PHENYTOIN INDUCED TOXIC EPIDERMAL NECROLYSIS (TEN) IN AN ADULT

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Abstract

A 38 year old male patient was treated with paracetamol and phenytoin tablets for fever and convulsions. On the fourth day of treatment, he developed generalised erythema and blistering of skin. A provisional diagnosis of toxic epidermal necrolysis was made. Both the drugs were stopped and he was treated with i.v. fluids, antibiotics and steroids. He completely recovered in 15 days.

TEN is a rare immune-mediated life-threatening reaction characterised by widespread erythema, necrosis, and bullous detachment of the epidermis and mucous membranes, resulting in exfoliation and possible sepsis and death. The possibility of occurrence of TEN with phenytoin must be kept in mind. Early diagnosis of the condition and proper treatment with steroids help in recovery.

Key-words: Pharmacogenetics . Toxic epidermal Necrolysis . Phenytoin . Dexamethasone . Adult

Key Messages:
1. Recurrences have been attributed to the same generic drug or compounds chemically related.
2. Patient should avoid reexposure.
3. First line relatives alerted to risk of reaction to same drugs.
4. More awareness in medical field about TEN.

INTRODUCTION:

Toxic Epidermal Necrolysis (TEN) is a rare immune-mediated life threatening reaction for which drugs account more than 95% of cases. Incidence of TEN is 0.4 to 1.2/million/year worldwide. Involves more than 30% skin exfoliation in body. Mortality rate is around 20% to 25%.

PHARMACOGENETICS:

There is strong genetic association between HLA alleles and drug hypersensitivity. Genetic associations can be drug specific, HLA-B1502 with carbamazepine, phenytoin and lamotrigine; HLA-B5801 with allopurinol, HLA-B5701 with abacavir and HLA-DRB10101 with nevirapine. Polymorphisms have been described in Fas gene, IL-13, IL-4R signalling pathway gene and Toll like receptor 3 gene. Phenytoin hypersensitivity syndrome appears to be associated with inherited deficiency of epoxide hydrolase.

CASE HISTORY:

A 38 year old male was brought with history of skin lesions of 4 days duration. There was history of fever and convulsions about a week back for which he was given paracetamol 500mg tablet and phenytoin 100mg tablet. On day 4 after starting the above drugs he developed generalised erythematous patches followed by blistering of skin and he was toxic.

INVESTIGATIONS:

Hb 13 gm%, TC 7000/mm³, DC N- 43, L- 50, E- 3, ESR-20mm/hr, platelet 2.4L/mm³, RBS 126mg/dl, Blood urea 20 mg/dl, Serum creatinine- .43mg/dl, Serum electrolytes Na⁺ 141 mEq/l, K⁺ 4 mEq/l, cl⁻ 100 mEq/l.

HISTOPATHOLOGY:

Epidermal keratinocyte necrosis, subepithelial bullae formation, vacuolation of basement membrane.

TREATMENT:

I.V. fluids, Ceftriaxone -500 mg IV QID – 5 days, Corticosteroids – Dexamethasone 1 amp [4mg/ml] 8th hourly for next 4 days, 1 amp 12th hourly for next 3 days, followed by 1 amp/day for another 3 days. He recovered completely by 15th day.

Figure 1: case pictures
DISCUSSION:

TOXIC EPIDERMAL NECROLYSIS (Lyell's syndrome) is a rare potentially life threatening medical emergency characterised by widespread epidermal sloughing of skin accompanied by mucus membrane involvement. SCORTEN is prognosis scoring for TEN.

CLINICAL FEATURES:

Rash, blisters on skin and mouth, ears, nose, genital area, persistent fever, swelling of eyelids, conjunctivitis, flu like syndrome, recent history of taken a prescription or OTC drugs.

ETIOLOGY:

Drugs, viral infections and vaccinations.

Drugs commonly associated with TEN are antibiotics like sulphonamides, tetracyclines and quinolones; Anticonvulsants like phenytoin, carbamazepine, phenobarbitol and lamotrigine; Antiretroviral drugs like nevirapine; Nonsteroidal anti-inflammatory drugs like phenylbutazone, meloxicam, piroxicam, tenoxicam, valdecoxib and GIT drugs like famotidine and miscellaneous drug allopurinol.

Vaccination with DPT, measles, polio, smallpox and influenza vaccines and contrast media like diatrizoate and iopamidol, vaginal suppository terconazole and toxic fumigant acrylonitrile.

Causality analysis by Naranjo scale reveals this adverse effect is probable.

CONCLUSION:

1. Recurrences have been attributed to the same generic drug or compounds chemically related
2. Patient should avoid reexposure.
3. First line relatives alerted to risk of reaction to same drugs.
4. More awareness in medical field about TEN.

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ACKNOWLEDGEMENT:

The completion of each task is accompanied by acquisition of knowledge and wisdom. Several individuals helped me in the completion of this endeavour. I take this privilege to thank one and all, with all humility and gratitude.