Chapter 6
Purpura

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Definition

Purpura is visible hemorrhage in the skin or mucous membranes [1–3]. The color of purpura is due to hemoglobin (bright red for fully oxygenated; reddish blue, blue-black, or purple for less saturated; and blue-black to black for hemorrhage due to hemorrhagic tissue necrosis) [3]. Primary purpura means that the mechanism of lesion production is the same mechanism that produced the hemorrhage (as opposed to secondary purpura which represents hemorrhage into lesions occurring from another primary process, for example, hemorrhage occurring into areas of stasis dermatitis on the lower extremities due to increased intravascular pressures) [1, 3].

By definition, a lesion of purpura must have a color characteristic of hemorrhage, and some of the color must remain despite the application of direct pressure to the lesion with a glass slide (diascopy) [1, 3]. The direct pressure compresses the dermal vessels in the lesion and displaces any blood that is free to move [1, 3]. In contrast, if blood is external to the lesional vessels or if the vessels are occluded by clot, then some color will remain (i.e., purpura) [1, 3].

Purpuric lesions can have varying degrees of associated inflammation. This can be assessed by evaluating how much of the color of the lesion is blanchable via diascopy. The blanchable component of the color (i.e., that which is displaced with application of direct pressure with a glass slide) represents erythema and is a surrogate marker for the degree of inflammation present [3]. The residual color that does not blanch represents hemorrhage (purpura) [3]. The ratio of erythema (inflammation) to purpura (hemorrhage) can help the clinician to determine the relative role of inflammation and hemorrhage contributing to the lesion [1].

Purpura can be either macular (flat) or palpable (raised or indurated). The palpability of a lesion is due to edema, extravasated fibrin, and inflammation present

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M. Matucci-Cerinic et al. (eds.), *Skin Manifestations in Rheumatic Disease*,
DOI 10.1007/978-1-4614-7849-2_6,

within the lesion [1, 2]. Retiform purpura describes a subset of lesions that have a branched or reticulated shape (either to the entire lesion or of its edges) [3, 4]; other lesions of purpura may assume a stellate shape (consisting of peripheral radiating extensions like a star) [2].

Differential Diagnosis

There are three main pathogenic mechanisms of purpura: simple hemorrhage, inflammatory hemorrhage (i.e., inflammation directed at the blood vessels), and occlusive hemorrhage with minimal inflammation [3]. The morphology of purpura at the bedside can be used to help a clinician determine the most likely mechanism for the purpura. The following six morphologic subsets of purpura can be used to generate an abbreviated differential diagnosis [1–3]:

1. ***Macular petechiae* (≤4 mm in diameter, flat, noninflammatory, type of "simple hemorrhage")**: Thrombocytopenia (due to numerous causes), abnormal platelet function (hereditary or acquired), pigmented purpuric dermatoses (Fig. 6.1), and elevated intravascular pressure spikes (e.g., Valsalva-like maneuvers).

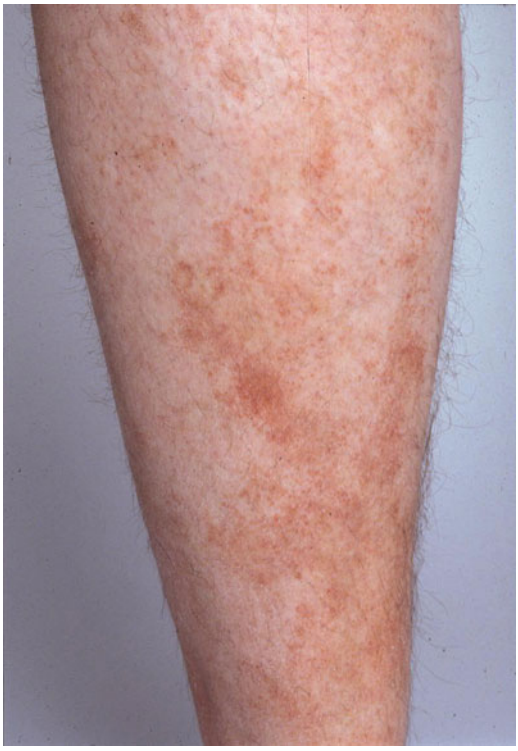

Fig. 6.1 Pigmented purpuric dermatosis (progressive pigmentary dermatosis [Schamberg disease]) occurring on the leg as reddish-brown patches with superimposed pinpoint petechiae

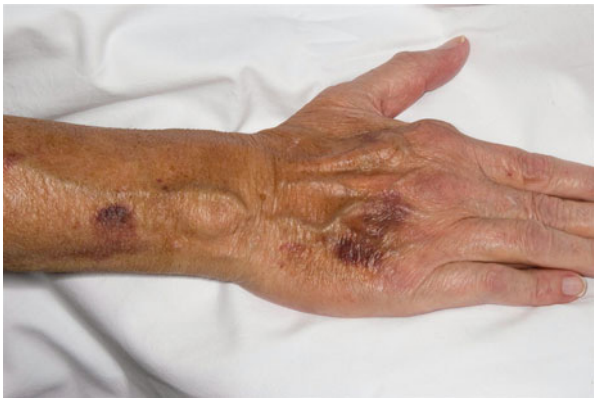

Fig. 6.2 Macular ecchymoses of the dorsal hand and forearm. These were due to long-term systemic corticosteroid therapy for rheumatoid arthritis

2. ***Intermediate macular purpura*** **(5–9 mm in diameter, flat, noninflammatory, type of "simple hemorrhage")**: Hypergammaglobulinemic purpura of Waldenström and other causes of macular petechiae and macular ecchymoses.
3. ***Macular ecchymoses*** **(≥1 cm in diameter, flat, noninflammatory, type of "simple hemorrhage")**: Hemophilia, anticoagulants, vitamin K deficiency, hepatic insufficiency, actinic purpura, corticosteroid therapy (topical or systemic; Fig. 6.2), vitamin C deficiency (scurvy), systemic amyloidosis, and Ehlers-Danlos syndrome.
4. ***Palpable purpura*** **(inflammatory purpura with prominent early erythema; round, port-wine color; partially blanches with diascopy indicating the presence of both inflammation and hemorrhage)**: The most important consideration in this category is cutaneous small-vessel vasculitis (e.g., leukocytoclastic vasculitis; Figs. 6.3 and 6.4). ANCA-associated vasculitides and vasculitides that affect both small- and medium-sized vessels can also present with palpable purpura. Targetoid lesions with a central purpuric component can be seen with IgA vasculitis and erythema multiforme. Pityriasis lichenoides et varioliformis acuta (PLEVA) can also manifest palpable purpura.
5. ***Noninflammatory retiform purpura*** **(minimal early erythema; some lesions are palpable; typically due to microvascular occlusion)**: Calciphylaxis (Figs. 6.5 and 6.6), heparin necrosis, warfarin necrosis, antiphospholipid antibody syndrome, cryoglobulinemia (monoclonal type only; mixed cryoglobulinemia usually presents with palpable purpura and demonstrates leukocytoclastic vasculitis on histology), hypercoagulable disorders (e.g., protein C or S deficiency), disseminated intravascular coagulation, cocaine use (levamisole-tainted), oxalosis, cholesterol emboli, livedoid vasculopathy, vessel-invasive infection (e.g., Aspergillus, ecthyma gangrenosum), malignant atrophic papulosis (Degos' disease), and marantic endocarditis.
6. ***Inflammatory retiform purpura*** **(early lesions have prominent erythema; some lesions are palpable)**: IgA cutaneous small-vessel vasculitis, vasculitis affecting both small- and medium-sized vessels (such as ANCA-associated and connective tissue disease-associated vasculitides), and chilblains (perniosis).

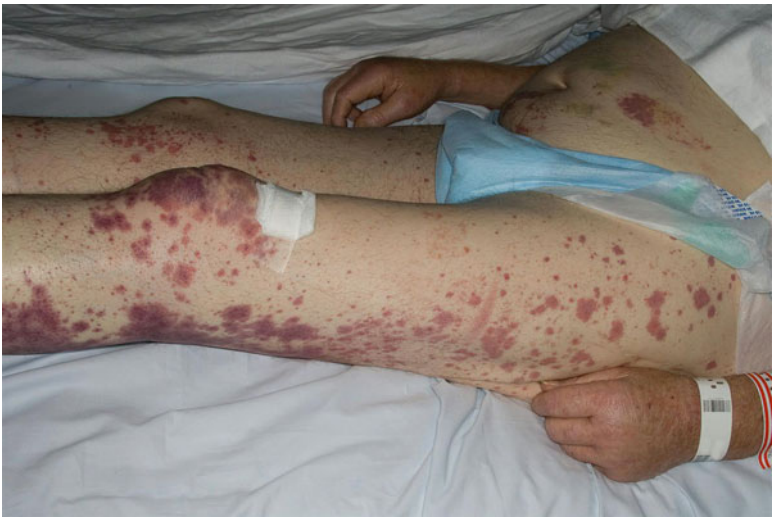

Fig. 6.3 Palpable purpura in a patient with cutaneous small-vessel vasculitis manifesting as purpuric papules and plaques on the lower extremities. Note the presence of both hemorrhage (purpura) and erythema (inflammation). Skin biopsy demonstrated leukocytoclastic vasculitis

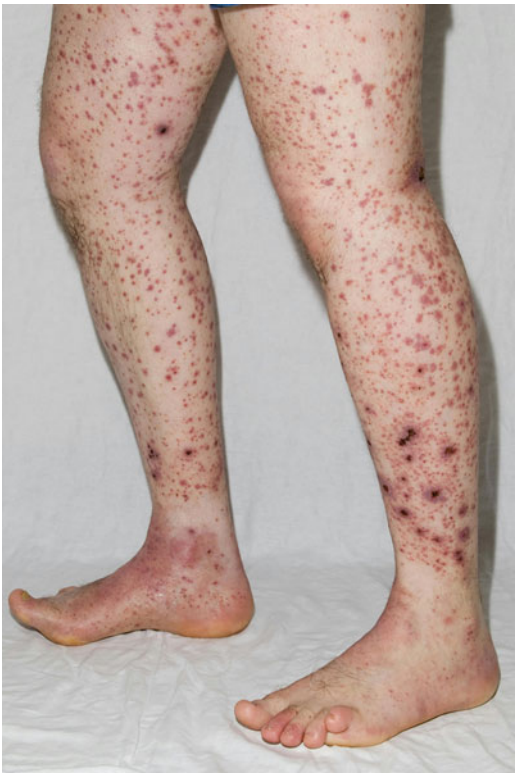

Fig. 6.4 Palpable purpura manifesting as purpuric papules and plaques (some with overlying necrosis) on the lower extremities. Skin biopsy demonstrated leukocytoclastic vasculitis, and direct immunofluorescence microscopy of lesional skin revealed the presence of IgA within superficial dermal blood vessels. Evaluation for associated causes of this patient's IgA vasculitis revealed the presence of renal cell carcinoma

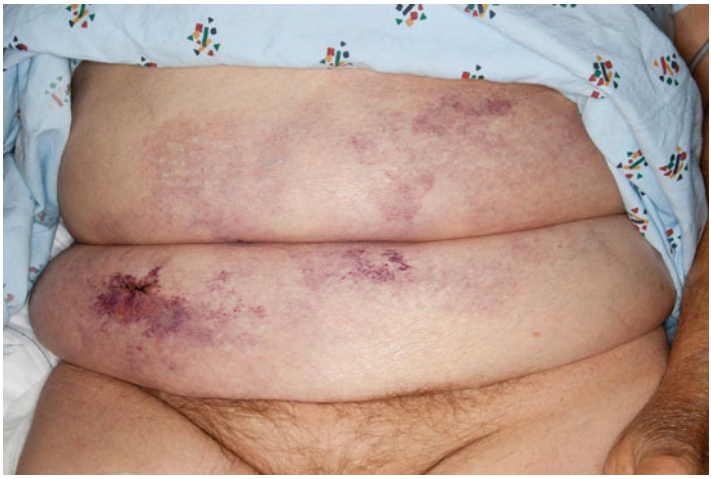

Fig. 6.5 Noninflammatory, retiform purpura manifesting as purpuric patches and indurated, exquisitely tender plaques on the abdomen. Skin biopsy demonstrated findings consistent with calciphylaxis

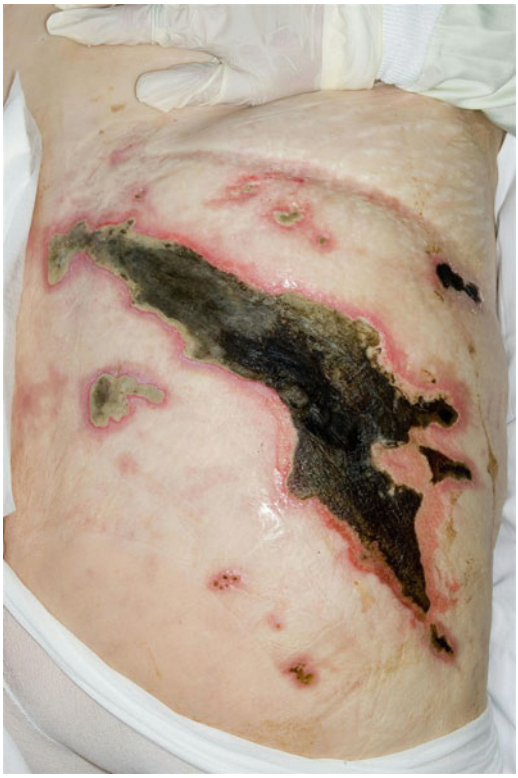

Fig. 6.6 Noninflammatory retiform purpura. Necrotic, stellate ulceration of the hip in a patient with calciphylaxis

Typical Locations of Purpura

Acral predominant (e.g., hands, feet, ears) can be due to various causes, including cryoglobulinemia, embolic phenomena (e.g., cholesterol emboli, endocarditis), antiphospholipid antibody syndrome, perniosis, cocaine use (particularly the ears), disseminated intravascular coagulation, systemic amyloidosis ("pinch purpura" around eyes), and cutaneous small-vessel vasculitis (associated with drug, infection, connective tissue disease, malignancy, ANCA-associated vasculitis).

Dependent areas (typically lower extremities, also sacral back and buttocks in a hospitalized patient lying down): Cutaneous small-vessel vasculitis (i.e., leukocytoclastic vasculitis), pigmented purpuric dermatosis, and secondary purpura (e.g., due to hemorrhage into stasis dermatitis or hemorrhage into an area of drug eruption due to thrombocytopenia [1]).

Areas of extensive subcutaneous fat (e.g., breasts, hips, buttocks, thighs): Warfarin necrosis and calciphylaxis (this typically also occurs on the lower extremities).

Common sites of trauma (dorsal hands and forearms): Actinic purpura and corticosteroid-induced purpura.

Site of subcutaneous injection (e.g., abdomen): Heparin necrosis (may also occur at sites distant from this).

Approach to the Diagnosis of Purpura (Fig. 6.7) [1–3]

(A) First determine if the lesion is:

Purpura? (via diascopy)
Primary purpura?

(B) Determine if the lesions are *palpable* (exclude major trauma-induced hemorrhagic contusions):

1. If none are palpable – represents "**simple hemorrhage"** – classify by size **(macular petechiae, ≤4 mm; intermediate macular purpura, 5-9 mm; macular ecchymoses, ≥1 cm)**.
2. If some are palpable, classify as one of the following:

   (a) Early lesions are round, port-wine colored, and have prominent erythema (partially blanch with diascopy) – represents **palpable purpura** (often due to cutaneous small-vessel vasculitis).

   (b) Early lesions lack erythema and demonstrate a retiform, branched appearance – represents **noninflammatory retiform purpura** (usually due to conditions associated with microvascular occlusion).

   (c) Early lesions have prominent erythema and demonstrate a retiform, branched appearance – represents **inflammatory retiform purpura** (usually due to IgA vasculitis or other subtypes of vasculitis).

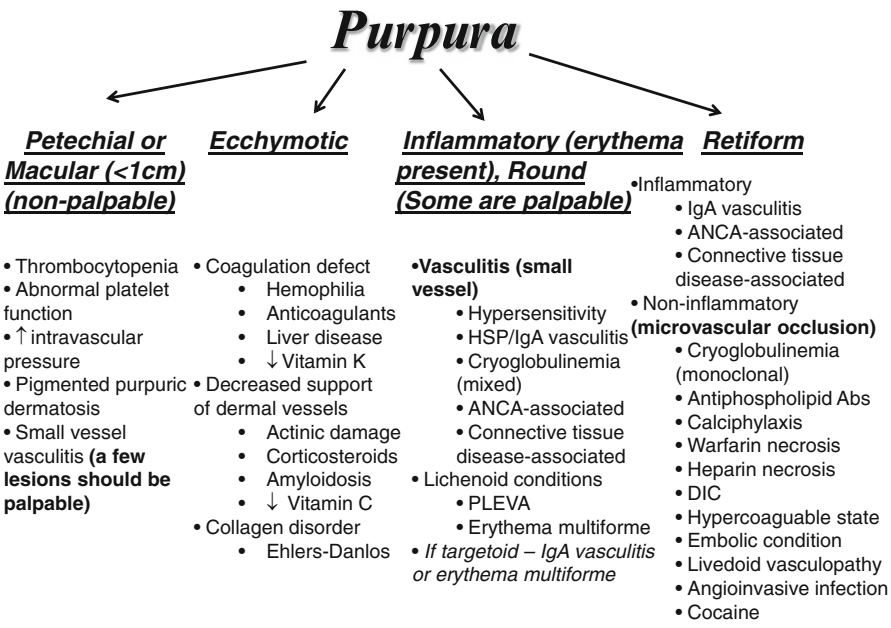

Fig. 6.7 Algorithm for approaching the patient with purpura (Adapted from Refs. [1–3])

(C) Perform history and review of systems to identify factors that may be contributing to purpura, guided by the differential diagnosis of the morphology of the purpura (e.g., preexisting medical conditions or medications that may affect coagulation and hemostasis).

(D) Pursue skin biopsy when the cause of purpura is uncertain.

1. *It is imperative to know the age of the lesion chosen for biopsy*, since late lesions of noninflammatory retiform purpura (due to microvascular occlusion) develop erythema (inflammation) as a wound healing response to ischemic injury or necrosis [3]. Thus, a late lesion of noninflammatory retiform purpura could appear clinically (and histologically) similar to an early lesion of palpable purpura (e.g., inflammatory hemorrhage due to cutaneous small-vessel vasculitis) [1–3].
2. Routine histopathology of palpable purpura should be from a lesion no more than 24–48 h old.
3. When the morphology of purpura is concerning for vasculitis, direct immunofluorescence studies should be performed on the skin biopsy (to rule out IgA vasculitis). Direct immunofluorescence in this setting should ideally be performed on an early lesion (less than 24 h old) to ensure the presence of the immune complex deposits.

(E) Targeted laboratory studies can be performed based upon the morphology of the purpura and its accompanying differential diagnosis (See section "Differential Diagnosis").

References

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