically.
No specific clinical finding has been described in newborns, but severe neonatal infections are possible.

In our patient expected cardiac (major cardiac anomaly, obstructive septal hypertrophic obstructive cardiomyopathy) and pulmonary (surfactant consumption) complications associated with uncontrolled diabetes were not present. Our patient developed pneumonia that required mechanical ventilation with findings consistent with the reported literature: consolidations, interstitial B Line pattern, and confluent B-lines; with an improvement after ventilatory management with consolidations gradually disappearing and B-lines pattern progressive reduction.

Ventilation with supplemental oxygen is the foundation of management in newborns with pulmonary hypertension\(^8\). In our case COVID pneumonia was diagnosed based on a positive RT-PCR, lymphocytic predominance on blood count, negative CRP (and posterior negative blood culture) and LUS described characteristics. As oxygenation secondary to parenchymal disease improved with optimal PEEP and pronation no further medication was necessary and no antibiotics were used. TnE demonstrated biventricular dilation with normal biventricular function, and managed with diuretics.

In the setting of a large PDA the need to evaluate the aortic arch from the referral Cardiologist was noted. As ductal tissue extending into the aortic wall is widely accepted as one important mechanism for coarctation\(^7\) and its challenging to diagnose it with a large patent ductus arteriosus, the carotid-subclavian index was calculated. Peng and colleagues demonstrated that less than 0.85 has a sensitivity of 0.83 and specificity of 0.86 with an area under the curve of 0.91 for coarctation\(^3\).

Other RNA virus related to tubular PDA is congenital rubella\(^9\). In this case where vertical transmission was a possibility it is interesting to consider an inflammatory state that interfered with the mechanisms of ductal closure leading to persistent patent ductus arteriosus that required device closure. As the patient was lost on follow up prolonged exposure to the PDA shunt leads to increased pulmonary vascular resistance and vascular remodeling that although it was a term newborn created a chronic lung disease phenotype with suboptimal growth, frequent upper respiratory episodes and chronic cough\(^10\).

REFERENCES:

Case Report


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