Livedo Reticularis and Livedo Racemosa

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Livedo is a relatively common physical condition of the skin, consisting of macular, violaceous, connecting rings forming a netlike pattern. In most cases, livedo reticularis is completely benign, related to cold exposure. However, there are many other possible causes of livedo reticularis, and of livedo racemosa, which is a constant pathological livedo. Livedo may be a sign of a wide range of systemic/internal diseases, some of which are potentially life-threatening or may result in disabilities. Evaluation of a patient presenting with this finding is therefore extremely important. This paper provides clinicians with guidance regarding the evaluation of patients presenting with livedo.

The term "livedo" describes a mottled, reticular, red-violaceous, vascular discoloration of the skin. Livedo mainly affects the limbs, but it can be generalized. It is secondary to dysfunction of the dermal arteries or arterioles, with a reduction or interruption of blood flow. This dysfunction may itself be related either to functional disorders (responsible for a vasospasm) or to organic disorders responsible for either an inflammation of the arteriolar wall (vasculitis) or a vascular obstruction (due to a thrombosis, an embolic event or vessel wall abnormalities) (1–3). The peculiar pattern of a livedo is due to the organization of the vascularization of the dermis (4). In brief, the arteriolar unit is a hexagon centred on an ascending capillary arteriole and surrounded by capillary venules (4). Livedo may be the first manifestation of a systemic/internal disease.

Differential diagnoses

The first step in evaluation of a livedo or a so-called livedoid eruption is to rule out the differential diagnoses (Table I). The main differential diagnosis is *erythema ab igne*, a reticular, telangiectatic, pigmented dermatosis occurring after long-term exposure to infrared radiation that is insufficient to produce a burn (Fig. 1). It is usually located on heat exposed areas (fireplaces, hot-water bottles, heating pad, computer laptop or car heating system), chiefly on the lower limbs, thighs or back (5, 6). Diagnosis is usually clinical. No biospy is needed to confirm the diagnosis.

Table I. *Differential diagnoses of livedo in adults*

Reticulated dermatoses
- Erythema ab igne
- Quinidine photosensitisation
- Reticulated erythematous mucinosis
- Lichen planus
- Lichenoid reactions (keratosis lichenoides chronica)
- Confluent and reticulated papillomatosis (Gougerot-Carteaud syndrome)
- Incontinentia pigmenti

Hereditary cutaneous conditions with reticulated pigmentation
- Xeroderma pigmentosum
- Zinsser-Cole-Engman syndrome (congenital dyskeratosis)

Poikilodermas
- Hereditary: Rothmund-Thomson syndrome, Weary-Kindler Syndrome, Bloom syndrome:
- Acquired: Parapsoriasis, discoid lupus, dermatomyositis, cutaneous Graft versus Host response, Civatte poikiloderma

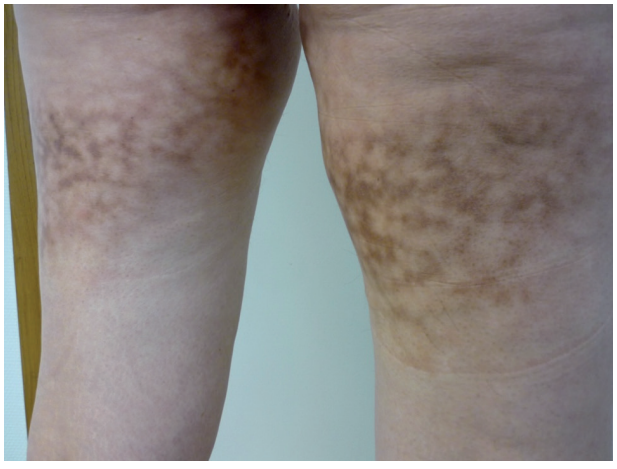

Fig. 1. Brown asymptomatic livedoid eruption of the thighs. Erythema ab igne.

Definition of "physiological" and "pathological" livedos

Definition of whether the livedo is physiological and benign or related to a condition (and therefore pathological) is made following a meticulous examination of the livedo (Table I). Physical examination is carried out with the patient lying down and then standing up. The physician must first describe the pattern, by answering the following questions:

- Are the lines of the livedo, thin and regular, or thick and irregular?
- Does the livedo show closed unbroken circles (resembling a fishing net) or open broken circles (resembling lightning)?
- On palpation, is the livedo infiltrated into any part?
- Is there any necrotic lesion on any part of the livedo?
- Are there any triggering factors?
- Is the livedo acute, transient or permanent?
- Is it worsened by cold exposure or standing?
- What was the age of onset of the livedo (early or late)?
- Where is the livedo localized on the body (lower limbs, face, trunk, buttocks, upper limbs)?
- Is the distribution generalized or patchy?
- Are there any other cutaneous symptoms that could arise suspicion for a pathological livedo: purpura, nodules, atrophic lesions, blue toe, etc.

Cutis marmorata, livedo reticularis or livedo racemosa?

One of the main issues regarding the diagnosis of "livedo" is the confusing terminology used in the medical literature, which can easily mislead the physician (1–3, 7).

"Cutis marmorata" is an English medical term referring to physiological livedo reticularis. Nowadays, it should be avoided for such purpose. However, the term "cutis marmorata" is still used in the newborn condition, cutis marmorata telangiectatica congenita (or Van Lohuizen syndrome). Briefly, this is a peculiar necrotic and atrophic livedo of newborns, that can be localized (on the limb, head, etc.) or diffuse. Its evolution is variable, ranging from regression to stability or scarring. Its diagnosis is clinical and it may be associated with various other genetic conditions (macrocephalia, homocystenuria, trisomy 21, Cornelia de Lange syndrome, etc.) (8).

Table II. *Signs of a "pathological" livedo*

- Thick, irregular lines
- Open circles
- Painful livedo
- Infiltrated livedo
- Necrotic livedo
- Localization on the trunk, buttocks and face
- Other cutaneous symptoms: purpura, papules, nodules, blue toe, etc.

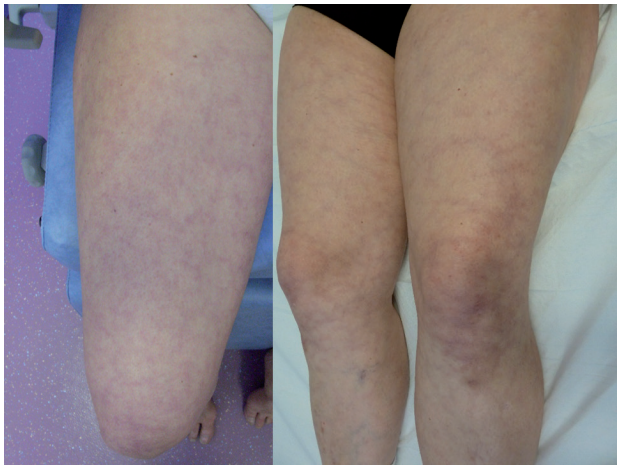

Fig. 2. Examples of physiological livedo reticularis appearing during the consultation.

"Livedo reticularis" describes a livedo that has thin and regular lines, closed, unbroken circles, in other words the typical "fishing net pattern" (Fig. 2). Livedo reticularis may be either physiological or pathological.

"Livedo racemosa", a term first used first by Ehrmann in 1907 (9), describes a livedo with irregular lines, open, broken circles, resembling "forked lightning" (Fig. 3). Livedo racemosa is always pathological and the underlying disorder must be actively managed.

Lastly, the term "retiform purpura" describes a peculiar purpura with stellated borders (Fig. 4). This is related to a vessel occlusion and subsequent haemorrhage secondary to a period of ischaemia. The causes of retiform purpura overlap the causes of an infiltrated and necrotic livedo racemosa (10).

Full clinical and physical examination

It is mandatory to avoid unnecessary exploration and to define the livedo. Personal and familial history should be fully

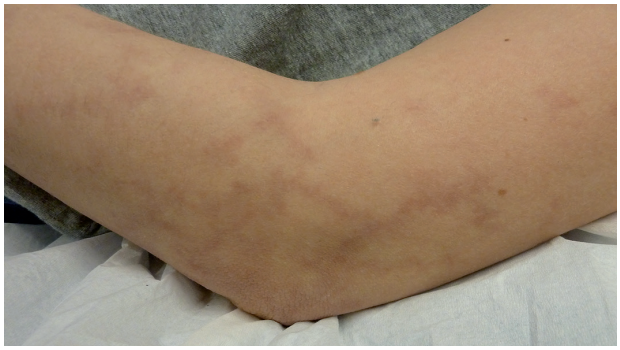

Fig. 3. Non-infiltrated livedo racemosa of the elbow.

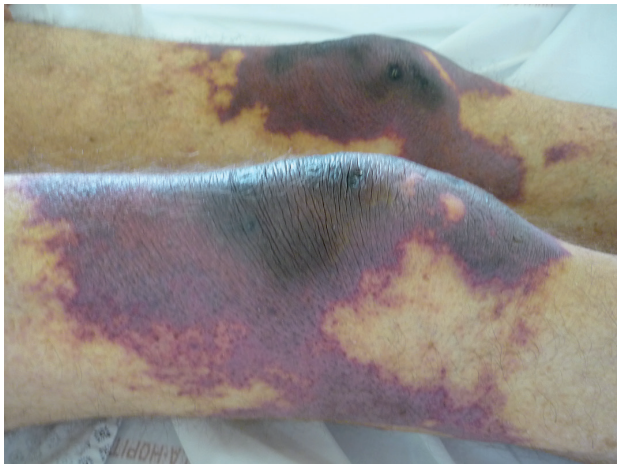

Fig. 4. Necrotic livedo/purpura retiform (notice the "stellate" borders) due to skin thrombosis related to cryoglobulin type I and multiple myeloma (11).

assessed, including systematic cardiovascular history (arterial hypertension, valvulopathy, atherosclerosis, thrombophlebitis, loss of consciousness, etc.), central nervous system diseases (migraines, stroke, transient ischemic attacks, seizures), ocular manifestations (diplopia, amaurosis, etc.), kidney (chronic renal failure, urolithiasis, etc.), pregnancies (spontaneous miscarriages, hypertension, eclampsia, prematurity). A complete physical examination must be carried out following the patient's history. Subsequently, the physician will be able to diagnose whether the patient has a livedo reticularis, and whether it is physiological or pathological, or if it is a livedo racemosa.

Physiological livedo reticularis

Physiological livedo reticularis is a common condition due to a vasospastic phenomenon affecting mainly neonates, infants and young people. It displays thin, regular lines, closed circles, and a fishing net pattern. It is aggravated by cold and improved by warming, affecting mainly the extremities and sometimes the trunk. It appears typically during the examination of a patient in underwear, if the room is a little cold. Women under 40 years of age may display other symptoms, such as acrocyanosis, chilblains and anorexia nervosa. Physiological livedo reticularis may be more extensive and not improved by warming. It does not require any additional exploration. There is no effective treatment, expect sun-tanning, which may mask the livedo (1).

Pathological livedo reticularis

Vasospam is responsible for livedo reticularis. The diagnosis of pathological livedo reticularis is rapid and easy due to the clinical history. A skin biopsy is not contributive and is of no use. The main causes include: low circulatory flow, in case of cardiogenic, septic shock or hypovolaemia especially. Neurological diseases in case of immobility stasis, reflex sympathetic dysfunction or dysautonomia may be responsible for such livedo. A few drugs are known to cause livedo reticularis, such as amantadine, a treatment for Parkinson's disease, multiple sclerosis or hepatitis C, and interferon or noradrenaline. Pheochromocytoma is a rare cause of livedo reticularis. However, this list of causes is not exhaustive.

Livedo racemosa

There are 3 pathological mechanisms that may be responsible for livedo racemosa: inflammation of blood vessels (vasculitis), thrombosis of blood vessels (Fig. 5) (11) and embolization process within the blood vessels (12).

A correct diagnosis of livedo racemosa can only be made at that stage by microscopic examination of a full-thickness biopsy up to the hypodermis. The most infiltrated or necrotic lesion should be chosen preferably for the biopsy. Punch skin biopsies should be avoided, as the sample could be too superficial and therefore miss the pathogenic process diagnosis. In the absence of any infiltration or necrosis within the livedo, the biopsy should be performed in the centre of the net/hexagon (where the central capillary arteriole is located) and in some cases also on the livedo itself (where the capillary venules are located). In some cases, multiple biopsies may be required to make a correct diagnosis. In addition, biopsies of other skin lesions may be performed.

According to the histological results, a wide number of causes may be responsible. The personal history of the patient and the clinical examination help to orientate the diagnosis. The list

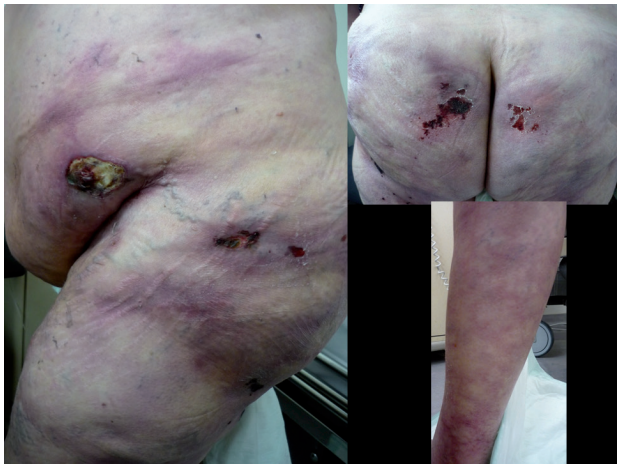

Fig. 5. Rapidly lethal generalized necrotizing thrombotic livedo racemosa of unknown origin in a middle-aged woman.

Table III. *Non-exhaustive list of diseases responsible for livedo racemosa (1–2)*

Vasculitis
- Any vasculitis can be responsible for a livedo racemosa (vasculitis associated with a connectivitis, systemic and cutaneous polyarteritis nodosa, mixed cryoglobulinaemia type II and III, deficiency of ADA2, etc.)

Thrombosis
- Coagulation disorders (protein S, protein C, anti-thrombin III deficiencies, factor V Leiden mutation; factor II (prothrombin) mutation, antiphospholipid syndrome, heparin and anti-vitamin K necrosis, disseminated intravascular coagulation, etc.)
- Myeloproliferative disorders (thrombocythaemia, polycythaemia vera)
- Cryoproteins (type I cryoglobulinaemia, cryofibrinogenaemia, cold agglutinins, paraproteinaemia)
- Primary oxaliuria (oxalosis)
- Cutaneous calcifications (calciphylaxis, primary hyperparathyroidism).
- Livedoid vasculopathy
- Sneddon's syndrome

Embolization disorders
- Fibrino-cruorinal emboli (intracardiac or vascular thrombus)
- Septic embolization (intracardiac or vascular)
- Cholesterol emboli
- Cardiac myxoma
- Gas emboli (decompression sickness)
- Fat emboli (severe trauma and multiple bone fractures)
- Tumoural and metastatic emboli (lymphoma; breast)
- Nicolau's livedoid dermatitis (embolia cutis medicamentosa) and accidental intra-arterial injection (intramuscular; sclerotherapy)
- Intravenous drug abuse (buprenorphine), cocaine

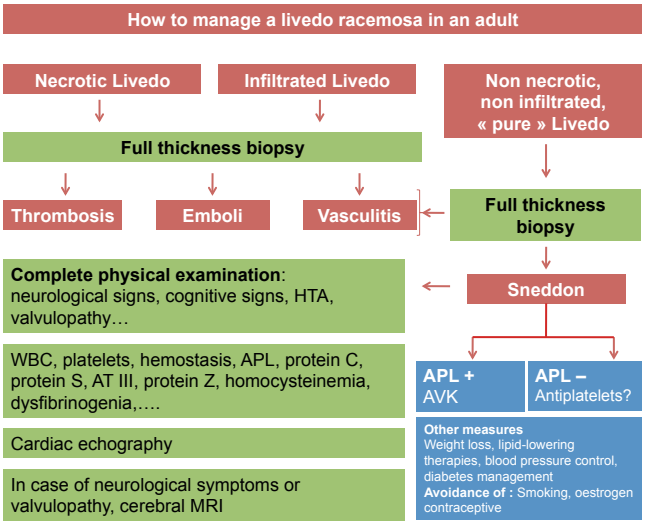

Fig. 6. Algorithm for the management of livedo in adults. APL: circulating antiphospholipid; AT III: Anti-thrombin III; AVK: anti-vitamin K treatment; HTA: health technology assessments; MRI: magnetic resonance imaging; WBC: white blood cells.

of possible causes of pathological livedo racemosa is wide. A non-exhaustive list of causes of livedo racemosa is summarized in Table III. PubMed and other databases should be consulted for more in-depth references regarding each disease (13–15).

Management of livedo racemosa

The management of livedo racemosa is directly related to the underlying disease. Management will rely on correction of the cause, the adjunction of corticosteroids and other immunosuppressive treatments, anticoagulation, antiplatelet or antivitamin K agents. An algorithm for the management of livedo racemosa is suggested in Fig. 6.

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