Chapter 11  Vasculitis, Purpura and Other Vascular Diseases

Vasculitis is divided into several types according to the diameter of the artery or vein at the principal site of inflammation (Fig. 11.2). In cutaneous vasculitis, there is frequently purpura or ulceration. Purpura may be an early sign of vasculitis.

Purpura is a general term for reddish-purple skin lesions produced by bleeding in the dermis or subcutaneous tissues. It is classified by the size of bleeding into petechia (diameter up to 2 mm) or ecchymosis (diameter larger than 2 mm). The major causative factors are ① vascular abnormality (from vasculitis or mechanical injury), ② blood flow abnormality (e.g., hypergammaglobulinemia, which often accompanies a systemic disease), ③ decrease or functional abnormality of platelets, and ④ coagulopathy (e.g., DIC). However, the etiology is unknown in many cases. This chapter discusses diseases with the symptoms listed above and diseases caused by circulatory disorder of the arteries, veins and lymphatic vessels.

Vasculitis

A. Vasculitis in small vessels

1. Cutaneous small-vessel vasculitis (CSVV)

Synonyms: Leukocytoclastic vasculitis, Necrotizing vasculitis, Allergic vasculitis, Cutaneous allergic vasculitis

Outline

● This is a group of diseases that are characterized by neutrophilic infiltration into the peripheral small dermal blood vessels.
● Various clinical features, including erythema, purpura, papules, blistering and ulceration, may be present, depending on the depth and severity of the vasculitis.
● Henoch-Schönlein purpura is a variant of CSVV.

Definition

Cutaneous small-vessel vasculitis (CSVV) is a general term for diseases that present pathological features of leukocytoclastic vasculitis, i.e., diseases with pathological perivascular neutrophilic infiltration and fibrinoid degeneration of the vascular walls (Fig. 11.1). Henoch-Schönlein purpura and urticarial vasculitis are included under a broad definition of CSVV; however, they are usually treated as distinct diseases. In its more restricted sense, CSVV is considered to be a disease caused by small-vessel vasculitis in the dermis (in and between the middle and deep layers of the dermis).

Clinical features

Purpura, urticaria, erythema-multiforme-like erythema,
Papules, nodules, pustules, blistering, erosion and ulceration occur, mainly in the lower extremities (Figs. 11.3-1 and 11.3-2). Nephritis, pulmonary infiltration, pleuritis, acute abdomen, cranial nerve symptoms, convulsive seizure, headache, myocarditis and epicarditis may accompany CSVV.

Pathogenesis

An immune complex of an antigen (e.g., bacterium, virus, drug) and the antibody against that antigen deposit on the arteriovenular walls. These activate the immune system and cause vasculitis (type III allergic reaction). Penicillin, sulfa drugs and other drugs, chemical substances, hemolytic streptococcus bacteria, or viruses may be the foreign antigen. Collagen diseases and antibodies against malignant tumors can also be causes.

Pathology

In the upper and middle dermal layer, fragments of nuclear debris and leakage of erythrocytes are found in the peripheral arteriola. Neutrophilic infiltration occurs in the arteriovenous small blood vessels and capillaries. Thickening of the blood vessel walls and fibrinoid degeneration are also found in many cases (Fig. 11.4).

**Palpable purpura, Non-palpable purpura**

When diagnosing purpura, it is important to distinguish between purpura caused by vasculitis and purpura caused by other factors (e.g., thrombocytopenia, capillary fragility). Purpura caused by vasculitis tends to be accompanied by palpable infiltration (palpable purpura), whereas in purpura caused by factors other than vasculitis, infiltration is not usually present. However, infiltration is impalpable in mild vasculitis.
Laboratory findings

Elevated erythrocyte sedimentation rate, increase of leukocytes and hypergammaglobulinemia may occur. The serum complement titer often decreases. Tests for immune complex are sometimes positive. When CSVV immunocomplex is accompanied by systemic symptoms, renal lesion tends to occur, and proteinuria and hematuria are found.

Diagnosis

CSVV is diagnosed by skin biopsy. Since there are many diseases that cause CSVV, special care should be taken in diagnosis.

Treatment, Prognosis

When the cause is a drug or infection, those should be removed. For a lesion in the lower extremities, the legs should be raised and kept warm and the patient should get bed rest. Oral application of NSAIDs and DDS (dapsone) is effective in relieving symptoms. Systemic corticosteroid therapy and immunosuppressants are useful for severe cases with systemic symptoms.

2. Henoch-Schönlein purpura (HSP) *

Synonym: Anaphylactoid purpura

Outline

- It is a specific type of cutaneous small-vessel vasculitis.
- The cause is IgA immune complex deposition on the vascular walls. HSP is a type III allergy.
- It is a leukocytoclastic vasculitis in which there are scattered nuclear fragments (nuclear dust), mainly in the subpapillary vessels of the dermal upper layer.
- Arthritic symptoms, abdominal pain, and renal symptoms occur.
- Bed rest and systemic steroid administration are the major treatments.

Definition

Multiple palpable purpura occur mostly in the lower legs, and they are accompanied by arthralgia, digestive disorder and kidney disorder. Henoch-Schönlein purpura (HSP) is in the pathological category of cutaneous small-vessel vasculitis (CSVV); however, it is localized in the dermal upper layer, and there is IgA deposition on the vascular walls.

Fig. 11.3-2 Cutaneous small-vessel vasculitis (CSVV). It presents various cutaneous clinical features from palpable purpura to deep ulcers, depending on the depth of the affected vessels.

Fig. 11.4 Histopathology of cutaneous small-vessel vasculitis (CSVV). Fibrinoid necrosis of the vessel walls in the upper dermis, hemorrhage with neutrophils, and nuclear dust (arrows) are present.

Fibrinoid degeneration

This is deposition of eosinophilic amorphous material on the vascular wall, and it appears in the early stages of vasculitis; the immunocomplex may be identified by fibrinoid degeneration (Fig. 11.4).
Clinical features, Classification

The most severely affected organs and locations are the skin, joints, digestive organs, and kidneys. Although children are most commonly affected, HSP may also occur in adults. It may be preceded by a headache, pharyngeal pain, and symptoms of the common cold. Disseminated palpable purpura of several millimeters to 10 mm in diameter occur, mainly in the lower extremities and dorsum of the foot, but sometimes on the thighs, upper extremities, and abdomen (Fig. 11.5). Blisters, ulcers, and old and new eruptions may be present together. In some cases there is transient edema with slight pressure pain. Arthritic symptoms in the legs, knees, hands and elbows, sharp pain in the abdomen, and gastrointestinal symptoms such as nausea, vomiting, hematemesis, and melena are found. HSP may be accompanied by renal symptoms including acute nephritis that progresses to nephrosis. Renal symptoms are closely related to the prognosis.

Pathogenesis

In children, the onset is mostly after upper respiratory infection; association with hemolytic streptococcus has been pointed out. Drugs (penicillin, aspirin) and certain kinds of foods (milk, eggs) are known to be antigens. These antigens combine with antibodies (mainly IgA) in the body, and the immunocomplex deposits on the vascular walls. Immunoreaction is induced to cause vasculitis and purpura.

Pathology

Leukocytoclastic vasculitis accompanied by fibrinoid degeneration is seen on the vascular walls in the upper dermal layer. IgA deposition is observed by direct immunofluorescence (Fig. 11.6). The histology of the kidney in HSP patients often shows crescentic glomerulonephritis.

Laboratory findings

When HSP is caused by hemolytic streptococcal infection, antistreptolysin O and antistreptokinase values increase. In half of the patients, serum coagulation factor XIII decreases. In cases with renal lesion, hematuria and proteinuria occur.

Differential diagnosis

When the purpura described above occurs in youth, HSP is suspected. History-taking should inquire into not only HSP but also other diseases before examinations and histopathological tests are conducted. It is necessary to differentiate HSP from other purpura, polyarteritis nodosa, Goodpasture syndrome, nephritis after infection caused by hemolytic streptococcus, and systemic lupus erythematosus (SLE). In adults, differential diagnosis from polyarteritis nodosa is important.

Treatment

Bed rest is the first-line treatment, followed by the administra-
tion of a vessel-strengthening drug and hemostatics, and systemic administration of steroids. When the disease is caused by hemolytic streptococcus, antibiotics are used. Administration of factor XIII may be effective.

**Prognosis**

HSP generally has a good prognosis and resolves within several weeks in most cases; however, it may recur. Serious complications may occur in other organs, such as nephritis with IgA deposition in the mesangium area, enterorrhagia, intussusception, intestinal perforation, or cerebral hemorrhage.

**3. Urticarial vasculitis**

When an urticarial eruption remains for more than 24 hours with purpura, urticarial vasculitis is suspected. It may be accompanied by systemic symptoms such as fever and a decrease in complement titer (Chapter 8).

**4. Erythema elevatum diutinum (EED)**

Erythema elevatum diutinum (EED) frequently occurs in men and women of middle age and older. It is a skin lesion that is accompanied by symmetrical infiltration on the extensor surface of elbows and knees. Although the pathogenesis is unknown, an immune reaction caused by deposition of immune complex in the blood vessels is thought to be involved. Appearing as soft, slightly elevated, purplish-red erythema at first, the eruptions gradually become fibrotic and keloidal. There is an atypical type with blistering (Fig. 11.7). Leukocytoclastic vasculitis occurs in the dermis. It is nearly asymptomatic, however, it recurs repeatedly and persistently. Oral ulcer, arthritis, lung fibrosis, IgA myeloma, and viral infection may accompany EED. DDS is an effective treatment.

**5. Granuloma faciale**

Granuloma faciale, a soft, infiltrative, reddish-brown plaque with a sharp margin, occurs on the face. It is known to be a chronic leukocytoclastic vasculitis. Deposition of immunoglobulins on the vascular walls has been reported, from which the possibility of an immunoreaction resembling that of EED has been pointed out. Granuloma faciale is intractable. Liquid nitrogen cryotherapy, local injection of steroids, and dye laser treatment have been used in recent years.