Topic-Adrenal Crisis: A Rare presentation of B/L Adrenal haemorrhage

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Abstract
Background: B/L Neonatal adrenal hemorrhage and B/L adrenal cystis a relatively uncommon condition (0.2-0.55%) [1, 2]. There are many risk factors. Birth asphyxia, sepsis, coagulation disorders, traumatic delivery, and perinatal injuries. Right adrenal gland is more frequently involved (70%) than left side. Only in 10% of cases bilateral adrenal glands are involved and bilateral involvement can lead to adrenal insufficiency.
Case presentation: A case of bilateral neonatal adrenal hemorrhage with bilateral adrenal cyst with adrenal insufficiency.
Conclusions: Adrenal hemorrhage is noticed most often after normal delivery. Symptoms are presented in rare situation. Most common being decreased activity, feeding and dyselectrolemia. Sometimes jaundice is early presentation.

Keywords: Neonatal adrenal hemorrhage (NAH), adrenal insufficiency, hyponatremia, hyperkalemia, 17-hydroxy progesterone

Introduction

Neonatal adrenal hemorrhage (NAH) is a relatively uncommon condition (0.2-0.55%) occurring during the neonatal period [1, 2]. Relatively large size of adrenal glands in newborns makes it prone to mechanical compression during delivery [3, 4]. In addition, any factor which leads to hypoxia results in redistribution of blood toward the central nervous system, heart, and adrenal glands [4]. The increased pressure associated with congestion and the damaged endothelial cells associated with hypoxia may cause adrenal hemorrhage [5]. Various risk factors have been reported in addition to birth asphyxia, such as sepsis, coagulation disorders, traumatic delivery, and perinatal injuries. A retrospective study identifies vaginal delivery, macrosomia and fetal acidaemia as the most important risk factors for NAH [6].

NAH is most commonly observed in term infants and mainly affects males, perhaps due to the different birth weight [7]. Asymptomatic cases are more common because of unilateral involvement so clinical manifestations are variable or even absent. Sometimes, there are intense jaundice, ischemia, palpable abdominal mass and anemia [3, 4]. Adrenal insufficiency rarely occurs, but when it does it usually appears in the first week of life. In fact, adrenal hemorrhage usually involves the right adrenal gland (about 70% of cases) whereas the bilateral adrenal gland is involved in only 10% of cases. Since the right adrenal gland blood flow drains directly into the inferior vena cava, it is more frequently affected by venous pressure changes and damage, and may be easily compressed between the liver and coastal bones [8, 9]. Severe unilateral cases often include a hypovolemic shock, while in bilateral events, signs of hypoadrenocorticism are more evident.

The adrenal gland has a considerable regenerative capacity and most NAH are not associated with significant adrenal insufficiency, but very rarely transient adrenal insufficiency noted, although prematurity and severe underlying diseases such as sepsis, DIC, perinatal hypoxia and intraventricular hemorrhage are also potential causes of adrenal insufficiency in these patients [10]. NAH is usually self-limited with resolution and a complete regression of lesions within the period of time that goes from the 20th to the 165th day of life as reported by Postek G. *et al*. [11]. In neonates, ultrasound (US) is the preferred modality for both the initial screening and the follow-up evaluation because it is portable, rapid, sensitive, non-invasive and free from ionizing radiation compared to CT and MRI.

Case presentation

A female infant was born at term (37 weeks of gestation) by spontaneous vaginal delivery following an uneventful pregnancy (no gestational diabetes or other complications). The labor delivery monitoring was without worthy alteration. Baby didnot required any resuscitation at birth and the Apgar score was respectively 8 and 9 at 1 and 5 minutes. Birth weight was 3035 grams (Appropriate for Gestational Age, AGA, 46 th percentile). Vitamin K 1 mg IM was given duly at birth. There was no evidence of trauma. Baby discharged Twenty-four hours after delivery.

At 76 hours of life baby had jaundice so referred to us with bilirubin of 21.6 g/dl. Baby was also hyporeactive and drowsy with vacant stare look, oxygen saturation and blood sugar was normal. Laboratory reports showed a slight increased C-reactive protein (CRP) of 12 mg/L for which antibiotic intravenous (IV) therapy was started and subsequently stopped after 2 CRP values were negative. Double surface phototherapy started. Direct Coombs Test was negative for ABO incompatibility). Jaundice decreased to 10.5 mg /dl after 48 hours so phototherapy stopped. Rebound was not in treatment range.

Baby also had hyponatremia (serum sodium was 115 meq/L) and hyperkalemia (serum potassium was 8.1 meq/L).

IV sodium supplementation was started to correct hyponatremia, and IV calcium gluconate infusion, inj insulin bolus in dextrose sodium bicarbonate infusion, salbutamol nebulization and potassium binder were started for the treatment of hyperkalemia. Gradually over time sodium and potassium values gets corrected owing to self-resolution of adrenal hemorrhage over time.

[Hyponatremia (meq/L)

(115→118→122→123→127→130→132→133→131→ 131→132→136→131→132→132→132→137)

Hyperkalemia (meq/L)

(8.1→6.93→6.45→6.92→7.75→7.15→6.67→6.47→7.1→ 7.7→6.4→ 6.99→6.29→5.71→5.12→5.17)

The hormonal tests performed for diagnosis revealed that her plasma renin activity was 8.4 ng/ml (normal range 2.4-37 ng/ml/h), while her aldosterone level was low with 3.3 ng/dl (normal range 19-141 ng/dl). The results of hormonal tests were as follows: serum adrenocorticotropic hormone (ACTH): 57.5 pg/ml (normal range 0‑46), cortisol: 29.05--23.78 µg/dl (normal range 5.5-22.0), 17-hydroxy progesterone (17-OHP): 2.66...2.32 ng/ml (normal range 0-6.3), Angiotensin Converting enzyme: 28 U/L.

There was normal coagulation profile, no urinary tract infection or other negative blood culture and negative research for invasive neonatal germs (real-time Polymerase Chain Reaction (PCR) method),

Abdominal ultrasonography revealed thick walled cystic lesion with echogenic contents and no internal vascularity noted in right adrenal gland measuring approx. 27x16x26 mm, volume approx. 6cc. There is cystic lesion with thin incomplete septa and subtle internal echoes noted in left adrenal gland measuring approx 27x23x29 mm, volume approx 9.9cc.

MRI Abdomen (17/01/2022)- B/L Well defined Cystic adrenal lesions 25x20x22 mm and 30x27x25 mm respectively, with altered contents ? sequelae of old adrenal hemorrhage? / nature. No evidence of any acute hemorrhage seen within.

Discussion

The cortex and medulla of the adrenal glands have different origins. The medulla originates from neural crest cells of the adjacent sympathetic ganglion, whereas the cortex develops from mesoderm of the posterior abdominal wall. The cortex eventually encircles the medulla

During fetal life, the fetal cortex produces large amounts of precursors of steroid hormones and placenta utilizes these precursors to produce progesterone to maintain pregnancy and inhibit uterine contractions.

The largest part of the adrenal medulla develops in the neonatal period and fetal catecholamines are produced by Zuckerkland organ and other paraganglia. During fetal life, developing adrenal medulla clusters of small medullary cells are distributed, irregularly, in highly vascular provisional cortex; when the latter degenerates, the clusters of medullary cells survive and, lacking the support of the cortical cells, aggregate together.

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NAH is usually self-limited condition due to its regenerative capacity which leads to complete regression of lesions after sometime. So the adrenal insufficiency initially associated with these lesions tend to recover with time with initial supportive treatment by correcting electolyte deficiencies, but may rarely require mineralocorticoid [10].

CAH is due to enzyme, 21 alpha hydroxylase, deficency which causes conversion of progesterone to deoxycorticosterone and subsequently to aldosterone, and also from 17 OHP to 11- deoxycortisol and then cortisol. So both aldosterone and cortisol are deficient in severe form. Severe form of CAH present as progressive weight loss, hyponatremia, hyperkalemia, hypoglycemia, anorexia, vomiting, dehydration, weakness, hypotension which develops at around 10-14 days.

At around 8 to 10 weeks of gestation, due to increased 17 OHP and progesterone which are diverted to form increased testosterone and subsequently abnormal genital development in females, enlarged clitoris, partial or complete fusion of labia. Internal organs are normal.

In Adrenocortical insufficiency, there is cortisol and adrenal deficiency with hypoglycemia often with ketosis. Cortisol deficiency leads to Hyponatremia and hyperkalemia, decrease vascular tone, decreased cardiac output, orthostatic hypotension leading to shock and low glomerular filteration rate.

Increased ACTH leads to hyperpigmentation of skin crease and mucosa.

Primary hypoaldosteronism typically causes vomiting, signs of dehydration, hypovolemia, and failure to thrive in the first weeks of life. The biochemical assessment revealed hyponatremia, hyperkalemia, increased plasma renin activity, and low aldosterone levels [12].

In this case, CAH was not considered because there were no signs of virilization and hyperpigmentation. Moreover 17-OHP, cortisol and adrenal androgen levels were all within normal limits and there was lack of virilization findings.

Primary hypoaldosteronism also not considered because of normal laboratory parameters of renin and aldosterone levels in blood with clinical signs not consistent with primary hypoaldosteronism.

Conclusions

NAH should be suspected for a baby delivered vaginal and has decreased activity with early initiation of jaundice and sepsis screen is negative

Moreover associated repeated electrolyte disturbances should also raise concern for adrenal involvement.

There is symptomatic improvement after electolyte correction so need for surgical treatment can be put on hold if there is no ongoing ultra sonographic evidence of ongoing hemorrhage.

In most cases, the event is asymptomatic but it could prove detrimental to determine death by bleeding or adrenal insufficiency.

So one should have high index of suspicion for diagnosing bilateral adrenal hemorrhage.

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