URTICARIA

Roundtable session
Common Referral Pitfalls

• All urticaria is allergic
• All angioedema is a prelude to anaphylaxis
• All peri-orbital swelling is ‘angioedema’
• Patch testing referrals for ‘urticaria’
• Skin prick testing for ‘cause of eczema’
• Allergy testing for ‘cause of chronic urticaria’
Aims

• Mechanisms of urticaria / angioedema versus eczema / contact dermatitis
• Differentiating clinically between these forms of allergy (including overlap cases)
• Which investigations and treatments can be carried out in primary care?
• When to refer to secondary care?
• Patient education / managing patient expectations
Urticaria

- Red/white, raised lumps (variable size) +/- flare
- Itchy
- Individual lesions last <24 hours
- Non-scarring/non-bruising
- No dryness, flaking, scaling
Mast cell degranulation

- Histamine, Leukotrienes, Heparin – superficial dermis and epidermis
Causes of Urticaria

• Triggered
  – Allergic
    • reproducible reliable trigger
  – Physical
    • Wind, cold, friction, pressure
  – Cholinergic
    • Heat, exercise, fever
  – COX
    • NSAIDs
  – Direct mast cell degranulation
    • Opiates, radiocontrast

• Spontaneous
  – Acute
    • <6 weeks
  – Chronic
    • >6 weeks

All can be exacerbated by:
  – Infection
  – Inflammation/ Systemic illness
  – Stress
  – Extremes of temp
  – Hormonal status
  – alcohol
CASE 1

• 34 y.o female c/o recurrent rash (typical urticaria) on and off last 6 months, symptoms everyday, pops up and down with no pattern, often wakes up with the rash, reliant on AH
CASE 1

- Angioedema - one or two episodes lip and face swelling, no resp distress
- Other – at wits end, excluded wheat, dairy, changed cosmetics and laundry products, affecting sleep and relationship, terrified of anaphylaxis because uncle has peanut allergy, wants steroids because they worked last year and doesn’t care about side effects.
Diagnosis?
Chronic Spontaneous Urticaria and Angioedema

- Why isn’t it allergy?
- How can we sure it’s histamine mediated and not another form of angioedema?
- Is there a risk of anaphylaxis?
- Management plan
  - Community based
  - Secondary care
Chronic Spontaneous Urticaria and Angioedema

- Why isn’t it allergy?
  - How can we sure it’s histamine mediated and not another form of angioedema?
- Is there a risk of anaphylaxis?
- Management plan
  - Community based
  - Secondary care
- Pattern
- Absence of other T1HS symptoms
- Duration
- Frequency
- Waking up with symptoms
Chronic Spontaneous Urticaria and Angioedema

- Why isn’t it allergy?
- **How can we sure it’s histamine mediated and not another form of angioedema?**
- Is there a risk of anaphylaxis?
- Management plan
  - Community based
  - Secondary care

- Response to antihistamines or steroids
- Typical appearance and behaviour of the urticaria
Chronic Spontaneous Urticaria and Angioedema

• Why isn’t it allergy?
• How can we sure it’s histamine mediated and not another form of angioedema?
• Is there a risk of anaphylaxis?
• Management plan
  – Community based
  – Secondary care

• Yes but rare
Chronic Spontaneous Urticaria and Angioedema

• Why isn’t it allergy?
• How can we sure it’s histamine mediated and not another form of angioedema?
• Is there a risk of anaphylaxis?

• Management plan
  – Community based
  – Secondary care

• Clinical review +/- Investigations
  – Infection/inflammation/systemic illness

• Rx
  – Antihistamines QDS
  – Rantidine
  – Montelukast
  – Emergency plan?
  – Exacerbators
    • NSAID’s
    • ACE-I
CSU&A – secondary care

• Objective assessment of symptoms severity
• Review of atypical features
• Specialist management
  – Omalizumab or Ciclosporin
  – Other agents
    • Hydroxychloroquine, dapsone, doxepin, sulfasalazine, methotrexate, mycophenolate,
    • Salicylate-free diet
  – CSU&A in pregnancy
What about????

- Pattern of symptoms suggest Type 1 allergy?
What about????

• Atypical appearance?
  – bruising, scarring, eczematosus

• Atypical behaviour?
  – Poor response to AH, steroids

Time for Case 2
CASE 2

• 34 y.o female
• Recurrent rash described as red patches with a raised edge, itchy but can be burning and tender. Rash has been there for weeks and individual patches last up to 3 days. A few episodes of facial swelling with residual bruising. Feels unwell in herself with fatigue, transient joint aches affecting different joints and recurrent abdominal pain with nausea. PMH: adult onset asthma with daily cough. Rash started infrequently but seems to be getting worse. Antihistammines are of some benefit for settling the itch but no affect on other symptoms. Has tried steroids but needs high dose to have any impact.
Point to pick up

• Differences from last case
• Investigations
• Management
CASE 2 – suspected Urticarial Vasculitis

• 34 y.o female
• Recurrent rash described as red patches with a raised edge, itchy but can be burning and tender. Rash has been there for weeks and individual patches last up to 3 days. A few episodes of facial swelling with residual bruising. Feels unwell in herself with fatigue, transient joint aches affecting different joints and recurrent abdominal pain with nausea. PMH: adult onset asthma with daily cough. Rash started infrequently but seems to be getting worse. Antihistamines are of some benefit for settling the itch but no affect on other symptoms. Has tried steroids but needs high dose to have any impact.
Point to pick up

• Differences from last case
  – Nature of rash, not typical urticaria, bruising, scaring
  – Systemic features
  – Response to treatment
  – Need to refer Dermatology or Immunology
    • Biopsy
    • Immune suppression
    • Review for systemic features
CASE 3

• 17 y.o male
• Recurrent angioedema for the last year. Typically affects hands but has had swellings affecting his lips, around his eye and on one occasion his genitals. Typically gets huge swellings at the sites of trauma (plays sports). He has woken up with swellings and they seem to be getting more frequent. He never gets a rash and no one else in his family has the same thing. Mum makes him take her AH at the start of swellings but still takes up to 5 days to go down.
Points to pick up

• How do we know not histamine mediated?
• What would indicate histamine involvement?
• What is the differential diagnosis?
• What if he were 60 or female?
• Management

• No response to AH, steroids or adrenaline
• No urticaria or itching
• No other T1HS symptoms
Points to pick up

- How do we know not histamine mediated?
- **What would indicate histamine involvement?**
- What is the differential diagnosis?
- What if he were 60 or female?
- Management

- Urticaria, T1HS symptoms – even infrequently
- Good/partial response to AH, steroids, Adrenaline
Inflammatory mediators in deeper dermis and subcutaneous tissue

• Mast cell degranulation
  – Triggered
  – spontaneous

• Bradykinin
  – ACE-I
  – C1 Inhibitor deficiency/dysfunction
    • Hereditary
    • Acquired
  – Type 3 HAE

Angioedema with or without urticaria
Good response to AH, steroids

NO urticaria
No response to AH or steroids
Points to pick up

- How do we know not histamine mediated?
- What would indicate histamine involvement?
- What is the differential diagnosis?
- What if he were 60 or female?
- Management

- C1 Inhibitor deficiency
  - HAE
  - Acquired Angioedema (AAE)
- ACE-I induced angioedema
- Spontaneous angioedema
  - CSU&A
Points to pick up

• How do we know not histamine mediated?
• What would indicate histamine involvement?
• What is the differential diagnosis?
• What if he were 60 or female?
• Management

• Older patients
  – AAE risk – clinical review for autoimmune disease and haematological malignancy
  – Avoid ACE-I
• Female
  – May exacerbate with oestrogen based medications
Points to pick up

• How do we know not histamine mediated?
• What would indicate histamine involvement?
• Can it be HAE without FH?
• What if he were 60?
• Management

• Refer
  – Confirm diagnosis
  – Prophylaxis
  – Emergency planning
  – Liaison with other specialities as required
Bradykinin Pathways

Factor XII → fXIIa → Plasma kallikrein → Bradykinin → Bradykinin B2 Receptor → Vasodilation and increase in vascular permeability

ACE = angiotensin converting enzyme, C1-INH = C1-esterase-inhibitor

ACE = angiotensin converting enzyme, C1-INH = C1-esterase-inhibitor

Assessment of urticaria and angioedema

Typical cutaneous presentation

Non-Allergic precipitant

Exclude underlying systemic condition

“Idiopathic” “Spontaneous” urticaria/angioedema

Allergic precipitant

Atypical presentation

Consider alternative diagnosis/biopsy

Confirm with SPT/blood test for specific IgE

“Idiopathic” “Spontaneous” urticaria/angioedema
Case 4

- 15 year old girl
- Admitted Maxillofacial team
- Periorbital oedema and erythema
- Weekly follow up for four weeks
- Recurrence A&E two months later
- Diagnosed as bilateral erysipelas
- IV antibiotics / oral
Points for discussion

- Mechanism based on clinical appearances?
- Investigations?
- Management?
Points for discussion

• Mechanism based on clinical appearances?
  – Oedema and swelling lasting several days
  – Crusting / epidermal change and dryness / scaling
  – Not ‘angiodema’

• Investigations?
  – Patch testing for delayed type allergy involving T-lymphocytes (not histamine-driven)

• Management?
  – Topical steroids – moderate potency
  – +/- Topical tacrolimus
Contact allergic dermatitis

Patch tests confirmed strong allergy to methylisothiazolinone (preservative in wet wipes, cosmetics, toiletries, paints, polishes, household products)
Patch testing
Case 5

Atopic eczema with urticated flare-ups

- 11 year old boy
- Eczema since birth
- Asthma and hay fever
- Multiple courses antibiotics and oral steroids
- Unable to swim or enjoy school / home life
- Father severe atopic eczema
Atopic eczema
Points for discussion

• Mechanism based on clinical appearances?
• Investigations?
• Management?
Points for discussion

• Mechanism based on clinical appearances?
  – Not ‘pure’ urticaria as urticated patches lasting > 24 hours and dryness / scaling
  – T-cell mediated inflammation
  – Itch not predominantly caused by histamine
• Investigations?
  – SPT / sIgE if reproducible urticarial flare-ups (but consider if likely to alter management)
  – Patch tests only if superimposed contact allergy suspected
• Management?
  – Topical steroids – moderate and potent
  – Consider topical tacrolimus
  – Oral antihistamine if regular urticarial flare-ups despite proactive topical steroid regime
Widespread urticated atopic eczema
Atopic eczema
Atopic eczema treatment

Topical steroid

Topical calcineurin inhibitor
Atopic eczema acute / flare treatment

- Topical steroid (first line therapy)
  - Mild
  - Moderate
  - Potent (avoid on face and flexures and in children < 12 months)
  - Daily for 1-2 weeks then twice weekly to reduce flares
Severe intermittent peri-orbital swelling/inflammation

GP Letter:
This 51 year old lady has had three episodes of peri-orbital swelling and inflammation in the last 6 months and I attach a copy of a photograph that one of my colleagues took in surgery. She initially had no idea of what the possible trigger was, she then thought it might be the furniture that she used in her cleaning job. However, she had avoided this prior to the most recent episode.

She has been taking antihistamines and using Hydrocortisone cream as well as anti-allergy drops. The swelling also affects the area around her mouth and she has been getting more cold sores recently. When the swelling occurs it isn’t particularly sore but for the 2-3 weeks after the swelling goes, it is then very itchy and at times sore.

She has also been using Calendula and Aloe Vera to moisturise her skin. Thankfully she has had no visual disturbance.

She has been offered steroids, but is very reluctant to take these – she really is just desperate to find out what the cause is and I think probably our best bet would be some patch testing.

Case 6
Points for discussion

• Mechanism based on clinical appearances?
  – Oedema but lasting days and leaving scaling and dryness and crusting

• Investigations?
  – Patch testing to standard and facial battery (not type 1 allergy tests)
  – Contact allergy to limonene and linalool (in cleaning and household products)

• Management?
  – Moderately potent topical steroid or oral prednisolone
Case 7

URGENT TELEDERMATOLOGY REFERRAL
Exfoliative dermatitis affecting sun exposed areas of face, neck and dorsum of hands on a background of previous severe hand dermatitis

I would be really grateful for your help with this 83 year old retired painter and decorator. Over the past three or four days, after spending some in the garden, albeit wearing a hat, he developed an acute erythrodermic reaction with exfoliation and serious ooze affecting his face, neck, ears and the dorsum of his hands. He is not systemically unwell and there is no extension of this erythroderma to other parts of his body.
Thank you for the images. This chap needs patch testing - he is likely to be allergic to compositae plants, but other air borne allergens such as methylisothiazolinone (in sprays, paints and polishes) are possible - please ask him to avoid gardening and sun exposure until we have arranged urgent patch testing. I agree with your management - 20-30mg prednisolone for 5-7 days then reduce by 10mg every 5 days, along with dermovate or elocon to body / hands. I would only use potent steroid on the face for 3 days then reduce to eumovate twice daily. I will send him an appointment for patch testing in a couple of weeks when he is off prednisolone.
Contact Allergies on Patch testing

• Compositae family of plants (daisies, dandelions, tansy, feverfew, chamomile, chrysanthemums) – lives next to dandelion bank of weeds which council had just strimmed
• Rubber (thiuram and carbamates)
• Epoxy resin (glues)
• Colophony (adhesives, elastoplast, pine trees)
Episodic, localised or persistent scaly skin reactions - think allergic contact dermatitis

• Discuss avoidance of common allergens with patient eg cosmetics, wet wipes, nail varnish, plants, polishes, sprays.

• If persistent, refer to dermatology for patch tests, especially if dermatitis involves face (air-borne allergens) or hands (multiple potential allergens).