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Two Cases of Quinine Induced Toxic Epidermal Necrolysis- A Case Report

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Abstract: *Toxic epidermal necrolysis is a common life threatening dermatological emergency. It occurs most often as an adverse drug reaction due to drugs like NSAIDS, antibiotics, anticonvulsants, quinolones. It is acute in onset and involves integumentary system and other systems having high mortality. This condition necessitates intense management because of acute skin failure characterised by confluent purpuric and erythematous macules evolving in to flaccid blisters and epidermal detachment predominantly on the trunk and upper limbs and associated with mucous membrane involvement. Awareness regarding drugs causing TEN is known but Quinine as an etiological factor is never reported as cause for TEN in existing literature. Here we are reporting three cases which developed signs and symptoms of TEN shortly after initiating Quinine therapy. The cause in this cases was found to be Quinine which was given to patients undergoing treatment for Malaria. Usage of Quinine in cases with Falciparum Malaria is still being practised by many physicians and awareness of this dreaded complication is important.*

Keywords: *Toxic epidermal necrolysis, Integumentary system, Quinine, TEN*

I. Introduction

Cutaneous drug eruptions are one of the most common types of adverse reaction to drug therapy, with an overall incidence rate of 2-3% in hospitalised patients (1, 2, and 3). Toxic epidermal necrolysis (TEN), or Lyell's syndrome, is a medical emergency. TEN is a life threatening adverse drug reaction and many drugs like NSAIDS, antibiotics, anticonvulsants, antiepileptics and anti-inflammatory drugs have drug eruption rates approaching 1-5% (4). Quinine has been used worldwide for hundreds of years in the treatment of malaria. However, quinolones have been implicated as etiological factors. Clinically it presents as confluent purpuric and erythematous macules evolving to flaccid blisters and epidermal detachment predominantly on the trunk and upper limbs and associated with mucous membrane involvement due to massive keratinocyte apoptosis (5). Main affector cells are cytotoxic T-lymphocytes (6). Incidence is 0.4 to 1.2 cases/million/year (7). Mortality is as high as 30% (6 & 7). More than 220 drugs have been implicated in TEN (10).

II. Case Reports

Case1: A 15 year old female patient came with chief complaint of generalised peeling of skin for 6 days.
Case2: A 18 year old female patient came with chief complaint of generalised peeling of skin for 7 days.

These cases were treated for fever with antipyretics, antibiotics. The patients did not respond. Then QBC was done and it is positive for P. falciparum. Then they were put on Quinine and artesunate. Shortly after Quinine therapy they initially complained bilateral conjuctival redness, later erythematous papules and macules on both upper and lower limbs occurred and later progressed to involve the whole body. These lesions progressed to form fluid filled lesions which denuded to form raw areas. Hoarseness of voice present difficulty in deglutition present. On general examination they were moderately built and nourished. They were in hypovolemic shock. On dermatological examination large bullae and vesicles distributed all over the body involving upper, lower limbs, trunk, and genitalia. Haemorrhagic crusting over both the eyes and lips, palms and soles also involved. Nikolsky's sign both direct and indirect positive in these two cases.
SCORE TEN for assessing the severity-1point for each parameter. Evaluation of prognosis including predicted mortality is done.

Parameter	Standard value	1st case	2nd case
Age	40yrs	15yrs	18yrs
HR	120	110	115
BSA	>10%	>70%	>60%
Bl. Urea	28mg/dl	22mg/dl	23mg/dl
RBS	252mg/dl	100mg/dl	100mg/dl
S. bicarb	<20meq/l	22meq/l	21meq/l
Malignancy	Present	Not present	Not present

It should be done at the time of admission and 3rd day.
Mortality basing on score TEN:

SCORE TEN	Predicted mortality (%)
0-1	3.2
2	12.1
3	35.3
4	58.3
5	90

Score Ten & mortality: 1st case: 3.2% and 2nd case: 3.2%

The lesions were biopsied in these two cases and the report came as features suggestive of TEN includes epidermal spongiosis, exocytosis and necrotic keratinocytes and Quinine was stopped and intense treatment was initiated with respect to maintain their fluid and electrolyte loss, using safer antibiotics to control infections. A short course of systemic steroids in the first week. Out of 2 cases, one case recovered completely and one patient died on 4thday.The person who died reported late and extensive involvement and died due to septic shock. This also necessitates the early reporting and intensive management.

III. Discussion

Complications of drug therapy are a major cause of patient morbidity and mortality. Drug eruptions present themselves as common eruptions to rare and life threatening situations like Toxic epidermal necrolysis. Incidence of TEN include 0.4-1.2 cases/million (7). It may occur at any age but incidence increases with age after 4thdecade.More common among female with M: F-0.6.patients infected with HIV virus, collagen vascular disease and cancer patients are at increased risk (8 & 9). More than 100 drugs have been reported as possible causes. Pathogenesis of TEN include widespread massive apoptosis of keratinocytes provoked by cell mediated cytotoxic reaction. TEN is clinically characterised by confluent purpuric and erythematous macules evolving to flaccid blisters and epidermal detachment predominantly on the trunk and limbs and associated with mucous membrane involvement. TEN characterised histologically by sparse apoptotic keratinocytes in the suprabasal layers, sub epidermal cleavage, mononuclear cell infiltrate in papillary dermis. Complications include sepsis, multiorgan failure and pulmonary complications leading to death. Late ophthalmic complications in 20-75% patients are also reported. Prognosis is not affected by type or dose of drug and it is estimated by SCORE TEN. These patients should be treated in intensive care unit. Early identification and withdrawal of susceptible drugs are essential. Symptomatic supportive care is very important. Short course of corticosteroids can be given (10).

IV. Conclusion

Drugs causing TEN are well documented in literature. Drugs like sulphonamides, NSAIDS, carbamazepine cause frequently but many others cause rarely. In the existing literature TEN due quinine not documented but for a few reports. Malaria being an endemic disease in south India the chances of getting this complication can be frequent. These cases give a note of caution to treating physician while prescribing quinine.

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Fig -1, Case report -1 the quinine induced TEN (18 year old female patient came with chief complaint of generalised peeling of skin for 7 days.)

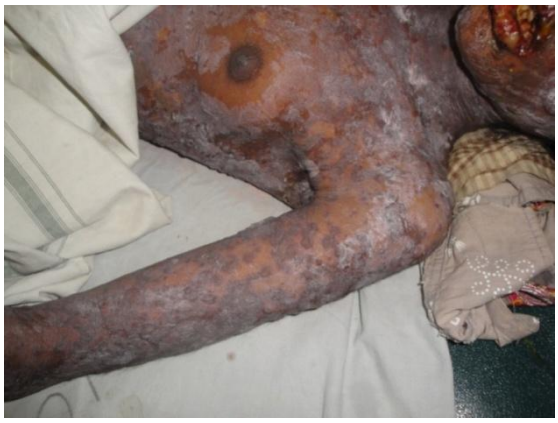

Fig -2, Case report -1 the quinine induced TEN (18 year old female patient with erythematous papules and macules on both upper and lower limbs and the whole body.)

Fig – 3 Case report -2 the quinine induced TEN (A 15 year old female patient came with chief complaint of generalised peeling of skin for 6 days)