AN ADOLESCENT WITH UNUSUAL CAUSE OF SEIZURES

T P VIGNESHWARAN
- 13 year old adolescent boy

- 2nd born to non consanguinuous parents, developmentally normal

- Admitted with
  h/o fever and altered sensorium for 2 days
  h/o recurrent seizures for 24 hours
- Seizures - iv lorazepam / iv fosphenytoin (loaded)
- Intubated - low GCS & unmaintainable airway
- 3% NaCl (loading foll. By maintenance)
- Past h/o:
  convulsions with fever - twice in last 3 months (nov 2013 & march 2014)
CT brain: bilateral globus pallidus calcifications
On examination:

- Febrile (100-101 F)
- No facial dysmorphism / neurocutaneous markers
- Systemic examination - non contributory

PROVISIONAL DIAGNOSIS:

- CNS infection - meningoencephalitis
- Seizure disorder
- Metabolic disorder
Base line investigations

- Blood counts - low normal platelets (1,51,000)
- Serum electrolytes - low Na (133) & k (3.2)
  - low Ca (7.6) & high phosphorus (9)
  - normal Mg (2.1)
- Blood sugar - 139
- LFT - SGPT (59), Alb - 3.7 & ALP -398
- RFT - normal
- Blood gas: 7.43/38.9/236/ 25.4 /1.1 / 0.45 ; iCa - 0.45
- LP - CSF analysis - protein elevated (139 mg%)
- MP QBC - negative
- blood and CSF cultures - sterile
- 2 D ECHO - Good biventricular function
  EF- 60% & Structurally normal heart
Day 1 of PICU admission

- Antibiotics - initiated
  ( ceftraixone / acyclovir / azithromycin & doxycycline)

- **10% Ca. Gluconate - bolus foll. By cont. Infusion**
  (After taking critical sample )
  ( ionic Ca - low in subsequent gases : 0.49 - 0.67 )

- AED - Fosphenytoin and leviteracetam

- ECG - QTc prolongation

- Endocrinologist opinion sought
Day 2:

- abnormal breathing + desaturation (SpO2 - 47%)
- fresh bleed thro’ ET tube + hematuria
- Vitamin k1 - 10mg stat
- Ventilator settings optimised
Probably

Pulmonary edema
? Neurogenic
? Cardiogenic

ARDS
- Urine M/E - turbid, plenty of RBC & pus cells
- Urine culture - sterile
- Repeat RFT - normal
- PT - 16/11, PTT - 37/27, INR - 1.5
- Urine for myoglobin - negative
- CPK (3414) & LDH - 1640
Serology for dengue / scrub / JE - negative

Vitamin D - 3.0 ng/ml ( <20 ng/ml - deficient)

PTH - 2.0 pg/ml ( N : 10-65 pg/ml)

Urine Ca creatinine ratio - 6.8 ( N <0.14)

Thyroid profile - normal

USG abdomen - normal study

Changes in management :

- Antibiotics discontinued
- Subsequent gases - low ionic Ca - Calcium infusion continued
12 hours later

- Hypotension - BP: 72/44 (54); HR - 95/min; CVP - 8

- No improvement with fluid bolus, inotropes initiation, stress dose of steroid

- Settled with bolus calcium infusion - BP: 123/59 (77)

- ABG: 7.33/31/156/18.2/-9.6 / 0.9; iCa - 0.27

- Calcium infusion was continued but at high dose (0.4ml/kg/hr)
Day 3

- Extubated - stridor - NIV
- Calcium infusion contd: (i.Ca- 0.32 - 0.34 - 0.43 - 0.63)
- Repeat Ca - 8.4 phosphorus - 6.8
- Cortisol - 9.0 (hydrocortisone added)
- Ophthalm exam - normal
- ACTH stimulation test - no evidence of primary adrenal insufficiency.
- Discharged on oral vitamin D, Ca & Leviteracetam
- Readmitted after 3 days with fever
- Clinically no focus of infection
- Inves: severe neutropenia
- Emperical antibiotics were initiated
- Cause of neutropenia: probably drug induced (leviteracetam)? Auto immune
- No evidence of hemolysis
- Counts improved with GM CSF
diagnosis

Hypocalcemic seizures secondary to hypoparathyroidism & hypovitaminosis D

? Autoimmune Polyendocrinopathy ? Genetic
Hypocalcemia occurs when serum Calcium is < 8.2 mg/dl (2.05 mmol/l) or ionized Calcium < 4.4 mg/dl (1.1 mmol/l) or below the minimum normal specified by the laboratory reference.

Calcium

↓ Calcium intake:
  - Nutritional deficit
  - Decreased absorption:
    * Vit D deficiency
    * Malabsorption

↑ Calcium loss:
  - Hypoparathyroidism
  - Pseudohypoparathyroidism
  - Decreased Magnesium
  - Increased Phosphorus
  - Hungry bone syndrome
Tetany is uncommon unless serum ionised calcium concentration falls below 4.3 mg% (1.1 mmol/L) or total serum Ca of 7 - 7.5 mg%.

Grand mal, petit mal and focal seizures can occur in hypocalcemia, and may be the sole presenting symptom.


Hypotension may complicate acute hypocalcemia

Decreased myocardial performance and even CCF have been reported

Hypocalcemia characteristically causes prolongation of QT interval in ECG

- Vitamin D deficiency - unrecognized and prevalent problem in adolescents

- adolescents - mostly asymptomatic.

- if symptomatic - signs of hypocalcemia - tetany and rarely seizures

- Moncrieff MW et al. Nutritional rickets at puberty. Arch dis child 1973: 221-224
Incidence of idiopathic hypoparathyroidism and pseudohypoparathyroidism have not been determined in US.

In Japan, a recent survey found the prevalence of idiopathic hypoparathyroidism to be 7.2 cases per million people and prevalence of PHP to be 3.4 cases per million people.

Hypoparathyroidism is equally prevalent in males and females.
Basal ganglia calcifications are a manifestation of long standing hypoparathyroidism

Usually asymptomatic, but variety of hypokinetiс and hyperkinetic movement disorders also seen

Increased intracranial pressure with papilledema also reported


kralik et al. The idiopathic hypoparathyroidism as a cause of intracranial hypertension in an infant. Acta univ carol med monogr. 1976;139-140
Hypoparathyroid myopathy with raised serum creatine kinase levels is another less common neurological syndrome

Autoimmune hypoparathyroidism

Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy syndrome - autoimmune polyglandular syndrome type 1

- mutations in Autoimmune regulator gene

- 3 principal findings:
  - Hypoparathyroidism - 90% after 3 yrs of age
  - Chronic mucocutaneous candidiasis - 70% before 5 yrs
  - Primary adrenal insufficiency - 90% after 6 yrs of age
Hypocalcemia

H&P

PTH, U.Ca: Cr
Bone profile

↓ / Normal PTH

↑ PTH

↑P, ↑U.Ca: Cr

Hypoparathyroidism

↑P, ↑U.Ca: Cr

PHP *

NI.25 (OH) D
↓ 1, 25(OH)2D

↓P, ↓U.Ca: Cr

Renal rickets

↓25(OH)D

Nutritional Rickets or vitamin D dependent rickets (secondary to liver disease or drugs)

* PHP: Pseudohypoparathyroidism
anticonvulsants such as phenytoin, phenobarbital, and carbamazepine are known to aggravate hypocalcemia which would further exacerbate the seizures.

- Unusual age - low serum calcium
- Unusual presentation - seizure with fever (recurrent)
- Unusual course of the disease - flash pulmonary edema
- Rare etiology of seizures - hypoparathyroidism
THANK YOU