CHRONIC SPONTANEOUS URTICARIA

HISTOPATHOLOGIC CHARACTERISTICS

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Urticaria is a dermatological disorder characterized by the sudden appearance of itchy hives (wheals), angioedema or both\(^1\)

A hive consists of three typical features:

1. Central **swelling** of variable size, usually surrounded by a reflex erythema
2. Associated **itching** (pruritus), or sometimes a **burning** sensation
3. Usually resolves within a few hours and always by 24 hours

The terms ‘itch/pruritus’, and ‘hive/wheal’ are interchangeable. For the purpose of this training tool, itch and hive will be used to describe these key symptoms of urticaria

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Urticaria is a dermatological disorder characterized by the sudden appearance of itchy hives (wheals), angioedema or both\(^1\)

**Angioedema** is typically characterized by:

1. Sudden, pronounced swelling of the lower dermis and subcutis
2. Sometimes pain rather than itching
3. Frequent involvement below mucous membranes
4. Up to 72 hours for resolution

Urticaria can be classified based on duration, frequency, and cause\textsuperscript{1}

**Acute < 6 weeks**

**Chronic > 6 weeks**

- **Spontaneous**
  - Known causes (including autoimmune, infection)
- **No obvious external specific trigger**
  - Unknown causes

Urticaria is more common than previously thought\(^1\)

- CSU affects up to 1% of the population at any given time, accounting for approximately two-thirds of cases of CU\(^1-3\)
- Female: male ratio is 2:1\(^1\)
- All age groups can be affected, but peak incidence is between 20-40 years of age\(^1\)

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CSU is a chronic disease whose duration is estimated to be 1-5 years in most cases\textsuperscript{1,2}

Of the diagnosed CSU patient population:

- 50% will resolve within 6 months of onset\textsuperscript{2}
- 20% will resolve within 3 years\textsuperscript{2}
- 20% will resolve within 5-10 years\textsuperscript{2}
- <2% will resolve within 25 years\textsuperscript{2}

In very rare cases, CSU can persist for up to 50 years

CSU skin lesions show recruitment of mast cells and also basophils, neutrophils, eosinophils and T lymphocytes\(^1\)–\(^5\)

EAACI/GA²LEN/EDF/WAO guidelines\(^1\) state that urticaria is a mast cell-driven disease

- Activated mast cells release histamine and other mediators
- These mediators activate sensory nerves
- Mast cell activating signals in urticaria are \textit{ill-defined} and likely to be heterogeneous and diverse

As IgE is key to the release of histamine and other pro-inflammatory mediators from mast cells and basophils following degranulation, it may play a role in CSU

Mast cell activation in CSU may either be via autoimmune, allergic or idiopathic mechanisms\(^1\text{-}^3\)

IgG anti-IgE cross-linking surface-bound IgE

Cross-linking of mast cell bound IgE activates mast cells

Histamine release

IgG anti-FcεRI cross-linking of FcεRI

The extent of impaired QoL in patients with CSU

- In addition to the classical symptoms associated with CSU, factors of major importance to patients that contribute to a reduced QoL include:
  - Unpredictability of attacks
  - Persistent lack of sleep
  - Fatigue
  - Disfigurement

- Patients with CSU may also have comorbidities such as depression and anxiety.

CSU has a high socioeconomic burden

- The socioeconomic cost of CSU is high in terms of direct medical costs and indirect costs, such as lost wages because of absences from work\textsuperscript{1,2}

Based on a CSU prevalence of 0.04% among the US population, estimated mean total indirect and direct costs would be $244 million per year

The aim of therapy for CSU is quick and complete symptom control\(^1\)

- Symptomatic treatment aims to reduce the effect of mast cell/basophil (effector cell) mediators, e.g. histamine, on target organs leading to the symptoms of urticaria\(^2,3\)

Treatment algorithm for urticaria according to the 2013 EAACI/GA\textsuperscript{2}LEN/EDF/WAO guidelines\textsuperscript{1}

First line

Second generation H\textsubscript{1}-antihistamines

Second line

Second generation H\textsubscript{1}-antihistamines at up to 4-fold increased dose\textsuperscript{§}

Third line

Add on to second line:* Omalizumab,\textsuperscript{‡} cyclosporin A\textsuperscript{§} or montelukast\textsuperscript{§}

*Exacerbations: short course (maximum 10 days) of corticosteroids

A number of additional treatment options are mentioned in the EAACI/GA\textsuperscript{2}LEN/EDF/WAO guidelines, but are not included in the recommended treatment algorithm due to limited supporting evidence;

*the order of third-line treatments does not reflect preference; \textsuperscript{†}Licensed in Europe and the US; \textsuperscript{‡}Not licensed.

\textsuperscript{1} EAACI = European Academy of Allergy and Clinical Immunology; GA\textsuperscript{2}LEN = Global Allergy and Asthma European Network; EDF = European Dermatology Forum; WAO = World Allergy Organization.

THE HISTOPATHOLOGY OF CHRONIC SPONTANEOUS URTICARIA - CLINICAL PATHOLOGICAL STUDY
The EAACI/GA\textsubscript{2}LEN/EDF/WAO Guideline for the definition, classification, diagnosis and management of urticaria: the 2013 revision and update:

Areas of further research in urticaria:

- Identification of new histological markers
- A search for more specific histological biomarkers for different subtypes of urticaria is desirable.
Background – The classic histopathological findings of urticaria include dermal edema and a sparse perivascular infiltrate of neutrophils, eosinophils, macrophages, and lymphocytes. However, this pattern is inconsistently described.
Two distinctive patterns of urticaria were recognized:
• Lymphocyte predominant characterized by a perivascular location.

• Neutrophil predominant associated with an interstitial location and a denser infiltrate.

Mast cells were relatively sparse, better demonstrated with special stains.
Objectives:

1. Validating the previous research regarding two histopathological entities of urticaria – Lymphocyte predominant & Neutrophil predominant.

2. Look into the clinical - pathological correlations of those entities in search of unique characteristics and possibly therapeutic implications.
A retrospective study in which the medical files and biopsy specimens of 88 patients with chronic spontaneous urticaria are reviewed.

Pathological parameters will be quantified.

A retrospective telephone questionnaire

- Duration of illness
- Frequency of attacks
- Duration of single lesion
- Pruritus intensity
- Secondary symptoms (hyperpigmentation/ purple/ purpuric)
- Treatments for CSU and effectiveness
- UAS7 (Urticarial activity score)
- UCT (Urticaria control test)
THANK YOU