Lymphocytic Vasculitis : Classification of 127 cases

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Abstract

Aim: Lymphocytic vasculitis is a morphological term which includes clinically heterogenous diseases like connective tissue disease, infection, lichenoid diseases, drug reaction, Behçet's disease, superficial thrombophlebitis and leukemic vasculitis. There are three forms of lymphocytic vasculitis : angiodestructive form, lichenoid lymphocytic vasculitis and lymphocytic endovasculitis. There is a need to classify the diseases with the pathologic diagnosis of lymphocytic vasculitis.

Materials and Methods: In this study, 127 cases of lymphocytic vasculitis diagnosed between 2001-2013 were classified according to the clinical setting. The histopathological diagnosis was given to the lesions with angiotropism/diapedesis by lymphocytes, erythrocyte extravasation and swelling of endothelial cells, with/without fibrinoid necrosis of the vessel wall.

Results: Clinical diagnoses were collagen vascular disease (CVD, n=25; including 6 dermatomyositis, 2 chillblain lupus, 2 morphea), urticarial/leukocytoclastic vasculitis (n=16), pitriazis lichenoides (n=15), drug reaction (n=9), Behçet's disease (n=8), figurate erythema (n=8), panniculitis (n=8), lichen planus (n=7), erythema multiforme (n=6), pigmented purpuric dermatitis (n=5), PUPPP (n=4), Gianotti-Crosti syndrome (n=4), FMF (n=3), spongiotic dermatitis (n=3), arthropod bite (n=2) and 4 other dermatoses.

Conclusions: Lymphocytic vasculitis is believed by some to be the late manifestation of LCV or a non-specific feature but some dermatoses without the characteristic defining pathologic criteria can be diagnosed by this finding. Finding lymphocytic vasculitis in CVD can be a hint for the endothelial cells to be a target, too.

Introduction

Vasculitis is a term defined as the inflammation of the vessel wall which shows some additional features, depending on the diameter of the vessel involved and the type of cells infiltrating the

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vessel. It can be classified by these different perspectives as small, medium-sized, large vessel vasculitis or acute and chronic vasculitis. Leukocytoclastic vasculitis (LCV) is the most commonly seen type of acute, small vessel vasculitis and bears polymorphonuclear leukocytes, nuclear dust, fibrinoid necrosis and destruction of the vessel wall usually along with C3 deposition. Chronic lymphocytic vasculitis (LV) is usually arbitrarily defined by different authors as to have lymphocytes attacking a small vessel, endothelial swelling with or without fibrin deposition. The definitions are criticised for the failure to provide objective diagnosis, because acute vasculitis may progress with time to a chronic stage and fibrin is rarely present in these lesions. Vasculopathic reaction pattern is a general term defining pathologic changes in blood vessels like endothelial swelling and inflammation with extravasated erythrocytes. As far as the controversy about the presence or absence of fibrin is concerned, the diagnosis can be given as "Perivascular dermatitis and vasculopathic changes". This needs dermatologists to be informed about the term and besides, some clinicians would prefer to get an exact diagnosis: "Is it vasculitis or not?". It may be reasonable not to use rigid criteria for the diagnosis of LV since otherwise 'perivascular dermatitis' becomes an underestimation of changes.

There are clinically heterogeneous group of diseases which may present as LV which include pigmented purpuric dermatoses, connective tissue diseases and drup eruptions among a long list, members of which can arbitrarily change depending on the author or the center in concern [1].

Three forms of lymphocytic vasculitis are defined as angiodestructive form, lichenoid lymphocytic vasculitis and lymphocytic endovasculitis. Angiodestructive form is usually seen in lymphoproliferative disorders. Lichenoid form is seen in inflammatory skin diseases as part of the pathologic features which are often characterized by lichenoid vacuolar change and erythrocyte extravasation. Endovasculitis aheads of thrombosis in obliterative conditions [2].

Materials and Methods

In this study, we examined our 127 cases diagnosed as LV retrospectively trying to classify them according to the clinical setting. The histopathological diagnosis was given to the lesions with angiotropism/diapedesis by lymphocytes, erythrocyte extravasation and swelling of endothelial cells, with/without fibrinoid necrosis of the vessel wall.

Results

All cases were sent to our pathology laboratory with clinical diagnoses of diseases which are commonly encountered to present as LV, like the generic term collagen vascular disease including dermatomyositis, lupus erythematosus and morphea; or some rarely applicable causes of LV like arthropod bite and spongiotic dermatitis (Figure 1).

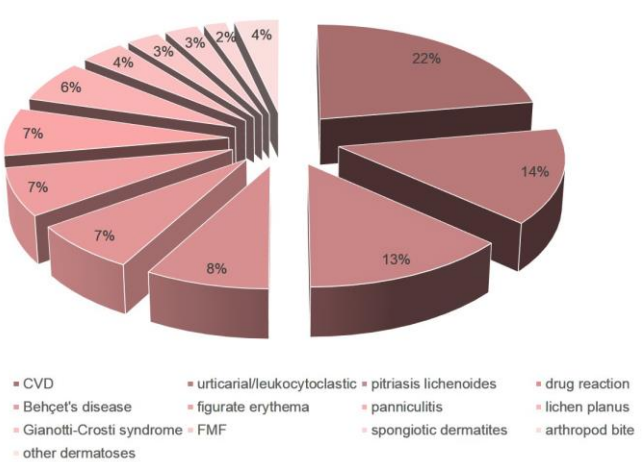

Figure 1. The distribution frequencies of clinical entities with a pathologic diagnosis of LV.

The following are four cases with different underlying causes but the same pathologic presentation as LV.

Case 1. A 31-year-old male patient had had pain on his heel twice a year for the past 4 years, and it had become permanent in the last two months. He had oral aphtous ulcers for the last 6-7 years. He had no genital ulcers or arthralgia. On blood examinations, C-reactive protein was 8.56 mg/dL (normal 0-0.8), hepatitis and HIV serology, as well as autoimmune antibody markers (such as anti-ds-DNA, ANA, ENA) were all negative. Upon administration, he had a subcutaneous nodule on the skin overlying his left gastrocnemius muscle. Clinical diagnosis was Behçet's disease. Biopsy revealed LV of small caliber vessels in the subcutaneous tissue septa without the whole picture of erythema nodosum like panniculitis which can be seen in Behçet's disease (Figure 2). Patient was followed up as such.

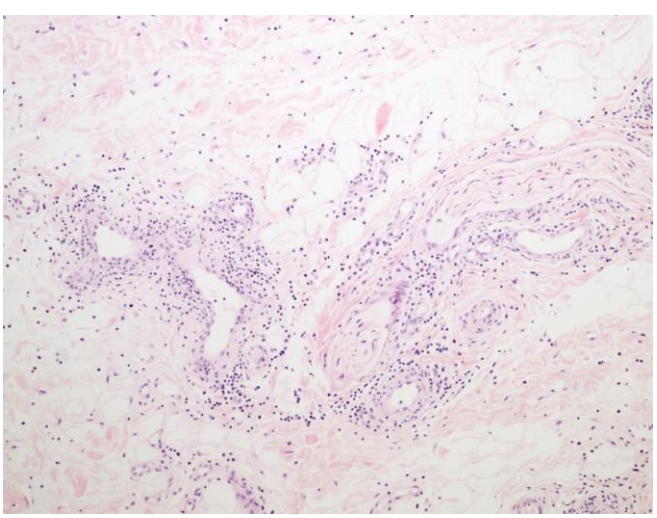

Figure 2. Lymphocytes at the periphery and the wall of the vessels in the subcutaneous tissue septum. Fibrin deposition or classical erythema nodosum picture are not seen (H+Ex100).

Case 2. A 29-year-old woman gave birth one month ago. At the end of postpartum first month, she had increasing pruritus and rash for 5 days. On dermatological examination, there were bilateral erythematous papules and plaques on her trunk. Clinical diagnoses were pruritic urticarial papules and plaques of pregnancy (PUPPP), pemphigoid (herpes) gestationis. Biopsy revealed LV, few eosinophil leukocytes and intraepidermal collection of Langerhans cells consistent with PUPPP (Figure 3). It was her first pregnancy, the rash resolved spontaneously and she did not have a similar eruption in her second pregnancy.

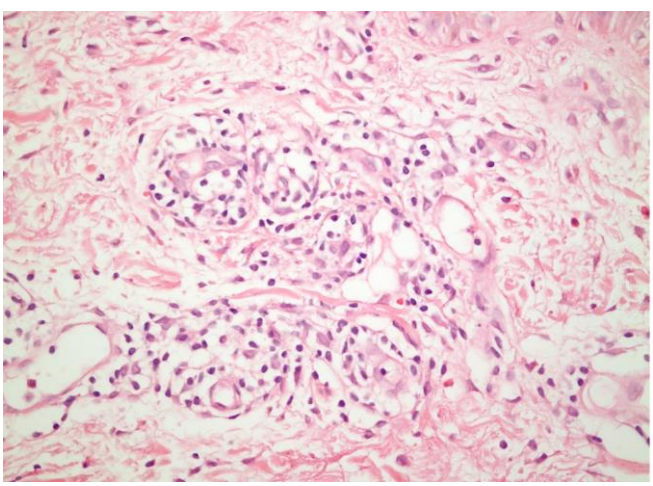

Figure 3. Vacuolization of the endothelia, erythrocyte extravasation and few eosinophils. (H+Ex400).

Case 3. A 23-year-old woman had erythematous papules predominantly on bilateral upper and lower extremities, declining steadily on her trunk. She had no vesicule or pustule formation. Oral mucosa was normal. On her blood test; autoimmune serology (such as Anti-cardiolipin IgM and IgG; Anti-Phospholipid IgM and IgG, Anti-ds-DNA), hepatitis and HIV serology were negative. EBV EBNA IgG was 682 RU/mL and EBV VCA IgG was 2657 RU/mL. Biopsy was taken from her forearm with the clinical diagnoses of viral eruption and Gianotti-Crosti syndrome. Pathologic examination revealed lichenoid vacuolar changes at the interface along with spongiosis and LV consistent with Gianotti-Crosti syndrome (Figure 4)

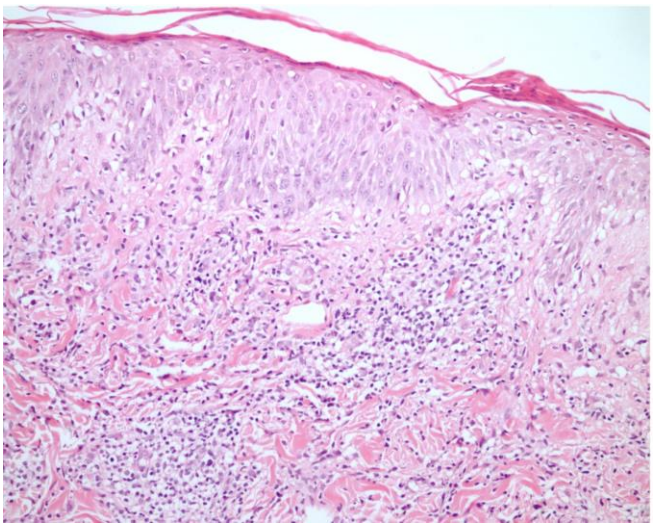

Figure 4. Basal vacuolization of the epidermis, dense lymphocytic reaction around and on the wall of the vessels in the papillary dermis. (H+Ex200).

Case 4. A 39-year-old male patient with a diagnosis of acute myeloid leukemia (AML) had palpable purpura on his bilateral lower extremity after the first dose of cytarabine therapy. Clinical picture was that of LCV, which is usually seen in sepsis or due to medications in these patients. Biopsy findings showed LV (Figure 5)

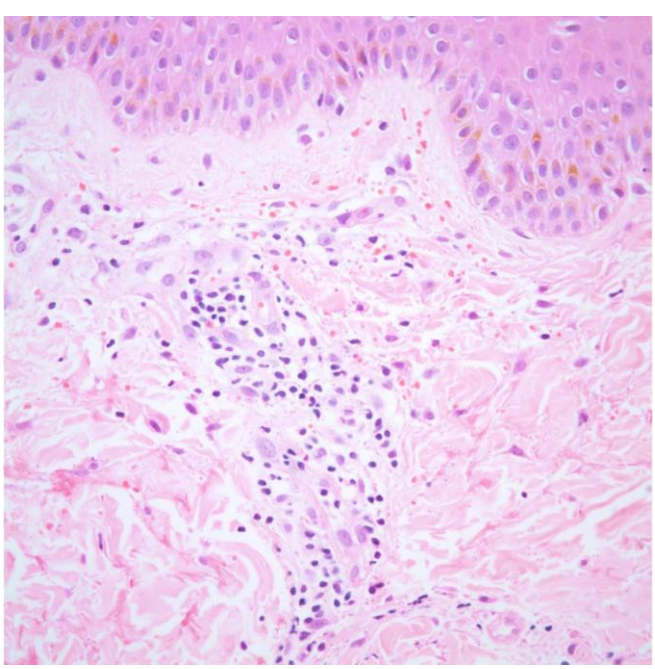

Figure 5. Endothelial swelling, lymphocytic infiltration of the vessel wall and extravasated erythrocytes. Leukemic infiltration is not present (H+Ex200).

Discussion

Vasculitis is a generic term for the inflammation of vessel walls. Many pathologists hesitate to give this diagnosis without a definable clinical condition explaining the presence of vascular damage. Also they should give explanatory notes about the type of vessel and the cellular constituents. A diagnosis of LCV is simpler for the clinician who is familiar with the underlying conditions than the diagnosis of LV which creates a confusion for how to find an appropriate place for this diagnosis in the clinical context for that particular patient. Since LV can have different clinical presentations, it is expected to have many different inflammatory skin diseases or vasculitic conditions included in the differential diagnosis. A pathologist almost never receives a clinical diagnosis of LV in the biopsy form but gives it as a diagnosis. For the pathologist's point of view, LV is a descriptive term defining a morphological change; the etiology leading to vascular damage, which is inflammation. This can fit to many situations [3].

If the term LV vasculitis is used by strict criteria, namely the presence of fibrin, then one should use the term vasculopathic reaction pattern for the lymphocytic reaction together with endothelial swelling or thickening of the vascular wall. This will lead to rarity of this diagnosis and perivascular dermatites will be assumed more important than they mostly are. Diseases showing vasculopathic reaction pattern can be listed as non-inflammatory purpuras, vascular occlusive diseases, urticarias, neutrophilic dermatoses and vasculitis (acute, chronic lymphocytic, granulomatous). The most important category

within this tissue reaction pattern is vasculitis. Then time comes to question the criterion for the vasculitis [4,5].

Chronic LV is a term used for a number of clinically heterogenous diseases. It is characterized by predominantly lymphocytic infiltrate involving and surrounding the small vessels in the dermis. There can be acute or chronic damage to the small vessel walls with fibrin deposition and/or lamination by pericytes. It is usually associated with endothelial cell swelling and erythrocyte extravasation. Nuclear dusting is uncommon. Acute vasculitis may progress with time to a chronic stage and fibrin is rarely present in these late lesions.

Regarding our cases, the distribution frequency of clinical conditions diagnosed pathologically as LV was within the expected range. Collagen vascular disease is a known and top list condition associated with LV [1]. Twenty-two percent of our cases had this diagnosis. One patient in this group had also myelodysplastic syndrome and one had colon carcinoma.

The percentage of the second most common clinical diagnosis, urticarial / LCV (14%) seems to be higher as compared to previous studies. The LV in these cases could represent the late manifestation of LCV [6]. Three patients in this group had accompanying lymphoma, AML and chronic renal failure.

Pitiriasis lichenoides, which makes up 13% of our cases is the prototype of lichenoid LV pattern. One patient had previously diagnosed as mycosis fungoides, 2 had colitis. Graft versus host disease (GVHD) which is said to be the first defined condition with a lichenoid LV was not present in our series. Patients who were diagnosed as GVHD in our department were usually in early phases with grade 2 features and probably the diagnostic / differential diagnostic work-up of GVHD did not involve searching for LV.

Drugs such as aspirin, paracetamol, lipid-lowering agents or herbal medicine may lead to lesions caused by LV [7]. Nine cases (8%) in our series had the clinical diagnosis of drug eruption. One patient was lost to hemophagocytic syndrome.

Behçet's disease, figurate erythema (erythema annulare centrifigum and granuloma annulare) and panniculitis (usually erythema nodosum) made 7% each of our cases.

Lichen planus and spongiotic (nummular) dermatitis were surprisingly present in the clinical diagnoses. These cases may suggest the dominance of vascular changes albeit the minor changes in the epidermis and the interface.

LCV bears neutrophils in the infiltrate and denotes an acute reaction. LV on the other hand, has lymphocytes which are cells capable of recruiting other inflammatory cells (neutrophils and histiocytes). Lymphocytes themselves are masqueraded in conditions like (late phase) LCV and granulomatous vasculitis. LCV is an immune complex mediated reaction and sometimes it can be seen in non-immunological conditions like with bacterial toxins and erythema elevatum diutinum. LV can represent the resolving phase of neutrophilic vasculitis after 24-72 hours. It is a cell mediated reaction causing its effects by cytotoxicity [2].

Conclusions

LV is an important part of diagnostic practice in dermatopathology since it can present as an heterogeneous group of diseases some of which do not manifest themselves clearly. The pathogenesis of LV interests researches since it has been shown that some molecular markers differ in LCV and LV.

References

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