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Bilateral adrenal hemorrhage and severe anemia in a neonate

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Summary

Neonatal adrenal hemorrhage (NAH) occurs in up to 3% of infants and is the most common adrenal mass in newborns. The most common presentation of NAH is an asymptomatic palpable flank mass which resolves over time without intervention. In rare cases, NAH can present as hemorrhage, shock, or adrenal insufficiency. This case describes a preterm infant born with severe anemia in the setting of bilateral adrenal hemorrhages with resulting adrenal insufficiency. The infant was successfully treated with blood transfusions and steroids. This is a unique presentation of NAH as it was bilateral, presented with severe anemia, and resulted in prolonged adrenal insufficiency.

Learning points

- Consider adrenal hemorrhage for cases of severe anemia at birth.
- Adrenal insufficiency is a rare complication of adrenal hemorrhage.
- Adrenal recovery can take months, if not years.

Background

Neonatal adrenal hemorrhage (NAH) occurs in 1.7 per 1000 to 3% of infants (1, 2) and is the most common adrenal mass in newborns (3). Peak incidence occurs during the neonates' first weeks of life (4) and is most commonly seen in term male infants (2, 5) often due to male infants displaying higher birth weight (4). Several factors make the adrenal glands uniquely susceptible to hemorrhage, including their large size relative to body weight and increased vascularity. The adrenals are more vulnerable to mechanical compression and sensitive to changes in venous pressures during delivery (4, 5, 6). During times of physiological stress, such as birth, adrenocorticotropic hormones are released from the pituitary and blood flow is further increased (1). Factors that may increase the risk of NAH include traumatic delivery, macrosomia, hypoxia, hypotension, coagulopathy, septicemia, shock, an underlying tumor, and hypothrombinemia (1, 2, 4, 5). There are cases, however, where the etiology of NAH is never established (4, 7). Overall, the rates of NAH have been increasing despite the falling rates of vaginal deliveries, which may be due to the increasing incidence of macrosomia (3).

The clinical presentation of NAH varies from most commonly asymptomatic (3), minimal bleeding, to fulminant hemorrhage and shock (2, 8). The most common presentation is a palpable flank mass (8). Clinical symptoms may also include abdominal mass, jaundice, anemia, poor feeding, vomiting, lethargy, hypotonia,

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hypertension, and scrotal edema (1, 4). Almost 70% of NAH is right sided and 5–10% are bilateral (1, 2, 4); the right adrenal gland is more prone to hemorrhage given its anatomy as it lies between the liver and the spine and is more likely to be compressed (1). Additionally, the right vein drains directly into the vena cava, which makes it more susceptible to changes in venous pressure (1). The most common imaging modality used to diagnose NAH is an abdominal ultrasound (1, 2, 6, 9).

The adrenal gland has highly regenerative capacities. NAH usually resolves in 3–9 months with one study showing an average resolution time of 18 weeks (3). Additionally, NAH rarely progresses to adrenal insufficiency (AI) given that the hemorrhage mostly occurs in the subcapsular region, and AI does not occur until at least 90% of the adrenal tissue is destroyed (1). A minimum of 10% of functional cortisol-producing tissue is enough to prevent progression to AI (3). In the cases of bilateral adrenal hemorrhage, it is less likely that both glands are impacted to the same degree (2). Otherwise, treatment is focused on the clinical outcomes of NAH. Anemia, although rare, is treated with blood transfusion, while AI is treated with steroids.

Case presentation

Our patient was a 35 2/7-week appropriate-for-gestational-age male born to a G1P1 mother. The pregnancy was complicated by elevated maternal BMI but otherwise unremarkable prenatal laboratory findings. His mother reported a 1-day history of decreased fetal movement without prior abdominal trauma, MVA, or falls. Given non-reassuring fetal heart tones, his mother required urgent C-section with delivery complicated by double nuchal cord without signs of placental abruption. The patient was born limp and pale and required intubation. APGAR scores were 2, 6, and 6 at 1, 5, and 10 min of life, respectively. His birth weight was 2690 g (59th percentile), length was 45 cm (22nd percentile), and head circumference was 32 cm (41st percentile). Initial physical exam findings were significant for pale mucous membranes, soft abdomen without palpable masses, diffuse hypotonia, and normal skin turgor without bruising, petechiae, or rashes.

The patient's initial CBC did not result due to too few blood cells. Labs drawn at 2 h of life were significant for hemoglobin 2.9 g/dL (12.8–20.4 g/dL), hematocrit 11.4% (42.0–60.0%), platelets 116 K/mcL (150–400 K/mcL), ABO set up (0+/A+/DAT-), no leukocytosis or bands, normal POC glucose, and unremarkable electrolytes. Chest X-ray was negative for acute cardiopulmonary findings. A 15 mL/kg of pRBC transfusion was given prior to same day transfer to University of Maryland's NICU for further evaluation and management.

Upon transfer to the NICU, the patient was noted to be very pale with a soft, full abdomen with LLQ fullness. To assess for potential sources of bleeding, head ultrasound showed small grade I germinal matrix hemorrhages. The abdominal ultrasound was significant for bilateral enlarged adrenal glands, with the right adrenal measuring 3.2 cm with maximal limb thickness 8 mm and left adrenal gland measuring 4.3 cm with maximal limb thickness of 8 mm, in addition to a hypoechoic cystic structure 9 mm × 8 mm in the left adrenal gland concerning for adrenal hemorrhage (Fig. 1). Given severe anemia and possible left adrenal hemorrhage, pediatric hematology and endocrinology were consulted within the first 24 h of life.

On day 1 of life, labs were significant for hyponatremia 133 mmol/L (136–145 mmol/L), normokalemia 3.8 mmol/L (3.7–5.9 mmol/L), and elevated AST 294 units/L (17–59 units/L). The ALT, direct and indirect bilirubin, and glucose levels were normal. Repeat labs completed on day 2 of life were significant for hyponatremia 132 mmol/L and low AM cortisol at 2.0 µg/dL (4.46–22.7 µg/dL), concerning for adrenal insufficiency. Thyroid function studies were normal. A cosyntropin stimulation test on day 4 of life was abnormal with an elevated ACTH 194.4 pg/mL (7.2–63.3 pg/mL), low baseline cortisol of 3.8 µg/dL, and subsequent cortisol measures of 4.1 µg/dL at 30 min and 4 µg/dL at 60 min. The normal response to cosyntropin stimulation test is a cortisol level >18 µg/dL at 60 min. The patient subsequently received 24 h of stress dose steroids (50 mg/m^2/day) then started on maintenance steroids (11 mg/m^2/day) to treat primary adrenal insufficiency. A repeat abdominal ultrasound showed redemonstration of enlarged bilateral adrenal glands, increased size of left adrenal hemorrhage, and new hypoechoic collection in right adrenal gland concerning for right adrenal gland hemorrhage. The patient did not show hypotension or hypoglycemia and maintained stable electrolytes throughout the remainder of his admission.

The patient was discharged at approximately 1 month of life with maintenance hydrocortisone and instructions for stress dose steroids. Remarkably, the patient did not demonstrate any clinical symptoms of adrenal insufficiency and met normal developmental milestones. He required stress dose steroids twice at 6 months and 12 months of age secondary to febrile illness and vaccinations, respectively, with no acute complications. His repeat abdominal ultrasound at 19 months of life demonstrated resolution of his bilateral adrenal hemorrhages. His maintenance steroids were weaned over the course of 4 months and completed just shy of his second birthday. Repeat cosyntropin testing at 28 months of life demonstrated recovery of his adrenal function with baseline cortisol 5.4 µg/dL and measurements of 16.6 µg/dL at 30 min and 19.6 µg/dL and 60 min consistent with a normal response to testing.

Regarding the anemia, the hemoglobin improved to 9.9 g/dL and hematocrit improved to 29% after his

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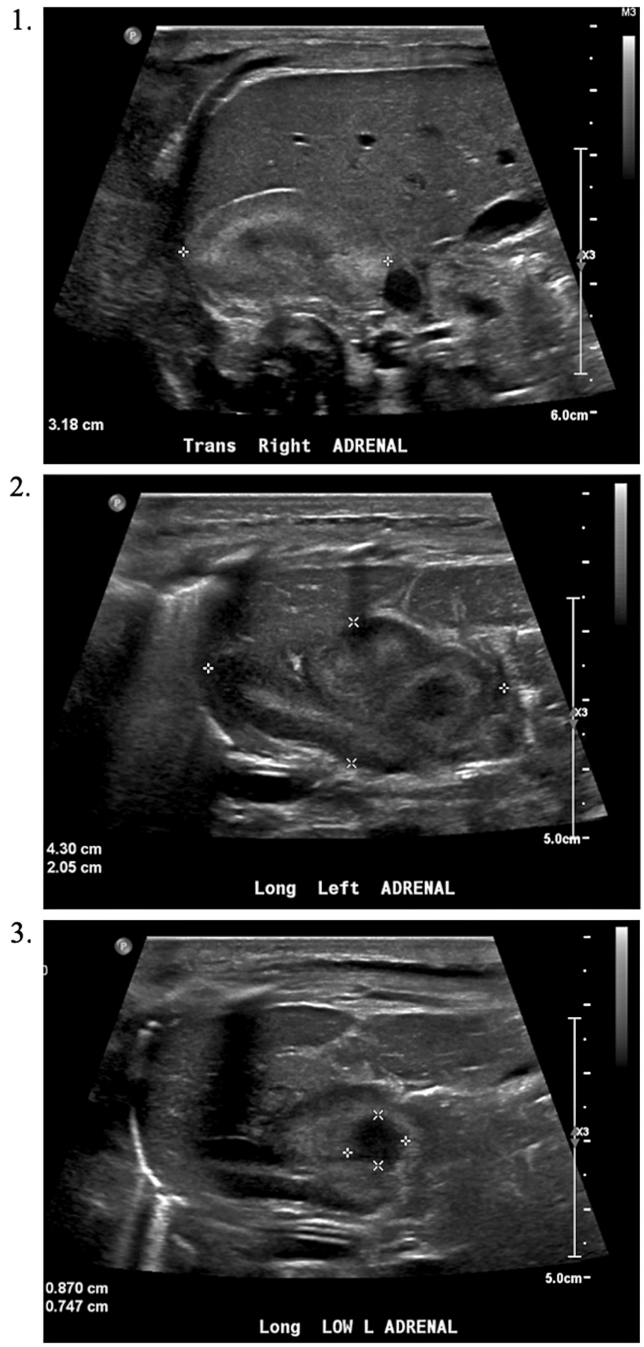

Figure 1

Ultrasound completed on day of birth showing bilateral adrenal gland enlargement. The right adrenal gland (1) measured up to 3.2 cm with a maximal limb thickness of 7 mm. The left adrenal gland (2) measured up to 4.3 cm with a maximal limb thickness of 8 mm. There was a hypoechoic cystic structure with an echogenic wall (3) that measured approximately 9 × 8 mm in the left adrenal gland.

first transfusion. The patient required two additional 10 mL/kg pRBC transfusions from day 1–2 of life due to declining hematocrit levels. The hematocrit subsequently improved and stabilized on day 3 of life. Coagulation studies, blood smear, and fecal occult blood testing were normal, and the patient did not require further blood transfusions throughout the remainder of his hospitalization. He was started on ferrous sulfate 2 mg/kg while admitted and discharged on Poly-Vi-Sol with iron. The patient continued to follow up with pediatric hematology as an outpatient. The patient did not show clinical signs of anemia. Hematocrit and hemoglobin remained stable. A hemoglobinopathy fractionation cascade was obtained at 1 year of age (as the newborn screen was obtained after the blood transfusion) and was normal.

Discussion

While literature has provided variable clinical presentations of adrenal hemorrhage, there are multiple case studies demonstrating anemia as a common clinical presentation (2, 3, 4, 6, 9). However, no other clinical case reports have demonstrated this level of severe anemia. This case is also unique in that the patient had prolonged adrenal insufficiency due to bilateral adrenal hemorrhage. Our patient required maintenance steroids until 19 months of age and demonstrated normal adrenal function at approximately 24 months of age.

Like other case studies that demonstrated male gender preference for NAH, our patient was male and displayed anemia, hypotonia, and abdominal mass on physical exam. However, our patient did not have any classic risk factors associated with NAH such as a traumatic or prolonged delivery, an assisted birth, perinatal asphyxia, septicemia, preexisting coagulation disorders, or fetal macrosomia. Pregnancy was only complicated by elevated maternal BMI. It was likely that the adrenal hemorrhage occurred prenatally and caused decreased fetal movement and non-reassuring fetal heart rates.

Zessis *et al.* describe a case of bilateral adrenal hemorrhage that resulted in prolonged adrenal insufficiency (3). Delivery was complicated by 6-min shoulder dystocia requiring episiotomy; the infant did not have a pulse initially and required chest compressions for the first 2 min of life. This patient was followed until 3 years of age, at which time the patient continued to require steroids for adrenal insufficiency. This case describes a patient who was much more ill at baseline with end organ damage due to hypoxia. Our patient had prolonged adrenal insufficiency; however, all other organ systems were functioning well.

Severe anemia and prolonged adrenal insufficiency are rare outcomes of adrenal hemorrhage. Adrenal hemorrhage should be on the differential when an infant is born with clinical and laboratory signs of anemia with no obvious cause. Although rare, any neonate with adrenal hemorrhage should be closely monitored for

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adrenal insufficiency. Prompt diagnosis with laboratory testing and abdominal ultrasound are critical for early recognition and treatment.

Declaration of interest
The authors declare that there are no potential conflicts (financial, professional, or personal) relevant to the content presented in this article.

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Patient consent
Written consent has been obtained from the patient's parent after full explanation of the purpose and nature of all procedures used.

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