Urticaria

1. Types of urticaria

Outline
- Urticaria is transitory localized erythema or wheals accompanied by itching.
- Acute urticaria occurs in episodes shorter than 6 weeks; chronic urticaria occurs in episodes of 6 weeks or longer.
- Vascular permeability increases. Edema forms in the dermal upper layer.
- In factitious urticaria, dermographism is positive.
- Oral antihistamines are the first-line treatment.

Clinical features
A slightly elevated, sharply circumscribed wheal or reddening with a circular, oval or map-like pattern suddenly appears, accompanied by intense itching (Fig. 8.1). Edema, the primary event in the dermal upper layer, may occur at any site on the body, especially at sites subjected to rubbing or pressure. Wheals may occur not only in skin but also in mucosa. When formed in the pharyngeal region, urticaria causes hoarseness and breathing difficulty. Urticaria usually begins to subside within several hours and usually disappears within 24 hours. In some cases, erythema and slightly infiltrative lesions remain for several days.

Pathogenesis, Classification
Chemical mediators such as histamines released from mast cells enhance vascular permeability, which causes edema to form in the dermal upper layer (Fig. 8.2). Even thorough examination is unable to detect the cause of urticaria in about 90% of cases (idiopathic urticaria). For that reason, urticaria is often classified by duration of episode. Urticaria in episodes shorter than 6 weeks is called acute; that in episodes of 6 weeks or longer is called chronic. When there is an identifiable cause, the urticaria is named after that cause (discussed later).

Diagnosis, Examinations
It is easy to diagnose urticaria by the clinical findings. History-taking on suspected causative agents of urticaria, such as
mechanical stimuli, the cold, foods and drugs, is helpful. Since urticaria sometimes accompanies systemic diseases, including collagen diseases, determination of the primary disease is necessary. Dermographism is positive (when the skin is rubbed, the site turns red; \textbf{Fig. 8.3}). Tests such as that for serum IgE levels, IgE RAST (radioallergosorbent test), intradermal allergic test and drug-induction test are conducted.

**Treatment**

Antihistamines are the first-line treatment. When the cause is identified, it should be removed. Oral or intravenous steroids are effective in severe cases, such as glottic edema. Urticaria resolves in several days in most cases; however, it may progress to chronic urticaria.

**Types of urticaria**

Typical types are described below.

1) **Acute and chronic urticaria**

Urticaria is divided by duration of episode into acute (less than 6 weeks) and chronic (6 weeks or longer).

2) **Contact urticaria**

Contact urticaria occurs at sites where a foreign substance comes into contact with and permeates the skin or mucosa. It is classified into allergic contact urticaria and nonallergic contact urticaria.

Patients with allergic contact urticaria have had previous contact with the substance and are sensitized to it. Nonallergic contact urticaria is caused by the first contact with a substance (MEMO).

3) **Physical urticaria**

Physical urticaria is an eruption caused by physical stimulation. It disappears in 30 minutes to 1 hour. It is divided into several subtypes according to cause. Factitious urticaria, also called mechanical urticaria, is produced by rubbing. Dermographism is positive in factitious urticaria. Solar urticaria is caused by sunlight. Cold urticaria is caused by exposure to the cold, such as cold water or wind.

4) **Cholinergic urticaria**

Cholinergic urticaria occurs when the body perspires after the body temperature rises from exercise or bathing (\textbf{Fig. 8.4}). The cholinergic nerves are thought to be involved.
Angioedema is caused by increased vascular permeability in the subcutaneous tissue at sites deeper than those of urticaria.

The pathogenesis can be hereditary or nonhereditary.

The eyelids and lips of mouth are the most frequently affected.

The treatment for nonhereditary angioedema is the same as for urticaria.

Clinical features

Localized edema suddenly occurs and remains for several days.
hours to several weeks. The size of the angioedema varies, with the diameter ranging from 1 cm to 10 cm. It is sharply circumscribed, and itching is not usually present. Although it may occur at any site on the body, the most frequently affected areas are the eyelids, lips and genitalia (Fig. 8.5). Angioedema may be produced not only on the skin surface but also in the glossopharyngeal areas, nasal cavity, bronchial mucosa, gut mucosa, intracranial region, heart or kidneys. It can be fatal.

**Pathogenesis, Classification**

Angioedema is produced by the increased vascular permeability in the subcutaneous tissue that results when histamines are released from mast cells in the dermal lower layer or the subcutaneous tissue or when some hereditary factor comes into play. Angioedema is divided into hereditary and nonhereditary. Nonhereditary angioedema is thought to be deep-seated urticaria.

Hereditary angioneurotic edema, caused by congenital absence of C1 esterase inhibitors (C1INH) is autosomal dominant in most cases and is rare in Japan. Because of the absence of C1INHs, there is activation of C1, kallikrein, Hageman factor (antihemophilic factor XII) and plasmin, which results in the production of C2 kinin or bradykinin. Angioedema is caused by a resulting increase in vascular permeability.

**Diagnosis**

Angioedema is easy to diagnose from medical history and clinical features. Serum C1 inhibitor activation assay is effective in diagnosing hereditary angioedema.

**Treatment**

The treatments for nonhereditary angioedema are the same as those for urticaria. For hereditary angioedema, the following are administered: C1 inhibitor; androgen, which enhances expression of the C1 inhibitor; or C1 inactivator, which strongly inhibits the action of C1.

**Prognosis**

Nonhereditary angioedema may heal naturally. Hereditary angioedema rarely subsides, and it may be accompanied by disorders such as those of the vocal cords.

**3. Urticarial vasculitis**

Urticarial or erythema multiforme-like eruptions that persist for more than 24 hours recur and heal with purpura or pigmentation. Urticarial vasculitis most frequently occurs in women. Systemic lupus erythematosus (SLE) like symptoms and decreased complement value are seen. Leukocytoclastic vasculitis is found histopathologically in many cases (Chapter 11). The etiology is unknown. It is divided into idiopathic urticarial vasculitis and secondary urticarial vasculitis, the latter of which occurs secondarily.
to a primary disease such as SLE, rheumatic arthritis or hepatitis B. Unlike in ordinary urticaria, type I allergy is not involved in urticarial vasculitis. However, the immune complex that indicates the involvement of a type III allergy is present.

4. Food-dependent exercise-induced anaphylaxis (FDEIA)

Physical stress – from exercise, for example – 1 to 4 hours after ingestion of certain foods may cause anaphylaxis and urticaria simultaneously. In Japan, food-dependent exercise-induced anaphylaxis (FDEIA) is most often caused by wheat, followed in frequency by shrimp, oysters and celery. Since exercise or ingestion of specific foods alone does not cause FDEIA, an induction test is necessary to confirm and diagnose FDEIA.

Prurigo

Outline

- Prurigo is a condition in which there are independent itchy papules or small nodular eruptions.
- It is induced by insect bite, allergy, or atopic condition.
- It may be aggravated by rubbing, whereby small intractable nodules form.

Clinical features, Classification

In prurigo, papules or small urticarial nodules are accompanied by intense itching that becomes chronic. These nodules are called pruritic papules (Fig. 8.6). There are various etiologies and clinical features; however, the condition is thought to be a specific inflammatory reaction. Prurigo is characterized by exudative inflammatory lesions (Fig. 8.7) and by its failure to develop into the other types of eruptions that are seen with eczematous and dermatitis lesions. Prurigo remains as chronic papules and nodules. It is often categorized as acute or chronic.

Pathogenesis

Prurigo is exudative inflammation that occurs in the dermal upper layer. It is accompanied by lymphocytic or neutrophilic infiltration. It is thought to be induced by specific inflammatory reaction (pruritic reaction); however, the causative agent is unknown in many cases. Insect bites, mechanical or electrical stimulation, certain kinds of foods, and chemical stimulation such as by histamines are thought to be causative factors. Prurigo may also accompany malignant tumor, leukemia or Hodgkin’s disease. Atopic dermatitis can also cause prurigo.

Fig. 8.6 Prurigo nodularis.
Small, severely itchy nodules of 5 mm to 20 mm in diameter are noted. Excoriation is also seen.