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A RETROSPECTIVE STUDY OF TEN CASES OF TOXIC EPIDERMAL NECROLYSIS AND THE ASSESSMENT OF PROGNOSIS BASING ON AETIOLOGY AND THE SCORTEN – A CASE SERIES

Dermatology

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ABSTRACT

Background: Toxic epidermal necrolysis(TEN) is an acute cutaneous drug reaction (ACDR) first described by Alan Lyell in 1956.1,2 It is a life threatening mucocutaneous reaction, with a mortality of 25 to 30%.3,4 Granulysin causes massive keratinocyte apoptosis, a hallmark of TEN,5 which has been recently termed as Epidermal Necrolysis (EN).1 EN is responsible for the loss of skin barrier function leading to acute skin failure.3 With multidisciplinary approach, morbidity and mortality could be significantly minimized. **Objective:** To elucidate the clinical features, treatment response of the patients on withdrawal of the offending drug, and to assess the prognosis based on the SCORTEN value. **Methodology:** All patients with the clinical diagnosis of TEN who had prior drug intake were admitted. **Results:** SCORTEN was recorded and the offending drug was withdrawn. Appropriate investigations were done. Three drugs were found to be implicated in descending order NSAIDS (50%), anticonvulsants (30%) and antibiotics (20%). With interdisciplinary approach, all the patients were treated. Among ten patients, one patient died and the remaining patients recovered well without morbidity. **Limitations:** Small sample size. **Conclusion:** Along with early admission, prompt withdrawal of the offending drug and co-ordinated multidisciplinary approach, the mortality rate could be minimized.

KEYWORDS

Toxic epidermal necrolysis, SCORTEN, drugs.

INTRODUCTION:

Toxic epidermal necrolysis is a drug induced acute cutaneous drug reaction(ACDR) affecting the skin and mucous membranes. TEN is characterized by fever, associated with wide spread necrosis and exfoliation of the skin along with erosions of the mucous membranes. The skin was tender for touch and more than 30% of the body surface area (BSA) is involved with systemic involvement having a mortality rate of 25 to 30%.[6] Recently granulysin was shown to be the main implicating factor in the occurrence of massive keratinocyte apoptosis.[5]

Most of the TEN cases were due to drugs and as per one study, measles-mumps rubella vaccine and mycoplasma pneumonia infection were also found to be the causative factors.[6]

Methodology:

All the patients were admitted in Intensive Medical Care Unit (IMCU) and a detailed history revealed that most of the patients have taken drugs prior to the present complaint of fever with rash. The results were tabulated in the following proforma:

(1) The interval between intake of drug and appearance of the skin rash
(2) Location of the rash first appeared over the body
(3) Prodromal symptoms such as fever
(4) Presence of tenderness over the involved skin
(5) Shape of the lesions
(6) Extension of skin involvement
(7) Involvement of mucous membranes
(8) Signs of systemic involvement.

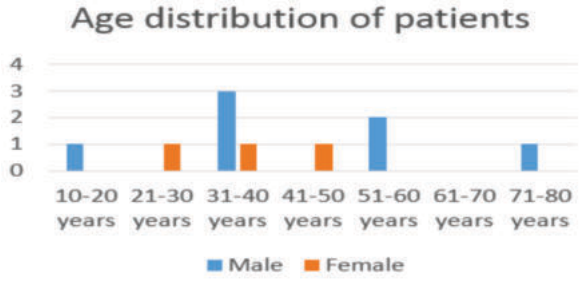
A battery of investigations were done and the SCORTEN value was recorded for all the patients. The offending drug was immediately withdrawn and the patients were treated with 1) Supportive therapy 2) Intravenous dexamethasone 3) Conventional antibiotics 4) Intravenous Immunoglobulins (I.V Ig). All the patients were followed for a period of 3 months for any recurrences.

RESULTS:

All the ten patients who attended the department of dermatology with the complaints of fever with rash were admitted. Among the ten patients, 7 were male and the rest of the three were female patients. The male patients were in the age group of 18 to 72 years and the female patients were in the range of 22 to 45 years. The mean age was 40 years with the male to female ratio of 2.33:1. In our group of ten patients, 4 patients were in the age group of 31 to 40 years.

Table 1: Showing the age distribution of the patients.

Age	Male	Female
10 - 20 years.	1	-
21 - 30 years.	-	1
31- 40years.	3	1
41- 50years.	-	1
51- 60years.	2	-
61- 70 years.	-	-
71- 80years.	1	-



The duration between drug intake and appearance of the skin rash was found to be between 5 days and 28 days.

Table 2: Showing the interval between the drug intake and the appearance of the rash.

Drug implicated	Appearance of rash after drug intake
NSAIDS	1 to 2 weeks
Ofloxacin	5 days
Anticonvulsants	3 to 4 weeks
Metronidazole	1week

Prodromal symptoms such as fever and malaise were present in all the patients except in the TEN case caused by metronidazole. In three cases, history of seizures were present and in another case systemic

lupus erythematous was present. In all the patients, primary site of involvement was the trunk followed by involvement of other parts of the body such as face, upper limbs, lower limbs and palms and soles. Oral, conjunctival and genital mucosae were involved in all the patients with complaints of burning sensation in the mouth, difficulty in swallowing and burning micturition. In all the patients, SCORTEN score was calculated at the time of admission

Table 3: Showing the SCORTEN score of all the patients with prognosis.

Case No.	SCORTEN	Predicted Mortality Rate
1. Male 55 years	3	35%. died
2. Female 45 years	2	12%
3. Male 72 years	3	35%
4. Male 33 years	2	12%
5. Male 36 years	1	3%
6. Male 18 years	1	3%
7. Male 32 years	1	3%
8. Female 22 years	1	3%
9. Male 53 years	3	35%
10.Female 32years	1	3%

Majority of the patients attended the hospital soon after the onset of fever, malaise associated with the skin rash, except Case 1, a male patient who was treated by a local village doctor not having medical registration and his SCORTEN value was 3 with a predicted mortality rate of 35% at the time of admission. The involved drug was an analgesic (NSAID) and the patient was brought to the hospital after the onset of systemic symptoms. SCORTEN score of the remaining patients was in the range of 3 to 12%, except case 3, a 72 year old male, presented with the SCORTEN value of 3 with good improvement after treatment and the culprit drug was ofloxacin. The interval between the consumption of ofloxacin and appearance of the skin rash was 5 days and the patient seeked treatment immediately. NSAIDs were found to be involved in 4 cases (case 1, 2, 4, 8, and 10). Anticonvulsants such as Phenytoin and carbamazepine were reported to be culprit drugs in 3 cases (case 5, 6 and 9). All patients who attended the hospital immediately after the onset of fever with rash were recovered completely except one patient who died and the following factors such as treatment by a quack doctor, and delayed hospitalization could be attributed for the cause of death.

Table 4: showing the culprit drugs and the number of patients affected

Implicated Drug	Number of patients
NSAID	5
Anticonvulsants	3
Ofloxacin	1
Metronidazole	1

DISCUSSION:

Men were more affected than women in our study where as other studies revealed female preponderance.[7,8]

The age of onset of TEN cases in our group was between second and eighth decades, with the occurrence of 4 cases in fourth decade and two cases in the sixth decade in concurrence with one previous study.[9] Sharma VK et al showed more number of cases in the second decade whereas in our study one case was observed which could be attributed to small sample size.[7]

History of drug intake was present in all the patients of our study and a similar observation was reported in a previous study.[7] Review of literature showed absence of drug intake prior to the appearance of skin rash in TEN cases, however similar feature was not observed in our study.[9,10] As in the previous studies, single drug was found to be an implicating factor in the occurrence of TEN cases in our study.[7,9,10]

In the present study, NSAIDS were reported to be associated with the occurrence of TEN cases followed by anticonvulsants and antibiotics. A similar observation was reported in the literature.[7] Among the anticonvulsants, carbamazepine in two cases (**Figure 1a,1b,2a,2b**) and Phenytoin in one case of TEN were reported to be the causative drugs constituting 30% in our group and a similar percentage of 35.08% was reported by Sharma et al[7] and a percentage of 35.73% was reported in another sturdy.[8]

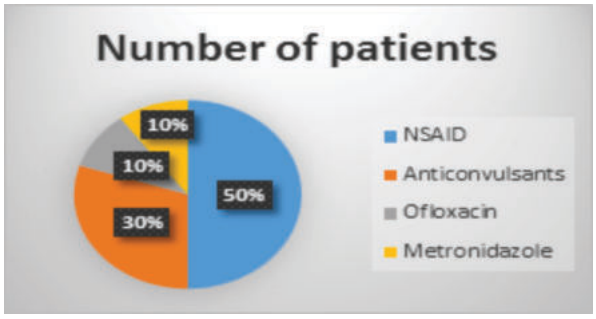


Figure 1a: 53 year old male patient – TEN due to carbamazepine (Pre-treatment)

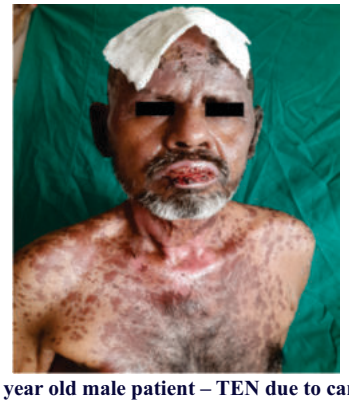


Figure 1b: 53 year old male patient – TEN due to carbamazepine (Pre-treatment)

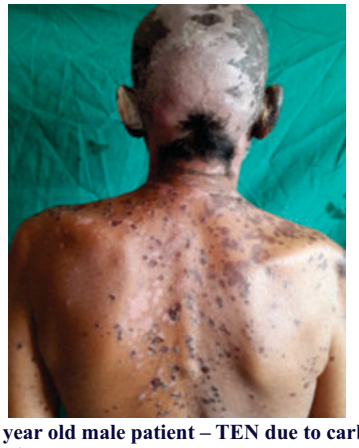


Figure 2a: 53 year old male patient – TEN due to carbamazepine (Post-treatment)

Figure 2b: 53 year old male patient – TEN due to carbamazepine (Post-treatment)

Few studies showed that anticonvulsants were the most common causes of ACDRs.[11,12] In one study, anticonvulsants were shown to be the culprit drugs of erythema multiforme (EM), SJS and TEN.[13] In our study, NSAIDS were found to be the common implicating drugs among five cases of TEN and a similar observation was reported in a French survey done by Roujeau JC et al in the year 1990.[9]

In our group the offending drug was withdrawn immediately and the patients were admitted in IMCU. After calculation of the SCORTEN value, general supportive therapy was instituted along with primary investigations and special tests were done as and when required. Under strict aseptic environment and barrier nursing care all patients were treated with antibiotics, intravenous dexamethasone, and in one patient Intravenous Immunoglobulin (IVIG) was given with good response (**Figure 3a,3b,4a,4b**).

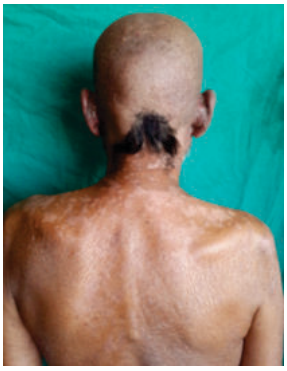


Figure 3a: 18 year old male patient – TEN due to carbamazepine (Pre-treatment)

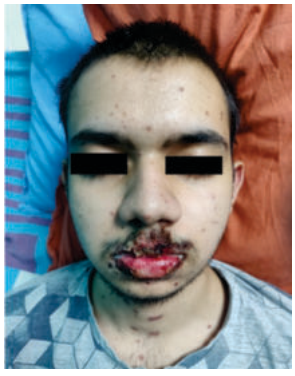


Figure 3b: 18 year old male patient – TEN due to carbamazepine (Pre-treatment)

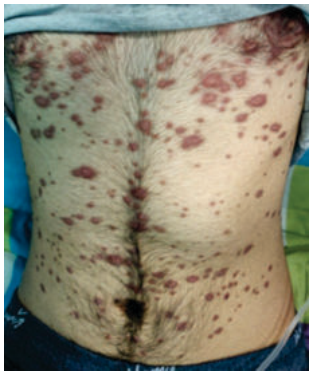


Figure 4a: 18 year old male patient – TEN due to carbamazepine (Post-treatment)

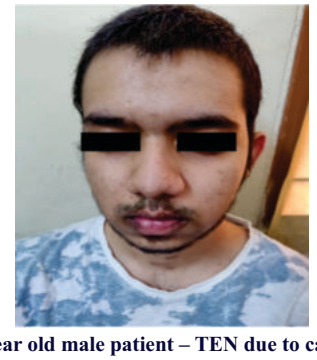


Figure 4b: 18 year old male patient – TEN due to carbamazepine (Post-treatment)

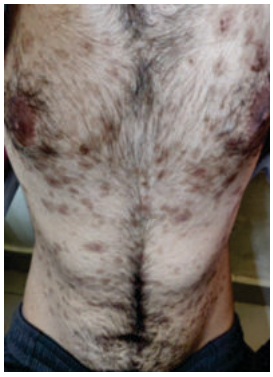


Figure 4b: 18 year old male patient – TEN due to carbamazepine (Post-treatment)

All the patients were recovered completely without scarring mucosal sequelae, except one patient died, the cause of death was found to be due to septicaemia and multiple organ failure which was in concurrence with other studies.[14] The bad prognosis in this case could be attributed to treatment by a quack doctor and delayed admission.

CONCLUSION:

Among all Adverse Cutaneous Drug Reactions, TEN is a dermatological emergency where more than 30% of the body surface area is involved. The common offending drugs in our study were NSAIDS and anticonvulsants. SCORTEN was a prognostic index to assess the severity. The mortality rate could be reduced by prompt withdrawal of the offending drug along with supportive therapy, IV dexamethasone, and prophylactic antibiotics.

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