CHRONIC URTICARIA

-AN APPROACH

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- Urticaria, also known as hives, is an outbreak of swollen, pale red bumps or plaques (wheals) on the skin that appears suddenly -- either as a result of the body's reaction to certain allergens, or for unknown reasons. Hives usually cause itching, but may also burn or sting.

Chronic urticaria refers to hives lasting longer than 6-8 weeks; identification of a cause is less than 5%

Differential Diagnosis: Non-Immunologic Causes More Often Responsible for Chronic Urticaria

- Physical hives (i.e., dermatographism, pressure, solar, cold…)
- Hereditary (i.e., cold, heat, vibratory, porphyria, C3b inactivator deficiency…)
- Vasculitis
- Neoplasms
- Infections
- Endocrine (i.e. Thyroid disorder)
- Drugs (i.e., aspirin/NSAIDs-exacerbate hives in up to 30% of cases)
- Psychologic? More a myth than fact

- **History and Physical Examination**

1. Onset (e.g. timing of symptoms with any change in medication or other exposures).
2. Frequency, duration, severity, and localization of wheals and itching.
3. Dependence of symptoms on the time of day, day of the week, season, menstrual cycle, or other pattern.
4. Known precipitating factors of urticaria (e.g. physical stimuli, exertion, stress, food, medications).
5. Relation of Urticaria to Occupation and leisure activities.

6. Associated angioedema, systemic manifestations (headache, joint pain, gastrointestinal symptoms, etc.)
7. Known allergies, intolerances, infections, systemic illnesses or other possible causes.
8. Family history of urticaria and atopy.
9. Degree of impairment of quality of life.
10. Response to prior treatment.
11. General and Systemic physical examination

Investigations for chronic urticaria

- Infectious diseases (e.g., *Helicobacter pylori*)
- Type I allergy
- Functional antibodies.
- Thyroid hormones and autoantibodies
- Skin tests (including physical tests)
- Tryptase (as indication of severe systemic disease)

- Lesional skin biopsy.
- The investigations below may also be helpful:
- ESR/CRP: elevated in chronic inflammation
- WBC count: lymphocytosis in viral infection; neutrophilia in bacterial infection, or eosinophilia in parasitosis or chronic allergy
- C1, C2, C4 level: typical patterns in complement- and kinin-dependent urticaria (e.g., C1 esterase deficiency)

- Serum IgE: elevated in allergic settings
- LFT: abnormal in recent hepatitis or EBV
- Hepatitis A, B, and C antibody titres
- Thyroid function testing for TSH, T4 and T3, radio-iodine uptake, anti-TPO and anti-TG antibodies: abnormal in active autoimmune thyroiditis or thyroid carcinoma.
- Antistreptolysin O (ASO) and EBV titre (where fever is associated)
- ANA test, anti-Ro antibody, anti-La antibody, and anti-Smith antibody: positive in lupus erythematosus or Sjogren's disease. These are performed for photosensitive patients.

- Suspected colon carcinoma: CEA antigen
- Known upper GI issues: *Helicobacter pylori* investigation.
- Family history of angio-oedema and suspected C1 esterase deficiency: C1 esterase level testing
- In patients with relevant travel history and suspected intestinal parasitosis: stool ova and parasites (O and P) test x3
- Suspected autoimmune disease, gammopathy, or multiple myeloma: gamma globulin and protein electrophoresis
- Complement component deficiencies: cryoglobulin

ALGORITHM FOR DIAGNOSIS

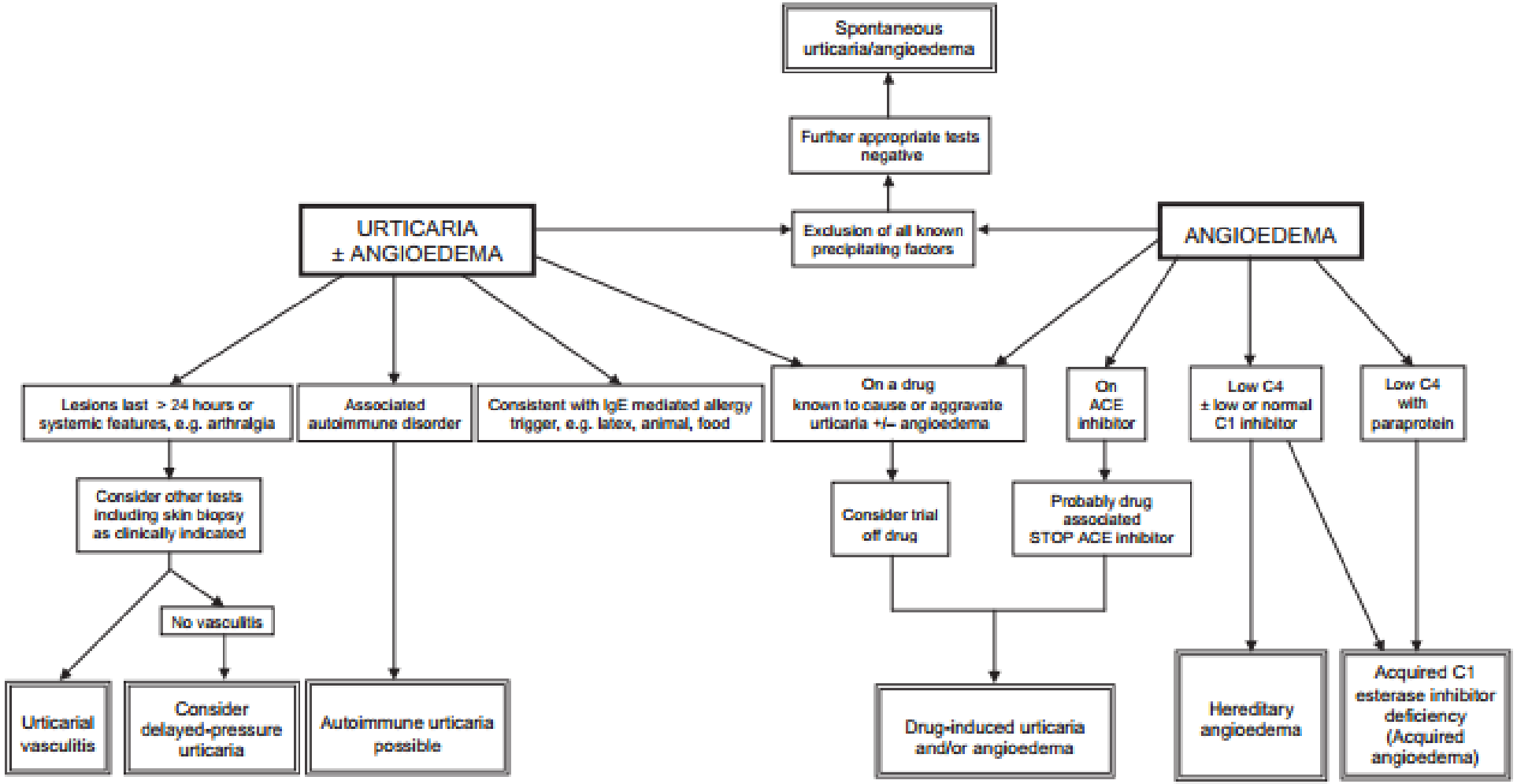

Fig. 1. Algorithm for diagnosis of chronic urticaria and/or angioedema.

TREATMENT

STEP 4
Add an alternative agent
- Omalizumab or cyclosporine
- Other anti-inflammatory agents,immunosuppressants, or biologics

STEP 3
Dose advancement of potent antihistamine (e.g. hydroxyzine or doxepin) as tolerated

STEP 2
One or more of the following:
- Dose advancement of 2nd generation antihistamine used in Step 1
- Add another second generation antihistamine
- Add H_2– antagonist
- Add leukotriene receptor antagonist
- Add 1st generation antihistamine to be taken at bedtime

STEP 1
- Monotherapy with second generation antihistamine
- Avoidance of triggers (e.g., NSAIDs) and relevant physical factors if physical urticaria/angioedema syndrome is present.

- Begin treatment at step appropriate for patient's level of severity and previous treatment history
- At each level of the step-approach, medication(s) should be assessed for patient tolerance and efficacy
- **"Step-down" in treatment is appropriate at any step, once consistent control of urticaria/angioedema is achieved**

- **Treatment used now a days:**

Drug (families)	Grade	Specific indication/comments/side-effects
Omalizumab	A	Used for chronic urticaria failed on higher dose antihistamines
Leukotriene receptor antagonists (montelukast[1], zafirlukast)	B[1]	Most effective in combination with antihistamines Autoimmune urticaria; chronic urticaria with positive challenge to food, food additives or aspirin; delayed pressure urticaria
Tranexamic acid	D	Showed reduced frequency of angioedema attacks.
Ciclosporin	B	Immunosuppresive, i.e. requires monitoring of blood pressure, renal function and serum levels if indicated; significant side-effects
Mycophenolate Mofetil	D	Used for chronic urticaria failed on higher dose antihistamines
Tacrolimus	D	Value in severe, steroid-dependent chronic urticaria needs further randomized controlled studies

Grade = Grade of recommendation (Table B2) [133, 134]. B[1] = Grade only refers to montelukast, but not to zafirlukas

THANK YOU