THE ROLE OF PATCH TESTING IN NON-IMMEDIATE CUTANEOUS ADVERSE DRUG REACTIONS

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Introduction

- Patch testing is a useful tool for evaluating delayed-type drug allergy when multiple drugs are suspected.
- It is helpful when positive, but does not exclude allergy when negative.
- It is considered extremely safe.
- It is especially helpful when there are multiple possible drug culprits.
- We will present two cases where patch testing was utilized to assess acute generalized exanthematous pustulosis (AGEP) and fixed drug eruption (FDE).

Methods

- Patients were patch tested to The North American Contact Dermatitis Group (NACDG) standard series and select series.
- Select medications mixed by our inpatient pharmacy diluted to 10 or 30% in petrolatum using IQ chambers and Scanpor tape.
- Patches were removed at 48 hours.
- Patches were read at 48, 72 or 96 and 120 hours.

Case #1: Acute Generalized Exanthematous Pustulosis

67 year old man presented with confluent erythematous patches studded with non-follicular pustules on the face, trunk and extremities (figure 1 and 2). Systemic features included associated fever, malaise, rigors and diarrhea. 24 hours prior to onset of rash, the patient received benzocaine spray for a dental procedure. A skin biopsy was performed and showed spongiform subcorneal and intra-epidermal pustules consistent with AGEP. The patient was treated with oral prednisone, topical corticosteroids and was discharged from hospital 3 days later.

Patch testing results:
- 3+ pustular reaction to benzocaine at 96 hours.
- Biopsy of patch site consistent with allergic contact dermatitis.

Patch Testing in AGEP

- Sensitivity of patch testing = 50-60%
- Positive patch tests show an spongiosis or can mimic AGEP at the site of testing.
- Positive results are observed most frequently with B-lactams, antiepileptics, diltiazem, quinolones, morphine, NSAIDs, pseudoephedrine.

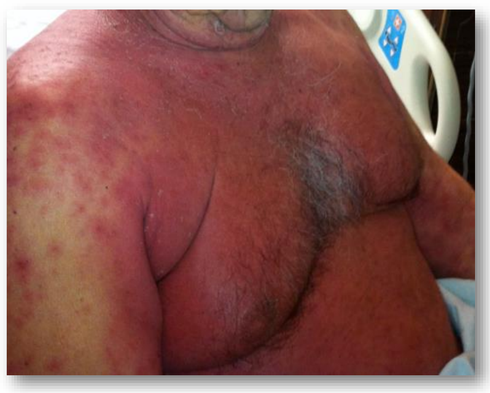

Figure 1

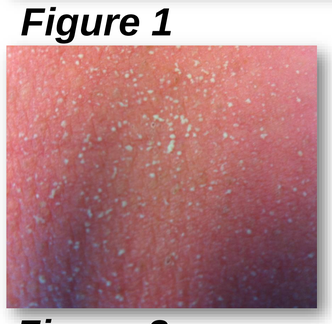

Figure 2

Case #2: Fixed Drug Eruption

A 56-year-old female who owns a lumber shop that supplies domestic and exotic woods presented with intermittent episodes of widespread eczematous dermatitis previously treated with prednisone, antihistamines and topical corticosteroids

The patient was patch tested to 1) NACDG standard series 2) Textile allergens 3) Plastics and glues (wood glues with phenol formaldehyde resin) 4) Domestic and exotic woods

Patch testing results:
- DalBergiones → **3+ blackwood 5%;** 2+ santose rosewood
- 3+ balsam of Peru
- 2+ paratertiary butyl phenol formaldehyde resin, fragrance mix 1, methyl dibromoglutaronitrile

Three years later, the patient developed pruritic annular erythematous patches on the palms, dorsal foot, back, legs and buccal mucosa (Figure 3). Twelve hours earlier, she was sawing blackwood. A skin biopsy revealed a vacuolar interface with dyskeratotic keratinocytes consistent with fixed drug eruption.

Patch testing was repeated. Final results at 120 hours
- 3+ to Dalbergiones → **Blackwood**, Cocobolo, Padauk, Pau Ferro
- 3+ beech, juniper
- 2+ PTBPFR, birch, cashew shell oil
- 1+ pine

One year later, the patient develops a urinary tract infection and was treated with ciprofloxacin.
She developed recurrence of multiple FDE's in the same sites as after inhalation of blackwood.
The patient was patch tested to 1) Ciprofloxacin 10% in petrolatum2) Ciprofloxacin 30% in petrolatum 3) Septra 10% in petrolatum 4) Septra 30% in petrolatum 5) Ciprofloxacin – chemo 10% in petrolatum 6) Norfloxacin – chemo 10% in petrolatum

Results = all negative at 48 and 96 hours

Patch Testing for FDE

- Fixed drug eruption is a presentation of systemic allergic contact dermatitis
- Sensitivity of patch testing = >40%
- Must be performed on previously affected sites
- Positive results are observed most frequently with NSAIDs and sulfonamide antibiotics

<u>Blackwood Allergy</u>
Blackwood is an exotic wood from the Dalbergione family. The allergens in blackwood are **2,6-dimethoxy-1-4-benzoquinone** and **6-methoxy-2-methyl-3,5-dihydrobenzofurano-4,7-dion** which are both quinones **and** melacacidin

<u>Putting it all together</u>
Our patient had
1) Physical contact with blackwood which presented with widespread eczematous dermatitis and positive patch testing to blackwood
2) Inhalation of blackwood sawdust which led to systemic allergic contact dermatitis presenting as multiple fixed-drug eruption
3) Multiple fixed drug eruption from ciprofloxacin, a quinolone antibiotics. Quinones (blackwood) and quinolones (ciprofloxacin) do not cross-react as the chemical structure is quite different. This is confirmed on patch testing with a negative result after testing to ciprofloxacin (a quinolone antibiotic). Unfortunately we were unable to prove a fixed drug eruption to ciprofloxacin with patch testing; the PPV of patch testing in FDE is only 43%.

Guidelines for patch testing for non-immediate cutaneous adverse drug reactions

- Current guidelines recommend patch testing between 6 weeks and 6 months after resolution of non-immediate cutaneous adverse drug reactions (NI-CADR) and at least 1 month after discontinuation of oral steroids .
- European guidelines suggest testing commercially available medications at 30% and 20% concentrations, although some have done 10% in petrolatum (either from pure drug or powder for IV injection). It is suggested to dilute further if the reaction is a severe cutaneous adverse reaction (SCAR; start 0.1% and increase to max of 10%). Read at 48 and 96 hours, if negative then read on day 7.
- Patch testing is generally performed on the back, with the exception of FDE and SDRIFE/Flexural exanthem which should be performed on a previously affected site.
- Patch testing for NI-CADR is considered safe. Barbaud et al. reported only 1 of 134 patients who underwent patch testing for NI-CADR with a clinically significant reaction requiring systemic steroids.
- The likelihood of a positive patch testing result varies depending on the type of NI-CADR and the culprit medication.
- Patch test sensitivity depends on the drug penetrability, concentration, drug metabolite rather than the actual drug is true culprit,
- There is significant correlation between the patch test result and the clinical probability of a CADR.
- False negatives are possibly related to the drug metabolite not being formed during skin application compared to metabolism in body.

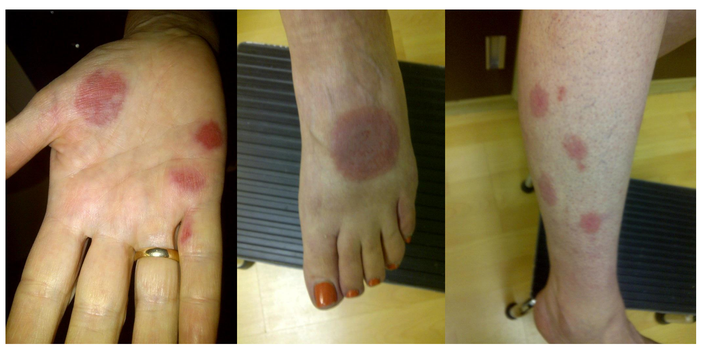

Figure 3

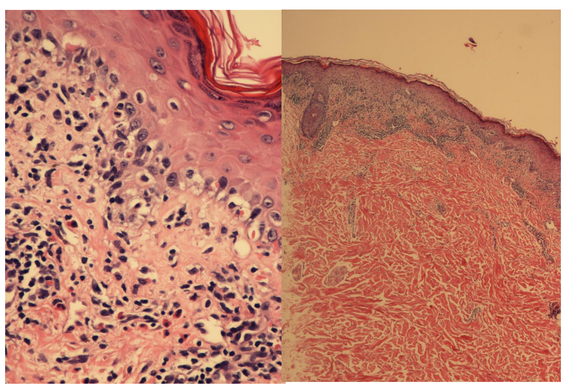

Figure 4

References

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