TOXIC EPIDERMAL NECROLYSIS IN MALAYSIAN ADULTS A RETROSPECTIVE STUDY

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SYNOPSIS

We report a retrospective study of all cases of toxic epidermal necrolysis admitted to the adult medical wards of the University Hospital in Kuala Lumpur over a 16 year period from 1967 to 1983. Over this period of time only 7 cases were encountered, suggesting the condition is rare in adults in our country. All the cases were females and the age ranged from 21 to 41 years. Four cases were due to drugs, 2 were idiopathic and one was attributed to Staphylococcal infection. One patient died. The other patients recovered completely with no sequelae.

INTRODUCTION

Toxic epidermal necrolysis (TEN) is a dramatic but rare dermatological disorder characterised by inflammed and necrotic epidermis which strips off easily, giving an appearance resembling extensive scalding. We report a retrospective study of the disease as seen in adult patients at the University Hospital in Kuala Lumpur over a period of 16 years from 1967 to 1983.

METHODS

A computer search of all admissions to the adult medical wards of the University Hospital over the period of study from 1967 to 1983 was programmed and carried out and the case records of those patients with the diagnosis of toxic epidermal necrolysis were reviewed. Clinical, laboratory and follow-up data were obtained from the case records. All the patients had been seen and managed by dermatologists. Most of the cases have photographic records which showed the distinctive lesions.

FINDINGS

Over the 16 year period reviewed in this study only 7 cases of toxic epidermal necrolysis were encountered. This accounted for only 0.001% of total medical admissions (71,355) to the hospital.

The patients ranged in age from 21-41 years. All the patients were females. Four of the patients were Chinese and 3 were Malays.

The clinical details of the patients are summarised in Table I. The typical appearance of the skin is illustrated by Figure 1 which is a photograph of Case 7. The results of investigations are shown in Table II while the etiological association, treatment and course of the disease are detailed in Table III.

TABLE I CLINICAL FEATURES

Case	Age (years)	Sex	Race	Duration of symptoms (days)	Itch	Pain	Fever	Extent skin lesions	Conjunctivitis	Buccal lesions	Lymph-adenopathy	Involvement other system
1	21	F	M	14	+	+	+	limbs & trunk	0	0	0	0
2	25	F	M	7	+	+	+	chest & lower limbs	0	0	0	0
3	30	F	C	3	+	+	+	generalised	+	+	0	0
4	30	F	C	10	0	0	+	generalised	0	0	0	0
5	41	F	C	3	0	+	+	generalised	+	+	0	0
6	25	F	M	4	+	0	+	generalised	0	0	generalised	0
7	24	F	C	14	+	+	+	generalised	0	0	inguinal	0

F = Female
M = Malay
C = Chinese
+ = present
0 = absent

Figure 1 Typical appearance of skin in TEN with necrolysis and separation of skin.

TABLE II INVESTIGATIONS

Case	Anaemia (<12G/dl)	Leucocytosis (>10,000/mm³)	Eosinophilia (>300/mm³)	Raised ESR (>10 mm/hr)	Proteinuria (>300 mg/24 hr)	Hematuria (>10/mm³)	Raised serum creatinine (>1.4 ug/dl)
1	0	0	0	+ (21 mm/hr)	0	0	0
2	+ (11G/dl)	0	+ (968/mm³)	0	0	0	0
3	0	0	0	+ (10 mm/hr)	+	0	0
4	0	+ (12000/mm³)	+ (720/mm³)	+ (44 mm/hr)	0	0	0
5	0	0	0	+ (20 mm/hr)	0	0	0
6	0	+ (1380/mm³)	+ (690/mm³)	+ (53 mm/hr)	0	0	0
7	0	+ (14400/mm³)	0	0	+	0	0

TABLE III ETIOLOGICAL ASSOCIATION, TREATMENT AND COURSE OF DISEASE

Case	Drug	Staphylococca infection	Systemic treatment	Progress	Follow-up period
1	0	0	Prednisolone	Healed after 1 week	5 years
2	+ ? name	0	0	Healed after 1½ weeks	3 years
3	+ (Beserol injection)	0	Prednisolone + cloxacillin	Healed after 3 weels	4 years
4	0	0	Prednisolone + cloxacillin	Healed after 2 weeks	2 weeks
5	+ (levamisole)	0	Prednisolone + cloxacillin	Died after 2 week	—
6	+ (penicillin)	0	Prednisolone	Healed after 4 weeks	1 year
7	0	+	Prednisolone + Fucidin	Healed after 2 weeks	4 weeks

DISCUSSION

Toxic epidermal necrolysis was first described in 1956 independently by Lyell in Scotland and Lang and Walker in South Africa (1). The condition is characterised by the acute onset of systemic symptoms in association with diffuse erythema and an easily detachable epidermis.

The syndrome was originally described in adults. However, in the 1960s several investigators recognised the clinical and histologic similarity between this and a clinical syndrome described in infants by Ritter in 1878 and it is now accepted that TEN is a syndrome that can occur in different age groups with slight variation in etiologicasl association and clinical manifestations. It has been stated (1, 2) that most cases of TEN in infants and children are related to Staphylococcal infection, epidermolysis tends to be extensive and though conjunctivitis is frequent, involvement of the buccal mucosa is uncommon. In contrast, in adults the majority of cases are related to drugs, epidermolysis may be less extensive and buccal mucosal involvement is a feature (in addition to conjunctivitis which is also frequent).

Our study is confined to adult patients. In our experience TEN is rare in the local adult population sampled in the study. Over a period of 16 years only 7 cases were seen. The incidence of TEN in adults has not been documented in the literature. However, it is generally considered to be rare in the Western countries too (3). For instance, Beare (4) reported that he saw only 1 case of adult TEN over a 2½ year period in a hospital in Northern Ireland.

All our 7 patients were females. In other reports the condition has been found to occur in both males and females, albeit with a female preponderance (2, 4). Lyell (2) has quoted an average female:male ratio of 3:2 in all groups of TEN. The lack of male patients in

our series is interesting but one should not attach too much significance to this observation as our series is small.

Our patients were all young and fell into the 21-41 age range. This is in contrast to the experience in Western countries where the majority of cases of adult TETN are middle-aged or older.

Clinically all but one of our patients had fever. The rash was very extensive in 5 patients but in 2 patients it was limited to certain parts of the body. In all cases there was sparing of the hairy parts of the body. This feature of sparing of the hairy parts has been noted by other workers (4). Some authors have stressed that the rash usually starts in the flexures and the neck (4) but in our patients the rash appeared to start simultaneously in several areas without any definite sequence. Pain and skin tenderness have been reported to be a striking feature in TEN. Five of our 7 patients did complain of these symptoms (Table I). However, an equal number also complained of mild pruritus in the early stage of the rash, a feature which has not been highlighted in other reports (1, 2, 4). In contrast to other reports (1, 2) too, conjunctivitis and buccal erosions were not frequent in our patients, and only 2 patients showed these signs. There was no clinical evidence of involvement of the lungs or other systems. This is in contrast to Stevens-Johnson syndrome, another condition with severe eruptions often due to drugs, where lung, renal and other visceral involvement are fairly common.

The laboratory investigations revealed anaemia in 1 patient; leucocytosis in 3 patients, eosinophilia in 3 patients, raised ESR in 4 patients and transient proteinuria in 2 patients. Transient proteinuria in TEN is well documented (2) but the white cell count and eosinophils are reportedly 'seldom raised' (2). Our experience suggests that leucocytosis and eosinophilia are in fact not uncommon.

Etiology wise, apart from drugs, which constitute the common cause of adult TEN, the syndrome in this age-group can also be:-

a) incidental to certain systemic disorders (like lymphoma, measles, vaccination, radiotherapy)
b) idiopathic, and
c) rarely due to Staphylococcus aureus infection (2, 5).

In our 7 patients, 4 had association with drugs, 2 were idiopathic and 1 was attributable to Staphylococcus aureus infection. The drugs implicated were penicillin in one case, beserol (a combination of paracetamol and chlormeranone) in another and levamisole in a third case. The fourth patient took a drug which was not identified. Levamisole in the third patient was given by a general practitioner for suspected systemic lupus erythematosus (she initially had a photosensitive rash with polyarthralgia). However subsequent investigations for systemic lupus erythematosus (complements, anti-nuclear factor, skin biopsy for histology and lupus band test were all negative). In the other 3 cases the drugs were prescribed for what in retrospective appear to be upper respiratory tract infections. The interval between drug ingestion and onset of TEN varied from 2 to 10 days. In the literature, the drugs which can cause TEN are chiefly: sulphonamides, sulphones, pyrazolone derivatives and barbiturates (2, 3, 5). Penicillin, aminopyrine, phenolphthalein and salicylates are also known to be associated with TEN (1, 5). To the best of our knowledge, TEN associated with levamisole therapy has not been previously reported. The case associated with Staphylococcal infection is worthy of comment too as this etiological factor, though common in paediatric patients with TEN, is very rare in adult cases (1, 6). When Staphylococcus-induced TEN is observed in adults, it may reflect defective host defence mechanisms (1), particularly a defect in cell-mediated immunity (2). Our case of Staphylococcal TEN occurred in a 24 year old female who was otherwise well clinically and was not known to have any associated debilitating disease or preceding treatment with immunosuppressive drugs. Unfortunately we did not do humoral or cell-mediated immunological studies on her and hence are not able to say definitely if she had any occult defect in her defence mechanisms. In this patient the TEN occurred a few days after she had a stye in the right lower eyelid. Staphylococcus aureus was cultured from the stye as well as from a specimen of mid-stream urine. No drugs were given before the onset of the TEN.

Of our 7 cases, one patient died, giving a mortality rate of 14%. An overall mortality for TEN of 23% has been reported by Lyell (2). In children the mortality rate is lower and has been observed to be around 3% (2, 3). In adults, though, the mortality has been estimated at 22% to 50% (3), with the prognosis being worst in those in the idiopathic group. Our only fatality occurred in one of the patients who had drug-associated TEN. In all the other cases the lesions healed after an average of about 2½ weeks and no recurrence has been observed in the patients over a period of follow-up (as long as 5 years in 1 case). Other authors (2, 5) have reported occasional instances of scarring but we did not observe any such complication. The idiopathic type of TEN in adults is also reported to have a tendency to recurrence (2, 6) but none of our 2 cases with this type of TEN had any recurrence.

All but one of our patients were treated with systemic steroid (prednisolone 40-60 mg per day). Parental fucidin was given in addition, in the patient with Staphylococcus-induced TEN. Two of the patients with drug-associated TTEN and 1 of the patients with idiopathic TEN were also given systemic cloxacillin for suspected secondary sepsis. The role of prednisolone in TEN is still unclear. A trial in 18 cases with Staphylococcal TEN showed that corticosteroids could be harmful (6). In non-Staphylococcal cases Lyell (2) is of the opinion that corticosteroid is not likely to play a major part in recovery from TEN. Esterly (1) and Sneddon (5) feel that there is a possible, though not proven indication for systemic prednisolone.

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