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 koplik 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

O/ E

- 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)PLT70000

Altered sensorium + Febrile neutropenia

- A/B escalated to cefepime.
- Rpt counts-rising trend-TC 1600,PLT73000.

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

	19/4/11	20/4/11	21/4/11	27/4/11
HB	9.1	8.7	7.9	8.6
PCV	27	26	26	27
TC	2300	2200	1600	7,300
DC	P60L36E4	P58L40E2	P43L45E2	P67L29E3
PLAT	1.53	86,000	70,000	1.17
SGOT	104	297	317	194
SGPT	67	216	223	112

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 HYERSENSITIVITY SYNDROME (AHS)

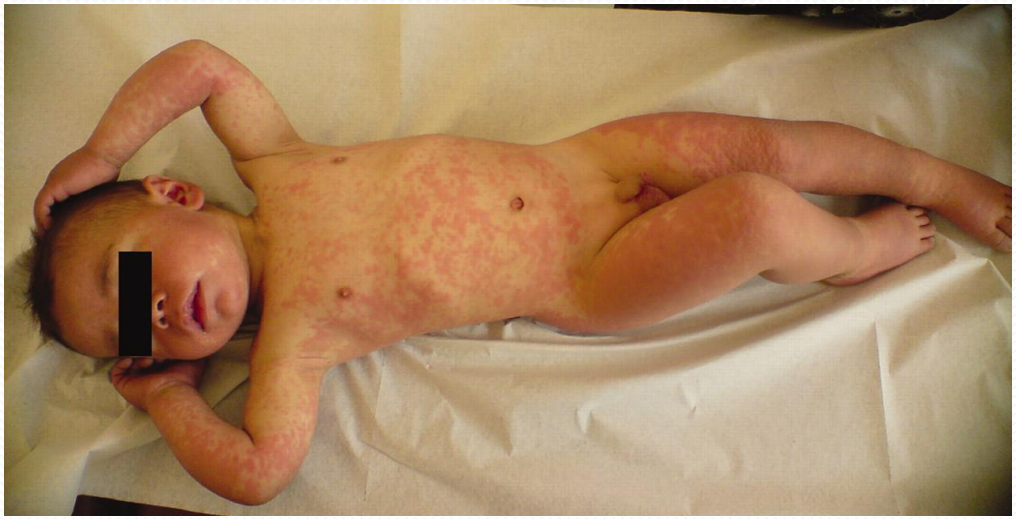
- (AHS) is an acute, life-threatening, idiosyncratic drug reaction seen within 1–8 weeks (usually 2 – 4 weeks) after administration of an aromatic antiepileptic drug - phenytoin, carbamazepine, lamotrigine, phenobarbitone.
- It's a clinical diagnosis.
- Multiorgan syndrome.
- More severe in previously sensitized individuals.

MECHANISIM

- 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 (Kawaski)
- 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