July/ 2022

Department of Health Research
Ministry of Health and Family Welfare, Government of India

Standard Treatment Workflow (STW)

CUTANEOUS ADVERSE DRUG REACTIONS- PART B

ICD-10-L27.0

Cutaneous adverse drug reactions (cADR) are undesirable clinical manifestations to a drug, which include predictable or unanticipated side effects, with or without systemic involvement.

COMMON TYPES OF cADR

NON- SEVERE cADR

- Fixed drug eruption (FDE)*
- Maculopapular/ Exanthematous reactions*

SEVERE cADR

- Drug induced hypersensitivity syndrome/ DRESS
- Acute generalized exanthematous pustulosis
- Angioedema/ Anaphylaxis*
- Erythema multiforme/ Stevens Johnson syndrome/ Toxic epidermal necrolysis

***Refer to separate STW on Urticaria/ Angioedema, and cADR Part-A for FDE/ Maculopapular/ Exanthematous reactions**

DRUG RASH WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME

- Potentially life threatening systemic adverse reaction
- Onset 2-6 weeks after start of drug intake (up to 12 weeks)
- The rash may continue to progress weeks to months after discontinuation of the drug
- Commonly observed with anticonvulsants, dapsone, allopurinol, abacavir, leflunomide, minocycline

When to suspect DRESS syndrome

- Exposure to a high risk drug
- Clinical presentation: fever (>38°C-40°C), rash, leukocytosis with eosinophilia, lymphadenopathy, hepato-renal dysfunction
- Features of the rash: involves >50% body surface area, facial edema, desquamation or dusky erythema
- Occasionally pustules and targetoid lesions may be seen

MANAGEMENT

PRIMARY CARE

- Withdraw drugs
- Assess vitals, stabilise the patient and refer to higher center
- Symptomatic relief: Antihistamines, emollients
- Do not add any unnecessary new medications

SECONDARY CARE

- Same as primary care
- CBC, absolute eosinophil count (optional), LFT, renal function- monitored at least weekly
- CXR, ECG and ECHO to rule out myocarditis
- **Treatment**
- If no evidence of major organ involvement
- First line- Systemic steroids- Prednisolone 0.5-2 mg/kg, slow taper after symptoms and signs resolve (over months if needed)
- Antihistamines-Pheniramine 25 mg TID, bland emollients like liquid paraffin
- If there is severe organ involvement- liver, renal or cardiac refer to tertiary center for multidisciplinary intensive care

TERTIARY CARE

- Same as primary/ secondary care
- Second line - Cyclosporine (if the renal function is normal)
- Management will require a multidisciplinary team approach, depending on the organ(s) involved
- In the presence of severe liver failure, hemophagocytic syndrome, gastrointestinal bleeding, multiorgan failure, the patient may require intensive care treatment

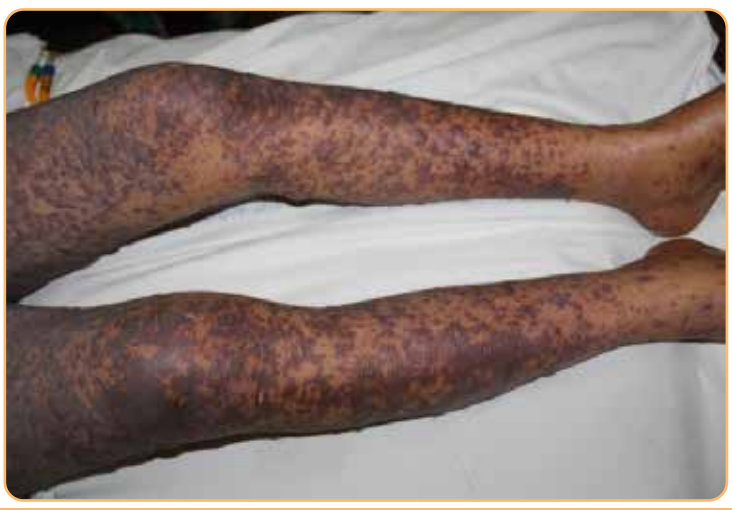
STEVENS JOHNSON SYNDROME (SJS) AND TOXIC EPIDERMAL NECROLYSIS (TEN)

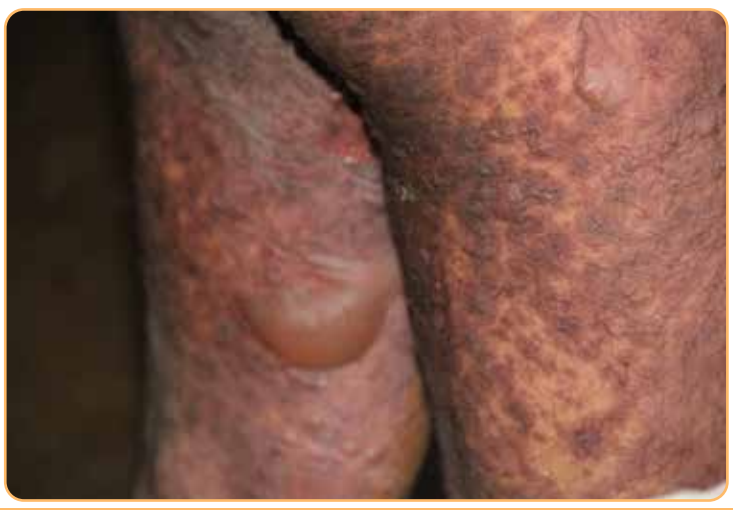
- Acute, severe mucocutaneous reactions associated with epidermal detachment and/ or tenderness, and widespread erythematous lesions with central dusky erythema or vesiculation often associated with high grade fever
- Usually observed with aromatic anticonvulsants, allopurinol, nevirapine, abacavir, NSAIDs, co-trimoxazole
- The classification of SJS, TEN is based on the extent of detachment
- D/d-Staphylococcal scalded skin syndrome, pemphigus

TYPE	DETACHMENT (% BSA)	WIDESPREAD ATYPICAL TARGETS *OR ERYTHEMATOUS MACULES
SJS	<10%	Present
SJS-TEN	10-30%	Present
TEN	≥30%	Present
TEN without SPOTS	≥10%	Absent

*Atypical targets (Red macules with purpuric vesiculations/ crusted centers)

TOXIC EPIDERMAL NECROLYSIS





PROGNOSIS

SCORTEN PROGNOSTIC FACTORS	POINTS
Age > 40 years	1
Tachycardia > 120 bpm	1
Neoplasia	1
Initial detachment > 10%	1
Serum urea > 60 mg/dL	1
Serum bicarbonate < 20mmol/L	1
Blood glucose > 252mg/ dL	1

Assess prognosis with a SCORTEN score done within 24 hours of presentation and repeated 3 days later

SCORTEN SCORE	ESTIMATED MORTALITY %
0-1	3
2	12
3	35
4	58
≥ 5	> 90

INVESTIGATIONS

- Chest X- ray
- ECG
- **Laboratory tests-** CBC, LFT, KFT, electrolytes, magnesium, phosphate, lactate
- Blood gas analysis
- **Microbiology-** Pus culture from infected areas and blood culture
- **Skin biopsy-** Not usually required unless the diagnosis is in doubt
- **Optional-** In TEN, biopsy and direct immunofluorescence is useful to rule out SLE and pemphigus

MANAGEMENT

PRIMARY CARE

- See primary care for drug rash with eosinophilia and systemic symptoms (DRESS)

SECONDARY CARE

- Assess vitals, stabilise the patient, nutrition and fluid replacement as appropriate
- Local care for skin and mucosae
- Skin care- dilute potassium permanganate baths/ saline compresses/ Chlorhexidine baths
  - Detached epidermis can be left in situ and covered with non-adherent dressing (sterile vaseline gauze)
  - Topical antibiotics (Mupirocin or Fucidin) on sloughed off areas
  - Oral care- Rinse mouth with Chlorhexidine 2-3 times, soft paraffin on lips as needed, steroid mouth washes
  - Eye care- refer to ophthalmologist
- Antibiotics-broad spectrum antibiotics (in case of sepsis or secondary infection) to cover staph, strep and pseudomonas. Change according to culture results and avoid suspected drug class
- Adjuvant systemic therapy (ideally within the first 24-72 hours of onset)
  - The role of systemic steroids is limited to early phase of SJS/TEN. High doses for longer periods can increase the risk of sepsis and metabolic complications. However judicious use of Prednisolone 1-2 mg/kg or equivalent dose of intravenous Dexamethasone for 3-7 days may be of benefit
  - Cyclosporine in a dose of 3-5 mg/kg for a period of 10-14 days (with monitoring)
- If skin detachment >10% refer to a center with an ICU familiar with management of skin failure
- If < 10% follow the treatment as described

TERTIARY CARE

- Admit in specialized units within dermatology wards if vitals are stable and follow secondary care treatment
- Barrier nursing
- If patient has SIRS/ sepsis or in shock, admit to ICU
- Long term follow up will be required to address complications: ophthalmic, skin and respiratory tract involvement

☛ ANY DRUG BELONGING TO ANY MEDICINAL SYSTEM CAN CAUSE cADR