Non-IgE Mediated Allergic Reactions

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Learning Objectives

• To recognise that some patients complaining of ‘allergies’ have disease that is not IgE-mediated
• To be able to describe some of the clinical features that differentiate IgE and non-IgE mediated ‘allergies’
• To be able to recall the features of some non-IgE reactions occurring commonly in clinical practice
• To be able to describe in simple terms some examples of mechanisms of non-IgE mediated ‘allergic’ reactions
IgE Mediated Allergy

- Time from exposure to symptoms is usually rapid (minutes)
- Small amounts of allergen > large reactions
- Recurs with re-exposure
- IgE can demonstrated by SPT or RAST

### IgE Mediated Food Allergy

- Skin (urticaria, angioedema, eczema)
- GI (vomiting, cramps, diarrhoea)
- Resp (wheeze, stridor, nasal Sx)
- CVS (hypotension, collapse)

### Non-IgE but Immunological hypersensitivity

- Food induced enteropathy (coeliac disease)
- Allergic eosinophilic gastroenteritis
- Contact dermatitis

### Idiosyncratic

- e.g. Irritable bowel syndrome, Chronic fatigue syndrome

### Non Immunological Food Intolerance

- Pharmacological (caffeine, nitrates)
- Metabolic (lactase deficiency > milk intolerance)

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RN – Allergy Clinic referral from GP

- 50 yrs ♂️ Professional musician

PC

- Episodic facial swelling for 3 months
HPC cont/d

- Starts early morning while still in bed
- Associated with itch and erythema
- Lasts between 2 and 3 days
- Only ever R side of face
- Onset coincided with anniversary of mother’s death
- Dyspepsia for 4-6 weeks

PMH

- Gastritis 2004
- Globus hystericus 1998
- Hayfever
- Childhood asthma

Angioedema

- Lifetime incidence: 10-15% of population
- Painless, well defined areas of oedema
- Due to vascular permeability
- Usually face, lips, mouth (but also any part of body)
- In severe cases: LARYNX > Obstruction
- Can involve bowel > abdominal pain
- Natural history variable

Can be associated with:

urticaria
Urticaria ↔ Angioedema

Superficial ↔ Deep

Activation of Mast Cells by Allergen

PLA₂ → PLD → Lipid Mediators

ARACHIDONIC ACID → DGLA, Eicosanoids

PKC → PLC, InsP₃, Ca²⁺
Activation of Mast Cells by anti-FceR1 auto-antibody

« Autoimmune urticaria »

Allergen-Independent Mast Cell Activation

Microbial components e.g. LPS

Toll like receptor 4

FceR1

Auto-antibodies

SCF (stem cell factor)

Intrinsic mast cell releasing activity
- Opioids
- Muscle relaxants
- Radiocontrast media

Enhances degranulation

mast cell proliferation
c-kit (RTK) D816V point mutation

SCF (stem cell factor)

mast cell proliferation

Enhances degranulation

Intrinsic mast cell releasing activity
  • Opioids
  • Muscle relaxants
  • Radiocontrast media

Auto-antibodies

Microbial components e.g. LPS

Toll like receptor 4

FcεR1

Allergen-Independent Mast Cell Activation

Chronic urticaria/angioedema

Acute urticaria
  (classically during URTI, Strep throat)

Systemic Mastocytosis
Possibly also Idiopathic anaphylaxis

“allergic reactions”

• Opioids
• Muscle relaxants
• Radiocontrast media
ANGIOEDEMA

Hereditary

Acquired
• Auto-Ab to C1-Est inh
• Consumption (lymphoma)

IgE-mediated
• Foods (nuts, fruits, seafood)
• Bee/wasp stings

No urticaria

Drugs (>90 of A&E cases)
• ACE inhibitors
• NSAID

Autoimmune
or Idiopathic
• ? stress
• ? trauma
• ? Helicobacter pylori infection

Idiopathic
• ? stress
• ? trauma
• ? Helicobacter pylori infection

No urticaria

Hereditary Angioedema
Hereditary Angioedema
(congenital C1-esterase inhibitor deficiency)

Kinin system: blood proteins that play a role in inflammation, blood pressure control, coagulation and pain
Lingual angioedema in a patient taking enalapril for 2 years

Alternative drug?

Urticaria

Ordinary urticaria
(‘? Allergic, autoimmune, infection, idiopathic)

Dermographism (physical urticaria)

'Ordinary' urticaria

Possibly idiopathic urticaria and angioedema but consider ACE-I

Hereditary angioedema

Superficial

Deep

Angioedema

Possible ACE-I

Likely ACE-I
Toxic effect: schromboid reaction

- Poorly preserved oily fish (e.g. tuna)
- Bacterial decarboxylation of histidine
- Histamine content may be increased > 100-fold (fish tastes funny)
- Tachycardia, erythematous flush w/o urtication

Sensitivity to Sulphites (1)

- Anti-oxidant used as preservative
- Sensitivity affects 1:100
- 5% of asthmatics react
- Uncommon in non-atopic non-asthmatics
Sensitivity to Sulphites (2)

Clinical features

- Bronchospasm - “wine sensitive asthma”
- Flushing/feeling of temperature change
- Vomiting
- Difficulty swallowing
- Dizziness
- Contact dermatitis

Sensitivity to Sulphites (3)

Mechanism?

- ? Non-IgE dependent mast cell degranulation
- ? Sulphur dioxide produced in stomach > inhaled > bronchospasm
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