Case Report

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Anesthetic Management in a Child of 11β Hydroxylase Deficiency at Rural Tertiery Care Centre, Loni

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Abstract

Congenital adrenal hyperplasia (CAH) is the result of an autosomal recessive disorder.It affects one of the step required for the synthesis of cortisol from cholesterol by the adrenal cortex. 11β-hydroxylase deficiency accounts for 5-8% of all cases of CAH with an incidence estimated at 1 in 100,000 - 200,000 newborns [1]. We present a 2.5-year-old girl with CAH due to 11β-hydroxylase deficiency who presented for surgical treatment of cliteromegaly with hypoplastic lower third of vagina for clitoroplasty with stage 1 vaginal reconstructions. The perioperative care of patients with CAH should address issues related to the deficient and excessive production of specific corticosteroids and mineralocorticoids by the adrenal cortex. We will discuss the perioperative implications of the disorder.

Keywords: Congenital Adrenal Hyperplasia(CAH); 11β-Hydroxylase Deficiency.

Introduction

Congenital adrenal hyperplasia (CAH) is a genetic disorder(autosomal recessive disorder) caused by mutations of the *CYP21A2* gene. Congenital adrenal hyperplasia (CAH) affects one of the several steps required for the synthesis of cortisol from cholesterol by the adrenal glands. Impairment in cortisol secretion alters the negative feedback loop leading to stimulation of the hypothalamic-pituitary-adrenal axis. High levels of ACTH over time result in hyperplasia of the adrenal cortex . The most common form of CAH, accounting for more than 90% of cases, results from the deficiency of the enzyme, 21-hydroxylase. CAH due to 11β-hydroxylase deficiency accounts for 5-8% of all cases with an incidence estimated at 1 in 100,000- 200,000 newborns [1]. The gene is located on the long arm of chromosome 8. This condition is more common in Moroccan Jews living in Israel, occurring in approximately 1 in 5,000 - 7,000 newborns[2]. 11β-hydroxylase mediates the final step of the glucocorticoid pathway, producing cortisol from 11-deoxycortisol in the adrenal. It also catalyzes the conversion of 11-deoxycorticosterone (DOC) to corticosterone in the mineralocorticoid pathway. These patients show androgenic and mineralocorticoid manifestations. Androgenic menifestations are partial virilization and ambiguous genitalia of female infants, childhood virilization of both sexes, rarer cases of virilization or infertility of adolescent and adult women and premature puberty. Due to mineralocorticod effect hypertension is usually present in 11β-hydroxylase deficiency which is clinical clue to differentiate patients from 21 hydroxylase CAH. The diagnosis of 11β-hydroxylase deficient CAH is confirmed by the demonstration of marked elevations of the substrates of the 11β-hydroxylase enzyme including 11-deoxycortisol and 11-DOC. Surgical intervention is required to correct

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the virilizing effects of the over production of adrenal androgens. Progressive adrenal hyperplasia due to persistent elevation of ACTH results in extreme over production of 11 deoxycorticosterone (DOC) by mid childhood. DOC is a weak mineralocorticoid, but usually reaches high enough levels in this disease to cause effects of mineralocorticoid excess such as salt retension, volume expansion and hypertension. We present a 2.5 year-old girl with CAH due to 11 beta hydroxylase deficiency who presented with cliteromegaly with hypoplastic lower third of vagina for clitoroplasty with stage 1 vaginal reconstructions surgery with borderline raised blood pressure . The perioperative implications of the disorder are discussed.

Case Report

A diagnosed case of congenital adrenal hyperplasia at KEM hospital Mumbai, came for surgical correction of cliteromegaly with lower third hypoplastic vagina. Our patient is a 2.5 year-old, 10 kg girl child who presented to clinic for evaluation and surgical correction. Patient is a 2nd child with parents of 3rd degree consanguious marriage. She was full term normal delivery at hospital and declared to have ambiguous genitals and not assigned any sex with advice to follow up in higher centre. Perinatal period was uneventful and her parents declared her as a male child. At 15th day she was shown to govt. medical college where some investigations were done including usg and her parents were told that she is a girl child and she was referred to KEMH Mumbai, for surgical correction. At age of 6 months again she was investigated with usg and cystogenitoscopy which shows hypertrophied clitoris with hypoplastic lower third of vagina and b/l nephrocalcinosis. Her general examination was normal except blood pressure 100/60 mmHg which was remarkably more for this age, all routine laboratory investigations were normal. As her brother was diagnosed case of 11 beta hydroxylase deficiency with hypertension on treatment, she was investigated for the same and 11 beta hydroxylase was 136.2 ng/ml (0.05-0.47ng/ml), genotyping was 46,XX.

Medications included tablet hydrocortisone 25 mg orally thrice a day. At present she has no complains.she has no history of salt loosing episodes, recurrent admission or hyperpigmention. She was reported to have no known drug or food allergies. Preoperative physical examination was notable for cliteromegaly and hypoplastic vagina, blood pressure

Fig. 1:

was 100/70 but was otherwise unremarkable,however, preoperative serum electrolytes, blood urea nitrogen, and creatinine were within normal limits.Her usg were normal too. Preoperative vital signs were as follows: blood pressure (BP) 100/70 mm Hg, heart rate 106 beats per minute, respiratory rate 18 breaths per minute, and oxygen saturation 99% on room air. The patient was scheduled for cliteroplasty with stage I vaginal reconstruction. The patient was held nil by mouth. A 22-gauge peripheral intravenous catheter was placed. Inj.gycopyrolate 0.04mg IV, Inj.Midazolam 0.25mg iv, inj Hydrocortisone 25 mg was administered intravenously prior to anesthetic induction. Intravenous induction was performed with Inj.Fentanyl 10 microgram iv, inj. propofol 20 mg iv patient was intubated with ETT portex 4.5 uncuffed after giving Inj.Scholine 20 mg iv, tracheal position of ETT confirmed and fixed. Anesthesia was maintained with 1.5% isoflurane in 40% oxygen 60% N_2O. The patient was positioned in the right lateral decubitus position for caudal block for reducing intraoperative drug requierement and postoperative pain control. The procedure was performed under standard sterile conditions at sacral region, sacral hiatus confirmed and 25G needle inserted and space confirmed by aspiration and it was negative for blood and cerebrospinal fluid, inj.bupivacaine 0.25% 8cc +Inj.Fentanyl 10 microgram injected without any resistance with no swelling at site of injection. The patient was then placed in supine position. At the time of surgery start, her vital signs were as follows: BP 84/48 mm Hg, heart rate 90 beats per minute, respiratory rate 14 breaths per minute, and oxygen saturation 100% with an FiO_2 40%. There was fall in blood pressure by 70/40 with an isoflurane concentration of 1% demonstrating adequate epidural

anesthesia. Approximately 15 min after surgical incision, the BP was 90/50 mmHg, ISoflurame was mainained at 0.4% with 60% N_2O and 40%O_2. Surgery completed in Approximately 1.5 hrs. Intravenous 200ml of RL+Dextrose infused in intraop, the patient showed vitals in normal range . extubation was done smoothly without any complication and patient was comfortable in the recovery room. That evening, her routine oral dose of hydrocortisone was 2.5mg was restarted and and shift to 1.25mg dose after suture removal. The remainder of the postoperative course was unremarkable.

Discussion

The perioperative care of patients with CAH should address issues related to the deficient and excessive production of specific mineralocorticoids and corticosteroids by the adrenal cortex. The mineralocorticoid manifestations of severe 11β-hydroxylase deficiency in CAH can be biphasic, changing from a salt-wasting presentation in early infancy to excessive production resulting in hypertension in childhood and adolescence. Although salt-wasting in early infancy is rare, it occasionally occurs in 11β-hydroxylase CAH because of the impaired production of aldosterone coupled with the normal inefficient renal sodium conservation of neonates and infants. The clinical manifestations are similar to those of the severe forms of 21-hydroxylase deficient CAH, including poor weight gain and vomiting in the first weeks of life, progressing to dehydration, hyponatremia, hyperkalemia, and metabolic acidosis which result in death if not effectively diagnosed and treated [1,2]. Therapy includes the administration of intravenous normal saline to restore intravascular volume, dextrose to correct hypoglycemia, and the administration of replacement doses of hydrocortisone, our patient shows none of the above at pressent. Despite the inefficient production of aldosterone, the more characteristic mineralocorticoid effect of the 11β-hydroxylase of CAH is hypertension. Progressive adrenal hyperplasia due to persistent elevation of ACTH results in the excessive production of 11-DOC by early to mid-childhood. Although DOC is a weak mineralocorticoid when compared to aldosterone, the plasma concentrations are high enough to result in the classic effects of mineralocorticoid excess including salt retention, volume expansion, and hypertension. Approximately two thirds of patients with CAH due to 11β-hydroxylase deficiency will manifest hypertension,typically developing within the first year or two of life. Excessive DOC also results in hypokalemia and alkalosis. The latter resulting from the excretion of hydrogen ion to maintain electrical neutrality in the kidneys as sodium is reabsorbed. Given these concerns, the preoperative assessment of electrolytes and acid-base status is suggested. The acid-base status as assessed by the serum bicarbonate can be used to generally assess the efficacy of corticosteroid replacement therapy [3]. Perioperative corticosteroid therapy is similar to that of 21-hydroxylase deficient CAH except that mineralocorticoids need not be replaced. The primary therapy of 11β-hydroxylase deficiency is lifelong glucocorticoid replacement in doses to prevent adrenal insufficiency and suppress excessive ACTH production. Suppression of ACTH results in limitation of excessive mineralocorticoid and androgen production. Perioperative corticosteroid therapy is recommended to avoid cardiovascular compromise due to the stress of surgery and anesthesia [4, 5]. While the time-honored therapy of patients on chronic glucocorticoid therapy has been to administer "stress doses" during the perioperative period with dosing calculated to match the maximum adrenal output (6 - 8 times the basal secretion), the need for such therapy has recently been questioned with the suggestion that many patients require only the continuation of maintenance corticosteroid therapy without stress dosing [4, 5]. This practice has been suggested given the potential adverse effect profile of high dose corticosteroid therapy including immune suppression, increased incidence of surgical site infections, delayed wound healing, hyperglycemia, and gastric bleeding [6-8]. In our patient, our plan was to administer a single preoperative dose of hydrocortisone; however. As the patients postoperative course was unremarkable, her routine dose of hydrocortisone was restarted same day night further supplementation was provided. Significant perioperative concerns may exist related to long term glucocorticoid therapy. Although necessary, chronic glucocorticoid therapy may result in hypertension related to abnormal renal sodium homeostasis, cataracts, osteoporosis, impaired wound healing, disordered glucose homeostasis, and cataract formation [6,8,9]. A large meta-analysis demonstrated that patients on chronic glucocorticoid therapy were 2.2 times more likely to be hypertensive, regardless of the duration of therapy [10]. As such, perioperative glucose monitoring is suggested in patients receiving chronic corticosteroid therapy. Treatment of hyperglycemia, depending on its magnitude, may also be indicated. In the diabetic patient with absolute or relative insulin deficiency,

surgical procedures and the associated stress response can lead to marked hyperglycemia and even diabetic ketoacidosis [11]. Hyperglycemia also can impair wound healing and increase the risk of surgical site infections [12-14]. Although clinical studies have not consistently demonstrated a significant relationship between perioperative glycemic control and short term risk of infection or morbidity, tight glucose control has been recommended by some investigators with a demonstration of decreased perioperative morbidity [15-17]. For major surgical procedures, a continuous intravenous infusion of insulin has been shown to be superior to subcutaneous injections in achieving perioperative optimal glycemic control [18-20]. Hyperglycemia may also result in glucosuria, polyuria, and electrolyte disturbances during the perioperative period. As noted in our patient, 11β-hydroxylase deficiency doesn't show any of these menifestations. Perioperative hypotension occurred after induction with the sympathectomy induced by the caudal epidural anesthesia. Restoration of adequate BP was accomplished by the administration of isotonic fluids with dextrose and titrating isoflurane, after that patient was heamodynemically stable and maintained on isoflurane 0.4% O_2 40%, N_2O 60%. Requirement of anaesthetic agent decrease through out surgery was due to adequate effect of caudal analgesia .The significant implications of CAH are illustrated by reports of death or malignant ventricular arrhythmias in undiagnosed newborns [3, 27]. Both volatile agents and total intravenous anesthesia have been used successfully. One report outlines the use of spinal anesthesia. No major intraoperative problems have been reported. In summary, we present the perioperative care of a 2.5 year old girl with CAH due to 11β-hydroxylase deficiency who presented for surgical treatment. She is having family history, her elderly brother 9 year old had normal male genitals descended gonads at birth was well till 2 year of age, when parents observed increase in size of gonads penis with mature look on face –shown to pravara rural medical college and he is also diagnosed with hypertension 140/90 BP, elevated DOC (863ng/dl) on tab hisone and amlodipine.Perioperative corticosteroid therapy is mandatory, controversy exists as to whether this should include continuation of the routine maintenance doses of corticosteroids or the administration of a perioperative "stress dose". Perioperative glucose homeostasis can be altered by corticosteroid therapy, pain, and the surgical stress response. As was used in our patient, neuraxial analgesia (caudal epidural) may be more effective in blunting the surgical stress response and its impact on glucose homeostasis than intravenous opioid therapy.

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