

Acute Demyelinating Encephalomyelitis in Malaria

The recent article on acute demyelinating encephalomyelitis in a patient with falciparum malaria is very interesting [1]. Indeed, the neurological complication of falciparum malaria is not uncommon but the acute demyelinating encephalomyelitis is extremely rare. Recently, a similar case was published in another journal [2]. It was proposed that the pathophysiology is due to immunopathological process [3]. The question is whether the acute demyelinating encephalomyelitis is an exact neurological complication due to falciparum malaria. In the present case, it is no doubt that both malaria and acute demyelinating encephalomyelitis existed. However, the question is whether this is an accidental concomitant occurrence. Some viral infections such as dengue are also endemic in the same setting as malaria [4] and can be the cause of acute demyelinating encephalomyelitis [5]. Since there is no laboratory test to

rule out concomitant viral infection, the conclusion can be only detection of two disorders in the patient.

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Glibenclamide for Neonatal Diabetes

Neonatal diabetes mellitus, defined as insulin-sensitive hyperglycemia involving the activating mutations in the *KCNJ11* gene encoding Kir 6.2, is diagnosed within the first six months of life presenting with glucosuria, polyuria, dehydration, failure to thrive, and diabetic ketoacidosis [1]. Treatment with insulin results in dramatic catch-up growth; insulin may be discontinued in about half these patients, as blood glucose is well-controlled on sulfonylureas (SUs).

We report a case of neonatal diabetes in a 4-month-old baby girl presenting with diabetic ketoacidosis due to p.R201H mutation in the *KCNJ11* gene, who was successfully changed from subcutaneous insulin to oral glibenclamide on an outpatient basis.

The patient, who was being treated elsewhere as Type 1 diabetic, had an HbA1c of 11.6% with low serum c-peptide levels (<0.3 ng/mL) on referral. Since autoimmune diabetes is less common before six months of age, we

considered other possible causes of diabetes. While awaiting results of genetic analysis, she was initiated on oral glibenclamide (as a powder dissolved in water) in a dose of 0.3 mg/kg/day, in three divided doses. Strict self monitoring of blood glucose was done and the insulin was gradually tapered off over next few days. Within four days of starting glibenclamide, repeat serum c-peptide levels done were better (2.25 ng/mL), indicating increased endogenous production of insulin. Genetic testing of both parents was negative for the mutations.

Presently, the patient is doing well, gaining weight, and is continuing on glibenclamide with a latest HbA1c of 7.6% and serum c-peptide level of 2.38 ng/mL. We therefore suggest an outpatient protocol for changing these patients from insulin to Sulfonylureas(SUs) [2].

SUs are introduced gradually over a period of weeks as an outpatient. Glibenclamide dose is increased each week by 0.2 mg per kg per day in divided doses up to a total daily dose of 1.0 mg per kg per day. It has been found that the pre-breakfast glucose may be very slow to fall and pre-lunch or pre-evening meal glucose values fall more rapidly and are generally a better marker of response to SUs. In

some patients there may be initial diarrhea but this settles on its own. Care must be taken to recognize and treat hypoglycemia including the use of 0.5-1 mg glucagon injection for emergency use if unable to take oral carbohydrate. The physician should see the patient every week, and be accessible by phone during the transfer.

We emphasize the need for medical practitioners to consider molecular testing for all patients who present with diabetes below 6 months of age as this will facilitate accurate diagnosis and appropriate therapy.

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Vitamin D Intoxication: Too Much of a Good Thing!

Vitamin D deficiency is common among Indian children [1]. The recommended therapy for vitamin D deficiency rickets is 1,00,000–6,00,000 IU [2]. The increasing awareness about beneficial effects of vitamin D has led to an increase in its prescription [3]. However, one needs to be cautious while prescribing vitamin D, as overdose can lead to severe hypercalcemia.

We present the case of an 18-month-old girl, referred with lethargy and vomiting for 10 days, and polyuria for 5 days. She was noticed to have bowing of legs 3 months ago, and diagnosed to have rickets. Her 25-hydroxy D₃ level was 37.5 nmol/L (normal: 75-250 nmol/L). She was started on oral calcium and cholecalciferol 60,000 IU per day, for 6 weeks. In follow-up, the prescription was repeated for another 6 weeks. Meanwhile, the parents consulted another practitioner for the 'persistent' bowing, who administered 6 lakh IU vitamin D₃ intramuscularly. The cumulative dose of vitamin D received by her was nearly ten times the therapeutic dose.

At presentation, the child was irritable and dehydrated, with BP of 136/94. Serum ionized calcium was 2.83 mmol/L, total calcium 20 mg/dL (normal: 9-11 mg/dL), phosphate 2.63 mg/dL (normal 2.5-4.5 mg/dL), alkaline phosphatase 513 IU/L (normal 240-840 IU/L), 25-hydroxy D₃ > 3500 nmol/L and parathormone level 23.48 pg/mL. Renal and liver function tests were normal. Urinary calcium/creatinine ratio was 2 (normal <0.2). Ultrasonography of kidneys and CECT brain was normal. Wrist skiagram showed healed rickets. She was started on intravenous fluids (1.5 times maintenance), furosemide and

hydrocortisone. Injection Calcitonin was added on 2nd day, in view of persistent hypercalcemia. Ionized calcium fell to 1.56 mmol/L initially, followed by rebound increase 48 hours later. For control of hypertension, child required amlodipine and enalapril. Child was discharged after 12 days with serum calcium 13 mg/dl and BP 106/70, on tapering doses of oral prednisolone, furosemide and anti-hypertensives.

Furosemide and enalapril were stopped after 3 weeks, whereas amlodipine was continued for 6 months in view of persistent hypertension. The serial serum Calcium was 10.5, 10.8 and 10.6 mg/dL, phosphate was 2.4, 5.1 and 5.6 mg/dL, 25-hydroxy D₃ was 3446, 3484 and 1785 nmol/L, and Parathormone was 16, 14.9 and 25 pg/mL at 2, 4 and 12 weeks after discharge. Ultrasonography at 3 and 6 months did not reveal nephrocalcinosis.

The manifestations of vitamin D intoxication are related to hypercalcemia, and require prompt treatment. Since vitamin D is stored in fatty tissues, the toxicity may last for up to 6-8 months. Calcium induced hypercatecholaminemia, and direct effect on vascular smooth muscle are responsible for hypertension [4]. Treatment modalities include diet with low calcium and phosphorus, hydration, loop diuretics, glucocorticoids, calcitonin and bisphosphonates [5]. Hemodialysis is useful in life threatening hypercalcemia.

Before starting vitamin D for children with rickets, parents should be asked about previous vitamin D administration. In case of doubt regarding either the diagnosis of vitamin D deficiency, or previous intake of vitamin D, it is prudent to check 25-hydroxy vitamin D levels. Parents should also be counseled that bowing of legs would take time to resolve and does not require repeated courses of vitamin D. Vitamin D needs to be used with caution, and only when indicated, to avoid adverse effects.