Bilateral Neonatal Adrenal Hemorrhage Associated With Severe Maternal COVID-19 Infection

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Abstract

Adrenal hemorrhage is the most common cause of adrenal mass in newborns. We present a case of a full-term male, born by cesarean section due to acute fetal distress from a mother with severe coronavirus disease 2019 (COVID-19) infection. He was diagnosed with hypoxic-ischemic encephalopathy, multifactorial shock, and early neonatal sepsis. On the seventh day of hospitalization, hemoglobin dropped and thus blood transfusion was required, and abdominal ultrasound showed bilateral adrenal hemorrhage. He developed relative adrenal insufficiency without either hemodynamic instability or electrolyte imbalances. The use of parenteral corticosteroids was not required. Follow-up ultrasonography and adrenal axis laboratory examination revealed complete resolution of adrenal hemorrhage. Neonatal adrenal hemorrhage has a wide variety of clinical manifestations. Ultrasound is preferred for both initial screening and follow-up evaluation. Adrenal insufficiency occurs rarely in neonatal adrenal hemorrhage. Treatment is usually conservative. We emphasize the importance of a timely diagnosis and clinical follow-up of adrenal hemorrhage in neonates with fetal distress born from mothers with severe COVID-19.

Introduction

Adrenal glands are relatively larger and more vascular early in life than in adulthood [1-2]. It generates greater vulnerability to mechanical compression and greater sensitivity to changes in venous pressure and redistribution of blood flow in cases of hypoxia [2]. Adrenal hemorrhage (AH) is more frequent in the neonatal period, it is currently considered the most common cause of adrenal mass in this age group [3-4]. Its incidence ranges between 1.7 and 3 cases per 1000 live births [1,3,5]; however, this value could be higher (16-29 per 1000 live births) since they are mostly asymptomatic [6].

AH is frequently seen in male neonates, 90% of cases are unilateral [1]. Clinical manifestations are variable although they are often absent, when symptomatic patients present with jaundice, ischemia, palpable abdominal mass, and anemia, in severe cases adrenal insufficiency (AI), hypovolemic shock, and even death may occur [2,4-5]. Development of adrenal insufficiency is rare since 10% of functional adrenal tissue produces enough amount of cortisol to meet the body’s needs [3,5]. It explains why most patients do not require treatment, and the process is usually self-limited with complete resolution within 20 and 165 days of life [2-3]. Even in cases where adrenal insufficiency developed and treatment is needed, complete resolution is achieved [3].

Adrenal hemorrhage in neonates has several risk factors, such as hypoxia, birth asphyxia, coagulation disorders, traumatic delivery, bacterial sepsis, and coronavirus disease 2019 (COVID-19) might be a new risk factor [2]. COVID-19 increases the rate of premature birth, fetal distress, and neonatal respiratory distress syndrome, these factors may contribute to the development of AH [7].

In this manuscript, we present the case of a newborn with a bilateral adrenal hemorrhage who developed relative adrenal insufficiency and whose mother had a severe COVID-19 infection.

Case Presentation

A male infant was born at 39 weeks of gestation from a 31-year-old mother with three antenatal check-ups during pregnancy. She presented to a primary care clinic with shortness of breath; her oxygen saturation was 90% on room exam. She tested immunoglobulin M (IgM)/IgG positive for severe acute respiratory...
syndrome coronavirus 2 (SARS-CoV-2) in an immunochromatography test; severe COVID-19 was diagnosed. Fetal ultrasonography revealed signs of fetal distress, thus an emergency cesarean section was performed. The neonate had adequate weight and height, Apgar scores were 3-6-7 at the first, fifth, and tenth minutes, respectively. He had marked respiratory distress nine hours after delivery. The patient was intubated and referred to a higher-level hospital.

On admission patient’s vital signs were as follow: blood pressure 75/49 mmHg, heart rate 130 beats per minute (bpm); respiratory rate 70 cycles per minute, body temperature 36.7 Celsius degrees, and oxygen saturation 96%, on oxygen fraction of 40% with a peak inspiratory pressure in 16 cm of water and positive pressure at the end of expiration (PEEP) in 5 cm of water. On physical exam, the patient was found stuporous, pale, with distal coldness, capillary filling equal to 3 seconds, perioral cyanosis, and presence of blood in the orogastric tube. On respiratory exam, an irregular respiratory pattern was observed and decreased breath sound bilaterally. Abdominal sounds were diminished and signs of inflammation around the umbilical stump were found. Pupils were miotic; there was little response to stimuli, hypotonia, no sucking reflex, and neither palmar nor plantar grasp were found.

Laboratory examination, blood cultures, arterial blood gas analysis (ABGA) (Table 1), and RT-PCR (real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2(severe acute respiratory syndrome coronavirus 2) infection were obtained. ABGA revealed metabolic acidosis, hypoglycemia, hyponatremia, and hypocalcemia. RT-PCR for SARS-CoV-2 was negative. Due to laboratory findings and physical exam hypoxic-ischemic encephalopathy and multifactorial shock, early neonatal sepsis was diagnosed. He was started on 3% sodium chloride, 10% dextrose, dopamine 8 ug/Kg/min, dobutamine 8 ug/Kg/min, sodium bicarbonate, calcium gluconate, phytomenadione, fresh frozen plasma, meropenem 80 mg intravenous every eight hours, and vancomycin 60 mg intravenous every eight due to abrupt clinical deterioration.

During hospitalization, the patient had subtle tonic seizures, a transfontanellar ultrasound showed signs of cerebral edema, therefore phenobarbital and subsequently levetiracetam were initiated due to a suboptimal response. On the seventh day of hospitalization, hemoglobin dropped up to 11 g/dl, which prompted blood transfusion. An abdominal ultrasound revealed on the right adrenal gland, a heterogeneous and hypoechoic encapsulated lesion, measuring 41 x 22 x 40 mm, with a volume of 21 ml; on the left adrenal region, another lesion with similar characteristics, measuring 40 x 17 x 30 mm, with a volume of 11 ml. AH was suspected thus abdominal contrast tomography was taken (Figure 1), which revealed a retroperitoneal hypodense collection on both adrenal glands, confirming the diagnosis of bilateral adrenal hemorrhage.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count on admission</td>
<td>Leucocytes: 18,000 cells per microliter (segmented neutrophils: 71%, abastonades: 3%), hemoglobine: 17.1 g/dl, platelets: 51000 cells per microliter</td>
</tr>
<tr>
<td>Coagulation profile on admission</td>
<td>TP: 10.97 seconds, fibrinogen: 3.75, TTPa: 43.11 seconds, INR: 0.97</td>
</tr>
<tr>
<td>Liver profile on admission</td>
<td>AST: 25 UI/L, albumine: 4.1 g/dl, total bilirubine: 8.74 g/dl, indirect bilirubine: 8.04 g/dl, GGTP: 163 UI/L, ALP: 226 UI/L</td>
</tr>
<tr>
<td>Biochemical profile and electrolytes on admission</td>
<td>Glucose: 87 mg/dl, serum sodium: 132 mmol/L, serum potasium: 4.3 mmol/L, total calcium: 8 mg/dl, magnesium: 2.26 mg/dl and serum phosphorus: 5.3 mg/dl</td>
</tr>
<tr>
<td>Renal function on admission</td>
<td>Creatinine: 0.48 mg/dl, urea: 21.4 mg/dl</td>
</tr>
<tr>
<td>Lipidic profile</td>
<td>Total cholesterol: 147 mg/dl, LDL cholesterol: 72 mg/dl, HDL cholesterol: 27 mg/dl, TG: 172 mg/dl</td>
</tr>
<tr>
<td>Hormonal profile</td>
<td>TSH: 3.58 mU/L (VR: 0.44-8.8 mU/L), T4 libre: 1.45 ng/dl (VR: 0.48-2.32 ng/dl), ACTH: 52 pg/ml (VR: 25-100 pg/ml), cortisol basal: 5 ug/dl (VR: 5-25 ug/dl), PTH: 10 pg/ml (VR: 9-52 pg/ml)</td>
</tr>
</tbody>
</table>

TABLE 1: Blood tests obtained during hospitalization


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FIGURE 1: Findings of abdominal CT with contrast, showing bilateral adrenal hematomas
Coronal (A) and sagittal (B) sections
Arrows indicate bilateral adrenal hemorrhage

The patient was evaluated by the surgery team; no surgical management was recommended due to comorbidities and unaltered hemodynamic status. He was evaluated by the endocrinology team, which ordered a lab examination (Table 2). After his reassessment, he was diagnosed with relative adrenal insufficiency. Since there wasn’t hemodynamic instability or electrolyte imbalances, clinical monitoring and periodic ultrasound were recommended. During the three-month follow-up, the adrenal hemorrhage and relative adrenal insufficiency resolved (Table 2).

<table>
<thead>
<tr>
<th>AT THE TIME OF DIAGNOSIS</th>
<th>1 MONTH LATER</th>
<th>3 MONTHS LATER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal ultrasound</td>
<td>Right adrenal hematoma (volume: 20 ml), Left adrenal hematoma (volume: 11 ml)</td>
<td>Right adrenal hematoma (volume: 14 ml), Left adrenal hematoma (volume: 8 ml)</td>
</tr>
<tr>
<td>Basal cortisol (ng/dl)</td>
<td>4.22</td>
<td>3.9</td>
</tr>
<tr>
<td>ACTH (pg/ml)</td>
<td>52</td>
<td>17.9</td>
</tr>
<tr>
<td>Serum sodium (mmol/l)</td>
<td>141.5</td>
<td>135.4</td>
</tr>
<tr>
<td>Serum potassium (mmol/l)</td>
<td>4.6</td>
<td>5.06</td>
</tr>
</tbody>
</table>

TABLE 2: Correlation between ultrasound findings, serum electrolytes, cortisol, and ACTH in the patient
ACTH: adrenocorticotropic

Discussion

AH usually occurs in the neonatal period. Newborns usually have a larger size and increased vascularity of the adrenal glands, which make them vulnerable to mechanical compression and increased sensitivity to changes in venous pressure during delivery [6]. In addition, hypoxia may cause a redistribution of blood to the central nervous system [6-8]. As a result, congestion and endothelial damage may lead to AH [9].

AH in neonates is considered a rare condition, which accounts for about 0.2% to 0.55% of adrenal mass cases [10-11]. It may actually have a higher incidence since it is mostly asymptomatic. AH is usually an incidental finding. It is generally unilateral, affecting the right adrenal gland in 70% of cases, only 10% of cases are
Adrenal insufficiency (AI) occurs rarely even in bilateral adrenal hemorrhage due to incomplete impairment of the adrenal gland since only 10% of the adrenal gland is needed to prevent AI [12]. Furthermore, hemorrhage usually occurs in the subcapsular portion of the adrenal gland, without affecting the adrenal cortex [17].

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Serum cortisol levels should be evaluated according to the clinical status of the newborn. A serum cortisol level within normal limits in a newborn under heavy stress does not exclude the diagnosis of adrenal insufficiency because, in these patients, normal cortisol may be indicative of relative adrenal insufficiency, normal cortisol may be relatively insufficient for heavy stress, as in the reported case [19].

Conclusions

Neonatal adrenal hemorrhage should be primarily suspected in patients with significant risk factors. Maternal severe COVID-19 may be a contributing factor to AH. It is usually asymptomatic, but it could lead to relative adrenal insufficiency and even death; therefore, monitoring clinical status is crucial. A conservative approach is the gold standard, early surgical approach should be avoided. Follow-up should include imaging and laboratory examination to assess the resolution of adrenal hemorrhage and relative adrenal insufficiency.
Additional Information

Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References