A rare case of Fever with rash

From

The Department of Pediatrics
Dr. Mehtas Hospital
Case history

- A 12 yr old girl:
- Fever – 5 days
- Redness of eyes & erythematous rashes over the body for 2 days

Past:
- Febrile fits at 9 mo. Of age
- Afebrile seizure GTCS 2 episodes-feb & may 2011
- EEG → B/L epileptiform discharges
- CT brain normal
- Started on carbamazepine past two weeks
O / E

- Febrile, sick looking
- Conjunctival Congestion
- No koplak Spot
- Mild erythema of lips
- Erythematous macular rashes all over body
- No significant Lymphadenopathy
- RR 26 /min  HR 120 /min Perfusion good
- BP 120/60 mm Hg
- Chest – Normal
- P/A- Liver palpable 2 cm Tender, No splenomegaly
- CNS: conscious, oriented, no meningeal signs
Problem: 1 wk fever, rash, on AED

Working diagnosis –
1. Viral Exanthematous fever
2. Dengue fever
3. Leptospirosis
Blood Investigation

- HB 9.1
- Dc - 2300 ( P60 L36 E4)
- Plt Count 1.53L  PCV 27
- CRP +ve 26
- SGOT 104
- SGPT 67

- WIDAL- Neg
- Lepto IgM-Neg
- Dengue Serology - Neg
- MP- Neg
- Urine-Alb-1+
  sugar-nil
  pus cell 3-5
- Chest x ray-normal
Day - 2

- Still febrile, toxic. No focus could be identified
- Repeat Counts:
  - Hb 8.4  Tc-2200(P48)  ANC 1200
  - Platelet Count - 86000
  - SGOT 297  SGPT 216 - a rising trend.
- PT / PTT, S.Electrolytes, urea, creat - NUSG Abdomen Mild Hepatomegaly
- Suspected: Carbamazepine Induced leukopenia
  Ceftriaxone added. CBZ stopped, phenytoin started
Altered sensorium

- Developed altered sensorium GCS 14/15 PERL
- No meningeal signs, No motor deficit BP 100/40
- Acute encephalopathy – Malaria, leptospirosis Viral Encephalopathy
- Acyclovir, Artesunate, Inj Ceftriaxone
- CT Brain – normal
- Rpt counts – further drop - TC 1600 ANC(668) PLT 70000
Altered sensorium + Febrile neutropenia

- A/B escalated to cefepime.
- Rpt counts-rising trend-TC 1600, PLT 73000.

All the following lab Normal

- Blood c/s, urine c/s, Scrub typhus Igm- neg
- S.ammonia, lactate – normal
- LP-Normal counts, biochemistry, HSV PCR-neg, c/s-neg
10 days of fever with rash, Encephalopathy, leucopenia
Most of the investigation for infection where Negative (Cultures, dengue, lepto, enteric, MP QBC, Smear. No eosinophilia, CSF )
But CRP (36), ESR high (30 min – 36, 60 min 54 ), Atypical lymphocyte
Is Drug induced fever? SJS (No mucosal lesions)
Collagen vascular disease?
Nosocomial sepsis ?
Repeat blood culture were done. Normal
Next day – giddiness, postural hypotension, fresh lesions, bullae over extremities – skin lesion s/o erythema multi forme

- ANA, Anti dsDNA-neg.
- On Phenytoin
- IMP - ANTICONVULSANT HYPERSENSIVITY SYNDROME Induced by PHENYTOIN, CARBAMAZEPINE
# Blood Investigation

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ACCURATE DIAGNOSIS MADE RX EASY

- Phenytoin stopped, changed to levetiracetam
- All A/B, Acyclovir stopped
- Started on antihistamine, glycerine magsulf for L/A
- Became afebrile, skin lesions healed, activity improved
- D/d with oral levipil & antihistamines
- With advice
  
  To avoid all aromatic anticonvulsants (CBZ, phenytoin, phenobarbitone, lamotrigine)
Course of events

- Ist week: fever with rash, Seizure on carbamazepine.
  AED carbamazepine to Phenytoin
- II week: leucopenia persisted. Encephalopathy.
  Common infection excluded
- DD: CVD, SJS, Other
- Mistake we made: Phenytoin as culprit
- AED sensitivity syndrome was not considered till 3rd wk
DISCUSSION

ANTICONVULSANT HYPERSENSITIVITY SYNDROME (AHS)
(AHS) is an acute, life-threatening, idiosyncratic drug reaction seen within 1–8 weeks (usually 2 – 4 weeks) after administration of an aromatic antiepileptic drug - phenytoin, carbamazepine, lamotrigine, phenobarbitone.

- It’s a clinical diagnosis.
- Multiorgan syndrome.
- More severe in previously sensitized individuals.
MECHANISIMS

- Phenytoin class of drugs is metabolised by cytochrome P-450 to intermediate metabolites, arene oxides.
- Arene oxides can contribute to an immunological response or even cause cell death.
- They are usually detoxified by epoxide hydroxylase but there is evidence that the individuals who develop AHS are unable to detoxify arene oxides.
CLINICAL SYMPTOMS

- Fever [90% - 100%].
- Rashes [90%] - macular erythema erythroderma.
- Tender lymphadenopathy [70%]
- Hepatitis [50%].
- Periorbital and facial oedema [25%]
LABORATORY VARIATION

- Elevated liver enzymes.
- Leukocytosis with atypical lymphocytes.
- Eosinophilia.
- Coagulopathy.
- Biomarkers [Deficient epoxide hydroxylase activity and deficiencies in free radical scavenging enzyme activity]
- Treatment of AHS is largely symptomatic.
- Drug should be stopped.
HIGH RISK GROUP ON VALPROATE

- Age < 2 yrs
- Multiple concomitant AEDs
- Underlying metabolic disease.
- Developmental delay.
Anticonvulsant Hypersensitivity Syndrome

DD:
- Usual seasonal illnesses
- Exanthematous illness
- Collagen vascular disease (Kawasaki)
- Malignancy
- Hemophagocytic syndrome
**TAKE HOME MESSAGE**

- Anticonvulsant Hypersensitivity Syndrome should be the first diagnosis in any patient treated with AED who presents with fever, rash or lymphadenopathy.
- The medication should be changed to a different class.
- Although it is rare, recognition is essential to avoid considerable morbidity and possible fatal outcome.
THANK YOU