not contributory in our case.

BMP4 loss of function mutations have been described in patients with SHORT syndrome, Axenfeld-Rieger malformation, growth delay, macrocephaly, and diaphragmatic hernia. The authors postulated the critical role of this in ocular development. Studies in animal models have shown that Bmp4 and Pitx2 act in a common pathway in craniofacial/dental and left-right asymmetry development [3]. However, the definite locus of SHORT syndrome gene still remains illusive.

Contributors: AS was involved in clinical case management and was the main author. RA did the opthalmoscopic evaluation and PS did the genetic studies.SK critically reviewed the manuscript, made the diagnosis and will act as guarantor for the manuscript
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Apparent Mineralocorticoid Excess (AME) Syndrome

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Apparent mineralocorticoid excess (AME) syndrome is a rare autosomal recessive disorder due to the deficiency of 11β hydroxysteroid dehydrogenase type 2 enzyme (11beta-HSD2). Mutations in this gene affect the enzymatic activity resulting to an excess of cortisol, which causes its inappropriate access to mineralocorticoid receptor leading to inherited hypertension.This is a potentially fatal but treatable disorder. We present clinical and molecular studies on two sisters diagnosed as AME.

Key words: *Hypertension,11β hydroxysteroid dehydrogenase type2 enzyme, Mutation.*

The syndrome of apparent mineralocorticoid excess (AME) arises from non-functional mutations in 11β hydroxysteroid dehydrogenase type2 enzyme (11beta-HSD2), an enzyme that inactivates cortisol and confers aldosterone specificity on the mineralocorticoid receptor. The imapaired conversion of cortisol (compound F) to cortisone (compound E) has been associated with low renin, low aldosterone hypertension with hypokalemia in children. The hypertension in the syndrome is presumed to arise from volume expansion secondary to renal sodium retention. This disorder is potentially fatal but treatable and hence early diagnosis is required to prevent the mortality.

CASE REPORT

Case-1: A one year old Kuwaiti girl, product of a consanguineous marriage; delivered by LSCS; IUGR with birthweight of 1.7 kg was admitted to our hospital with the history of polyuria and polydypsia for one week duration. On examination, the child's weight and height were both below 3rd centile. Her blood pressure was high (130/88 mmHg) at the time of admission. She had marked dystrophic squint and other systemic examination was unremarkable. Biochemical findings indicated hypokalemia with metabolic alkalosis. With this clinical and biochemical presentation Bartter syndrome was suspected, but the patient was further investigated to rule out other possibilities. Her plasma renin activity was low (<0.2 pmol/L/mL/h); serum aldosterone was low (<75 pmol/L); low serum renin and aldosterone level were against the diagnosis of Bartter syndrome. Chromatographic determination of urinary steroid

metabolites showed an abnormal elevation of tetrahydrocortisol (THF) and allo-tetrahydrocortisol compared to tetrahydrocortisone (THE). High ratio of cortisol to cortisone metabolites was suggestive of defect in 11β hydroxysteroid dehydrogenase type 2 enzyme. Renal ultrasound revealed the presence of bilateral nephrocalcinosis. Genetic study proved homozygous missense mutation c.710C>T;p.A273V in *HSD11B2* gene confirming the diagnosis of apparent mineralocorticoid excess (AME) syndrome. Patient responded well to spironolactone along with amiloride, with good control of blood pressure and electrolytes. Patient is being followed regularly in pediatric endocrinology and nephrology clinics.

Case 2. A 8-month-old girl (sister of above mentioned patient), product of a consanguineous marriage; full term delivered by LSCS with birth weight of 2.5 kg with uneventful neonatal period was admitted as a case of acute bronchiolitis. On examination, the child's weight and height were both below 3rd centile. Her blood pressure was high (114/78 mmHg) at the time of admission. Her systemic examination was unremarkable except for wheezes on auscultation of chest. Biochemical findings indicated hypokalemia (serum potassium-2.8 mmol/L) and normal sodium (136 mmol/L) with metabolic alkalosis; keeping in mind of the diagnosis of apparent mineralocorticoid excess (AME) syndrome in her elder sister, she was screened for the same too. Chromatographic determination of urinary steroid metabolites showed an abnormal elevation of tetrahydrocortisol (THF) and allo-tetrahydrocortisol compared to tetrahydrocortisone. High ratio of cortisol to cortisone metabolites was suggestive of defect in 11β hydroxysteroid dehydrogenase type 2 enzyme. Renal ultrasound revealed the presence of bilateral nephrocalcinosis. Genetic study proved homozygous missense mutation c.710C>T;p.A273V in *HSD11B2* gene confirming the diagnosis of apparent mineralocorticoid excess (AME) Syndrome. Patient responded well to spironolactone along with amiloride and is currently under regular follow-up.

DISCUSSION

The syndrome of apparent mineralocorticoid excess of AME is a form of low-renin hypertension that is caused by congenital deficiency in the activity of the enzyme HSD11β 2. AME is usually diagnosed within the first years of life and is characterized by polyuria and polydipsia, failure to thrive, severe hypertension with low renin and aldosterone levels, profound hypokalemia with metabolic alkalosis, and most often nephrocalcinosis [1,2]. Stroke has been observed before the age of 10 years in untreated children. Transmission is autosomal recessive and AME is caused by homozygous or compound heterozygous loss-of-function mutations or deletions in the *HSD11B2* gene (16q22) [3,4]. In all cases, these mutations lead to abolition or a marked decrease in the activity of 11-beta-hydroxysteroid dehydrogenase type 2 (11-beta-HSD2), an enzyme involved in the conversion of cortisol to cortisone [5,6]. Diagnosis should be suspected on the basis of the clinical and biochemical characteristics. Detection of a marked increase (10 to 100-fold) in the ratio of cortisol/cortisone (F/E) or of the tetrahydroxylated metabolites (THF+alloTHF/THE) in plasma and urine is a strong indication for diagnosis. Differential diagnoses include pseudohyperaldosteronism (particularly Liddle syndrome), as well as other forms of early-onset childhood hypertension (particularly renal hypertension) [7,8]. For families in which the disease-causing mutation has already been identified, prenatal diagnosis may be considered in case of a life-threatening event in a previous child. Early diagnosis and treatment is important to prevent end-organ damage (central nervous system, kidney, heart and retina). Two main strategies can be used to treat AME. The first is the blockade of the mineralocorticoid receptor by spironolactone (2-10 mg/kg/day), combined with thiazides to help to normalize blood pressure and reduce hypercalciuria and nephrocalcinosis [9]. The second and complementary strategy, is the administration of exogenous corticoids to block ACTH and suppress the endogenous secretion of cortisol. This strategy has proven efficacy on blood pressure, renin and aldosterone levels but has little effect on urinary cortisol, cortisone and corticosterone concentrations. The loss of functional epithelial sodium channel (ENaC) explains why amiloride is only an effective means of long term blood pressure control [8,10]. In the absence of treatment, the prognosis for AME is severe with malignant hypertension, stroke, cardiac and renal insufficiency. However, the prognosis for patients with appropriate treatment appears to be good.

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Fulminant Epstein Barr Virus Encephalitis

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Epstein Barr virus (EBV) encephalitis is rare in children but can have severe neurological complications and sometimes fatal. It can manifest with varied neurological presentations like meningoencephalitis, brain stem encephalitis, GBS etc. This can appear alone or with clinical picture of infectious mononucleosis. Establishing a diagnosis of EBV encephalitis is difficult and consequently molecular, serological and imaging techniques should be used when investigating a child with encephalitis. To highlight this entity we report two fatal cases of EBV meningoencephalitis presenting with sole neurological manifestations .

Key words: *Encephalitis, Epstein Barr virus.*

EBV virus infection is a common usually benign systemic viral illness in children. In few cases it is associated with variety of CNS manifestations including meningoencephalitis, cerebritis, transverse myelitis, neuropsychiatric syndrome, GBS and cranial nerve palsies.This occurs after usually 1-3 weeks of illness; rarely these can manifest at the onset of illness.

Case 1: A 7-year-old boy was admitted with history of fever, unsteady gait and drowsiness of 2 days duration. He was found to have wide-based gait, nystagmus and increasing drowsiness. Other system examinations was unremarkable. There were no focal neurological deficits, no seizures and no signs of raised intracranial tension or signs of meningeal irritation. Initial routine investigations and basic metabolic screen were normal. CT brain also revealed no abnormality. CSF analysis was done and microscopy and biochemistry was normal. CSF PCR for EBV virus was positive and EBV serology was also positive in blood. Immunological profile was normal. He was treated as meningo-encephalitis with broad-spectrum antibiotics and acyclovir. One day after admission, he was found to have deteriorating level of consciousness with low GCS and required mechanical ventilation. He was not showing any improvement in his neurological status, and he received intravenous immunoglobulin empirically. MRI brain showed abnormal signal intensity in pontine region suggestive of pontine encephalitis. Child had persistent fever, his general condition deteriorated and on 5th day of illness, he developed hypotension which was refractory to fluids, with GI bleeding and DIC with multiorgan failure and succumbed to the illness.

Case 2: An 8-year-old boy was admitted with low grade fever and drowsiness of 2 days duration.There was no history of convulsions or vomiting and there were no signs of raised intracranial tension. Clinical diagnosis of encephalitis was made at the time of admission and other systemic examination was unremarkable. Initial routine investigations and metabolic screen were normal. CT brain was also normal. CSF biochemistry and microscopy were normal. He was started on broad spectrum antibiotics including antiviral drugs along with other supportive treatment. He developed generalised tonic