Skin Manifestations of Drug Reactions

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What are the Skin Manifestations of Drug Reactions???
<table>
<thead>
<tr>
<th>Cutaneous Manifestation</th>
<th>Most Commonly Eliciting Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urticaria</td>
<td>NSAIDs, antibiotics, narcotic analgesics</td>
</tr>
<tr>
<td>Angioedema</td>
<td>NSAIDs, ACE inhibitors, angiotensin antagonists</td>
</tr>
<tr>
<td>Anaphylactic reactions</td>
<td>NSAIDs, antimicrobials, neuromuscular blockers</td>
</tr>
<tr>
<td>Erythematous eruptions</td>
<td>Antibiotics, sulfonamides, antiepileptic drugs, non-nucleoside reverse transcriptase inhibitors</td>
</tr>
<tr>
<td>Acneiform eruptions</td>
<td>ACTH, androgens, bromides, glucocorticoids, isoniazid, iodides, lithium, phenytoin, selective serotonin reuptake inhibitors, vitamins B1, B6, B12, cyclosporine, sirolimus, isoniazid, EGF inhibitors, bevacinumb, TNF-alpha inhibitors</td>
</tr>
<tr>
<td>AGEP</td>
<td>Aminopenicillins, macrolides, carbamazepine, quinolones, diluiazem, antimalarials, mercury</td>
</tr>
<tr>
<td>Pseudoporphyria</td>
<td>NSAIDs, antibiotics</td>
</tr>
<tr>
<td>Drug-induced LABD</td>
<td>Vancomycin, paracetamol, amiodarone, ceftriaxone, furosemide, metronidazole, phenytoin</td>
</tr>
<tr>
<td>Drug-induced pemphigus</td>
<td>Penicillamine and other thiol drugs</td>
</tr>
<tr>
<td>Drug-induced pemphigoid</td>
<td>Psoralens, furosemide, ibuprofen, ACE inhibitors, spironolactone, ampicillin, penicillin, levofloxacin, penicillamine, metronidazole, chloroquine</td>
</tr>
<tr>
<td>Lichenoid eruptions</td>
<td>Beta-blockers, penicillamine, ACE inhibitors</td>
</tr>
<tr>
<td>Cutaneous pseudolymphoma reaction</td>
<td>Anticonvulsants</td>
</tr>
<tr>
<td>Drug-induced vasculitis</td>
<td>Allopurinol, penicillins, sulfonamides, phenytoin, thiazides</td>
</tr>
<tr>
<td>Drug-induced lupus</td>
<td>Hydralazine, isoniazid, penicillamine, minocycline</td>
</tr>
<tr>
<td>Allergic contact dermatitis to drugs</td>
<td>Topical: antibiotics (neomycin, gentamycin, bacitracin), glucocorticosteroids, antiseptics (chlorhexidine, quinolones, benzalkonium chloride)</td>
</tr>
<tr>
<td>Photoallergic dermatitis to drugs</td>
<td>NSAIDs</td>
</tr>
<tr>
<td>Phototoxic reactions</td>
<td>Psoralens, thiazides, chlorpropamide, nalidixic acid, phenothiazines, tetracyclines, hormonal contraceptives</td>
</tr>
<tr>
<td>FDE</td>
<td>Ibuprofen, sulfonamides, tetracyclines, quinolone</td>
</tr>
<tr>
<td>SJS/TEN</td>
<td>Allopurinol, antiretrovirals, aromatic amine anticonvulsants, NSAIDs, sulfa-antimicrobials</td>
</tr>
<tr>
<td>DRESS</td>
<td>Allopurinol, anticonvulsants, antiretrovirals, NSAIDs, minocycline, sulfasalazine, dapsone, fluindione, proton pump inhibitors, strontium ranelate</td>
</tr>
</tbody>
</table>
Common in Paediatric population: Severe Cutaneous Adverse Reactions (SCAR)

- Acute Generalized Exanthemeatous Pustulosis (AGEP)
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN)
Exfoliative Dermatitis
(Erythroderma)

- Abnormal redness (erythema) covering more than 90% of body surface

- e.g. Red men syndrome - to Vancomycin

- Impaired Temp control

- Protein loss

- Water loss

- Oedema

- Lymphadenopathy
The first skin lesions typically develop on the trunk. The mucous membranes and nails are spared.

Possible causes:
- Beta-blockers, penicillamine, ACE inhibitors

Figure 1. (a and b) Lichenoid drug reaction showing depigmentation, hyperpigmentation and fissuring. (c) Clinically improved skin 1 week after completing antituberculosis therapy.
Severe Cutaneous Adverse Reactions (SCAR)

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Why such phenotypic diversity?

Drug

Structure

Metabolism (Cytochrome P450)

Immunogenic HLA

Immune toxic response

SJS/TEN??
AGEP??
DRESS??
Severe Cutaneous Adverse Reactions (SCAR)

- Acute Generalized Exanthematous Pustulosis (AGEP)

- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

- Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN)
DRESS associates with specific HLA antigens—certain ethnic groups

- HLA-B*58:01 allopurinol-induced
- HLA-B*57:01 Abacavir-induced
- HL-B*51:01 Phenytoin-related

Drug Reaction with Eosinophilia Systemic Symptoms (DRESS)
Severe Cutaneous Adverse Reactions (SCAR)

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Severe Cutaneous Adverse Reactions (SCAR)

STEVEN'S JOHNSON SYNDROME (SJS)
- <10% BSA skin detachment
- Mortality 1-5%
- Presents with fever & malaise
- Combination of Erythema multiforme (EM) & mucosal lesions
- Mucosal involvement - mouth, eyes & genitalia

TOXIC EPIDERMAL NECROLYSIS (TEN)
- >30% BSA skin detachment
- Mortality 25-35%
- Sudden onset of diffuse macules, EM-like lesions
- Progression to skin necrosis and peeling. Loss of hair and nails
- Mucosal involvement
SJS/TEN-Dermatological emergency

Skin failure:

• Loss of function: Temperature control, fluids, electrolytes, nutrition, mechanical barrier

• hypovolaemia, severe hypotension, organ failure.
Treatment: SJS/TEN

- Good supportive care and conditions arising from the erythema and exfoliation such as dehydration, high output failure and hypothermia must be addressed
- Fluid management
- Prevent infection
- Topical treatment should be bland, stop all non-essential drugs
- Treat the underlying cause
Treatment guidelines - SJS/TEN

- Stop causative drug + chemical related agents
- Burns unit/specialized unit wherever possible
- Rescucitative efforts as for major burns
- Sepsis control
- Steroids - only ocular; IVIG ?still undecided - debridement ?danger; ?prophylactic anti-biotics
- Enteral feeds in preference to parenteral
Patient assessment

• Clinical appearance
• How long (is the eruption)?
• Associated symptoms - fever, pruritus, L/N
• Time lapsed between drug intake + SCAR onset
• Exam: description; skin and mucosal
• Blood tests/Skin Biopsy
• SJS/TEN/ DRESS ? - Refer
Decisional algorithm for SCARs

Tu Anh Doung, et al. (2017) S0140-6736 (16) 30378-6
Conclusions

- A drug history - essential part of every patient with a skin lesions

- Do not rule out a drug history even if you cannot pinpoint a drug history at that time

- Management is hugely variable – early drug withdrawal – improves diagnosis

- Challenge??
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