

## An approach to the diagnosis of neutrophilic dermatoses: A histopathological perspective

K. C. Nischal, Uday Khopkar\*

Department of Dermatology, Adichunchanagiri Institute of Medical Sciences, Bellur, Karnataka, \*Department of Dermatology, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra, India.

**Address for correspondence:** Dr. K. C. Nischal, Department of Dermatology, Adichunchanagiri Institute of Medical Sciences, Bellur - 571448, Karnataka, India. E-mail: kc\_nischal@yahoo.com

### ABSTRACT

Neutrophilic dermatoses comprises of non-infective dermatoses which are histopathologically characterized by neutrophil predominant infiltrate and clinically, respond promptly to corticosteroids. Conditions primarily with vasculitis though neutrophilic are excluded from this group. In this article we intend to briefly outline the approach to diagnose these conditions with histological perspective. The ambiguity regarding few recent dermatosis viz., rheumatoid neutrophilic dermatosis, bowel associated-dermatosis-arthritis syndrome etc. with regard to their inclusion in this group has also been highlighted.

**Key Words:** Neutrophilic dermatoses, Histopathology, Pustule

The term 'neutrophilic dermatosis' (ND) was initially used by R. D. Sweet in 1964 as 'acute febrile neutrophilic dermatosis' to describe Sweet's syndrome.<sup>[1]</sup> However, over the years, this terminology has been adapted to denote non-infective dermatoses that exhibit a predominantly neutrophilic inflammatory infiltrate and promptly respond to corticosteroid therapy. Largely, dermatoses with associated vasculitis are not included in this spectrum though some researchers include these too under this broad entity. As histopathology plays a pivotal role in the classification of this group of diseases, which are diverse in their etiology, neutrophilic dermatosis is a histopathological rather than a clinical entity.

### DEFINITION AND SCOPE OF NEUTROPHILIC DERMATOSES

Neutrophilic dermatoses are inflammatory dermatoses characterized histologically by a predominantly neutrophilic infiltrate in the absence of any infective pathology.<sup>[2]</sup> Although some of these conditions may occasionally show features of small vessel vasculitis, all dermatoses with primary leukocytoclastic vasculitis (viz. polyarteritis nodosa, microscopic polyangiitis, hypersensitivity angiitis) are

excluded from this group of disorders.<sup>[3]</sup>

However, there are some grey areas in defining a ND; it is the purpose of this section to list entities that do not exactly fit this definition and are not discussed further in this review. These conditions are discussed in brief below.

Rheumatoid ND comprises papules, plaques, nodules,<sup>[4]</sup> wheals or ulcers on extensor aspects in both seropositive and seronegative rheumatoid patients.<sup>[5,6]</sup> Histologically it is characterized by dense infiltrate of neutrophils mixed with eosinophils, plasma cells and lymphocytes spanning the entire dermis and may extend into subcutis. Though leukocytoclasia is prominent, vasculitis is not seen. These features are reminiscent of Sweet's syndrome except for the absence of dermal edema and presence of a mixed inflammatory infiltrate. Probably, the condition described as 'neutrophilic lobular panniculitis associated with rheumatoid arthritis' and which Requena *et al* have reclassified as lobular neutrophilic panniculitis is nothing but an extension of this process itself.<sup>[7]</sup>

Although in many instances like pustular psoriasis, the predominantly epidermal neutrophilic infiltrates satisfy the

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technical criteria for a ND this review is focused on dermal neutrophilic infiltrates. Other causes of the epidermal pustule include irritant dermatitis, and acrodermatitis enteropathica. However, these and other conditions associated with secondary neutrophilic infiltration of the skin due to epidermal or dermal necrosis (which include spider bites) have been excluded from this discussion for the sake of convenience.

The term pyoderma vegetans is now preferentially used to denote pemphigus vegetans of Hallopeau type. It is histopathologically characterized by pseudocavicular epitheliomatous hyperplasia with multiple eosinophilic microabscesses and immunofluorescence is typical of pemphigus. Rarely, blastomycosis like pyoderma is also referred to as pyoderma vegetans. Here the microabscesses are predominantly neutrophilic; but as it is infective in etiology (usually *Staphylococcus aureus*), it does not merit inclusion as a neutrophilic dermatosis.

Pyoderma faciale, whose classification as a variant of acne or rosacea is still debated, cannot be included in this category of histological pattern as there is evidence of both Gram positive (*Staphylococcus aureus*) as well as Gram negative (*P. acnes*) organisms being grown from these lesions.

Even though bowel-associated dermatosis-arthritis syndrome is histologically characterized by perivascular neutrophilic infiltrate with dermal edema, the established role of peptidoglycans released from the intestinal flora, especially *E. coli*, puts a question on its inclusion in the spectrum of neutrophilic dermatoses.<sup>[8]</sup>

## **HISTOPATHOLOGICAL CLASSIFICATION OF NEUTROPHILIC DERMATOSES**

Keeping neutrophil-predominant infiltrate as the basic feature, we have attempted to classify the neutrophilic dermatoses based on the associated histological patterns [Table 1].

### **PREDOMINANTLY EPIDERMAL INFILTRATE NEUTROPHILIC PUSTULE / ABSCESS**

Collection of neutrophils in the epidermis can occur in a variety of conditions ranging from inflammatory dermatosis like psoriasis, neonatal disorders e.g. transient neonatal pustular melanosis to neoplasms viz. keratoacanthoma. Hence identification of the associated epidermal or dermal patterns helps in differentiating each of these conditions

from one another.

Pustules with epidermal proliferation are a feature of psoriasis, pustulosis associated with autoimmune diseases, halogenoderma and keratoacanthoma. Although amicrobial pustulosis associated with autoimmune diseases (APAD) presents with intraepidermal pustule, the acanthosis is not as regular as in psoriasis and parakeratosis is rather focal as mounds.<sup>[9,10]</sup>

Intraepidermal pustules along with epidermal proliferation are also found in halgenodermas. However, the pustules harbor eosinophils in addition to neutrophils. The epidermal hyperplasia is either in the form of papillomatosis (bromoderma > iododerma > fluoroderma) or pseudocarcinomatous type (arising from the appendageal epithelium). Ulceration of the plaque is more common with iododerma.<sup>[11]</sup> As the lesion evolves, a mononuclear cell infiltrate predominates. Epidermal proliferation in keratoacanthoma is irregular, folliculocentric and contains numerous dyskeratotic cells as well as atypical mitotic figures.

In psoriasis, neutrophilic collections occurring in the stratum malpighii layer are associated with spongiosis and hence referred to as 'spongiform pustule of Kogoj'. The same pustule as it moves up the epidermis, becomes more compact sine spongiosis and presents as Munro's microabscess.

Epidermal pustules without epidermal proliferation occur in transient neonatal pustular dermatosis (TNPd), acropustulosis of infancy, pustular psoriasis, palmoplantar pustulosis, acute generalized exanthematous pustulosis, pustular variant of Kawasaki's disease, IgA pemphigus and subcorneal pustular dermatosis (SCPD). Among these, eosinophils are admixed in neutrophilic infiltrate in transient neonatal pustular dermatosis (TNPd), palmoplantar pustulosis, subcorneal pustular dermatosis and acute generalized exanthematous pustulosis.<sup>[12]</sup> The number of eosinophils within the pustules is more in TNPd than in acropustulosis of infancy. The healed lesions of TNPd reveal focal hypermelanization of keratinocytes. It is almost impossible to histologically differentiate subcorneal pustular dermatosis and subcorneal pustular dermatosis subtype of IgA pemphigus.

Epidermal neutrophilic abscess may occasionally occur in the pustular variant of Kawasaki's disease. In addition, they have sparse superficial and deep perivascular mixed infiltrate made up of lymphocytes and neutrophils. However, these features are neither characteristic nor diagnostic of this variant of Kawasaki's disease.

**Table 1: Histopathological classification of neutrophilic dermatoses**

<b>Predominantly epidermal infiltrate</b>	
Epidermal neutrophilic pustule / abscess	Pustular psoriasis Palmoplantar pustulosis Subcorneal pustular dermatosis Acropustulosis of infancy Acute generalized exanthematous pustulosis IgA pemphigus Pemphigus foliaceus Transient neonatal pustular melanosis Amicrobial pustulosis associated with autoimmune diseases (APAD) Kawasaki disease, pustular variant
Neutrophilic vesicles / bullae	Subcorneal pustular dermatosis IgA pemphigus Pemphigus folicaceus Hydroa vacciniforme
<b>Predominantly dermal neutrophilic infiltrate</b>	
Neutrophilic vesicles / bullae in upper dermis	Dermatitis herpetiformis Pyoderma gangrenosum, bullous variant Bullous lupus erythematosus Linear IgA dermatosis Drug-induced linear IgA dermatosis Epidermolysis bullosa acquisita
Neutrophilic diffuse dermal infiltrate	Sweet's syndrome Pyoderma gangrenosum Behcet's disease Erythema elevatum diutinum Granuloma faciale Bowel-associated dermatitis-arthritis syndrome Halogenoderma Rheumatoid neutrophilic dermatosis Urticaria (some cases)
Neutrophilic infiltrate with granulomatous reaction	Pyoderma gangrenosum, superficial granulomatous variant Cutaneous Crohn's disease Behcet's disease, late stage Rheumatoid nodule Palisaded neutrophilic and granulomatous dermatitis of connective tissue disease Pseudofolliculitis, late stage
Neutrophilic infiltrate predominantly perivascular	Prurigo pigmentosa Solar urticaria Urticaria (some cases) Vesiculopustular eruption of hepatobiliary disease
<b>Predominantly appendageal neutrophilic infiltrate</b>	
Neutrophilic infiltrate predominantly follicular	Pyoderma gangrenosum Pseudofolliculitis Sterile neutrophilic folliculitis with perifollicular vasculopathy
Neutrophilic infiltrate predominantly eccrinal	Neutrophilic eccrine hidradenitis Idiopathic recurrent palmoplantar hidradenitis

Neutrophilic spongiosis may also be occasionally observed in Sweet's syndrome.<sup>[13]</sup>

In any of the above conditions, the neutrophils may cause secondary acantholysis and hence this feature is not of any diagnostic relevance.

**NEUTROPHILIC VESICLES / BULLAE**

Vesicles / bullae predominantly containing of neutrophils may have a normal overlying epidermis or necrosis of its roof. The latter is more common with hydroa vacciniforme. Reticular degeneration due to intercellular edema is

observed in early lesions of hydroa vacciniforme. These lesions as they enlarge, form a vesicle containing fibrin, neutrophils and lymphocytes and later develop confluent necrosis of roof of the blister.

Vesicopustules occurring in subcorneal pustular dermatosis (Sneddon-Wilkinson disease) are identical to those in IgA pemphigus. Also, intercellular IgA deposits are observed in both but the different antigen specificities has separated these conditions. Sparing of hair follicles, propensity for necrosis of blister roof and absence of intercellular IgA deposits favor a diagnosis of hydroa vacciniforme. Foci of neutrophilic spongiosis may also occur in pemphigus foliaceus.<sup>[14]</sup>

## PREDOMINANTLY DERMAL NEUTROPHILIC INFILTRATE

### *Neutrophilic vesicles / pustule*

This group of disorders poses a great challenge in diagnosis because of relatively identical histopathological appearance. The clues to diagnosis are occasionally very subtle, sometimes require special staining techniques and most of the times clinical correlation.

When a biopsy specimen from an early papule or a plaque reveals papillary dermal microabscess with or without neutrophilic spongiosis, a diagnosis of dermatitis herpetiformis (DH) is more likely. Rarely, erythema elevatum diutinum (EED) may sport a similar finding.<sup>[15]</sup> However, rarity of vesicles/blisters, presence of fibrosis and frequent presence of leukocytoclastic vasculitis helps to distinguish EED from DH. A uniform infiltrate of neutrophils in the subepidermal zone is more common with linear IgA dermatosis. Absence of such infiltrate in epidermolysis bullosa acquisita differentiates from DH, linear IgA dermatosis and DH-like drug eruption.<sup>[16]</sup> In drug-induced linear IgA dermatosis, there is lympho-eosinophilic perivascular infiltrate along with a few eosinophils in dermal infiltrate.

A well-developed vesicle or blister of dermatitis herpetiformis has features similar to any of the disorders enlisted in this section. In such cases, immunofluorescence plays an important role in the diagnosis of this condition.

Focal interface dermatitis or vacuolar dermatitis, superficial and deep perivascular and peri-appendageal lymphocyte admixed neutrophilic infiltrate, mucin in between collagen bundles and leukocytoclastic vasculitis occurs in bullous variant of acute cutaneous lupus erythematosus. Occasionally, dermatitis herpetiformis-like pattern may be seen in bullous SLE. Subepidermal blister with diffuse dense dermal infiltrate of neutrophils with or without leukocytoclasia and vasculitis is a feature of bullous variant of pyoderma gangrenosum. As bullous lesions are more common in association with underlying hematological malignancies, the infiltrate may contain atypical cells of myeloid or lymphoid lineage and serves as a vital clue in diagnosis.

## NEUTROPHILIC DIFFUSE DERMAL INFILTRATE

Dense diffuse dermal infiltrate predominantly composed of neutrophils and leukocytoclasia is very common in pyoderma gangrenosum (PG) as well as Sweet's syndrome (SS). Features of folliculitis, lack of papillary dermal edema and rarity of ulceration tends to differentiate the former from the latter.

Pyostomatitis vegetans is considered as a mucosal variant of pyoderma gangrenosum.

A slightly less dense neutrophilic infiltrate with or without leukocytoclastic vasculitis occurs in the early neutrophilic stage of Behcet's disease (the other two stages being, lymphocytic and granulomatous, in succession). Thus it is obvious that at times it is very difficult to histologically distinguish PG, SS and early Behcet's disease.

Diffuse infiltrate of neutrophils with eosinophils sans Grenz zone and fibrosis is found in some cases of urticaria, which includes not only chronic, cold and cholinergic urticaria but also some patients with acute urticaria and dermographism.<sup>[17]</sup> Features reminiscent of neutrophilic urticaria but with subepidermal and epidermal abscesses can occur in prurigo pigmentosa. However, with age, the lesions of prurigo pigmentosa develop scale-crust containing neutrophils and a rather more focal lichenoid lymphocytic infiltrate than neutrophil predominant infiltrate.

Erythema elevatum diutinum and granuloma faciale have similar histopathological features viz. diffuse dense nodular mixed dermal infiltrate of neutrophils, eosinophils and plasma cells on a background of concentric laminated fibroplasia around the involved vessels. Presence of a subepidermal infiltrate-free zone is characteristic of granuloma faciale. Overt vasculitis may or may not be present. However, careful search does reveal some neutrophilic nuclear dust and fibrin within and around small vessels. The fibroplasia is more pronounced in older plaques while vasculitis is more visible in the newer lesions.

Diffuse dense dermal infiltrate of neutrophils when admixed with eosinophils and present along with epidermal abscesses, epidermal hyperplasia (papillomatosis or pseudocarcinomatous hyperplasia) and with or without ulceration, halogenoderma should be borne in mind as a possibility. A variable amount of necrosis of keratinocytes along with interstitial and superficial perivascular mixed cell infiltrate consisting predominantly of neutrophils along with a few eosinophils is seen in toxic shock syndrome. Subepidermal blisters can occur in toxic shock syndrome.

## NEUTROPHILIC INFILTRATE WITH GRANULOMATOUS REACTION

This group of disorders is characterized by the presence of granulomas either ill-defined or well-defined in addition to neutrophil-predominant infiltrate. Ill-defined granuloma

is common with superficial granulomatous variant of pyoderma gangrenosum and late stage of Behcet's disease and granuloma faciale.

Ill-defined granulomas made up of aggregations of epithelioid cells, Langhan's giant cells, histiocytes occur in superficial granulomatous variant of pyoderma gangrenosum. However, in contrast to dense neutrophilic infiltrate seen with other neutrophilic dermatoses, neutrophils are sparse in this variant of PG. Poorly defined granuloma with varying degree of fibrosis occurs in the late stage of Behcet's disease.

Well-defined epithelioid cell granuloma with Langhan's giant cells occurring in foci or along neurovascular bundles admixed with neutrophils and leukocytoclasia occur in cutaneous Crohn's disease. Follicular hyperkeratosis leading to follicular dilatation and subsequent rupture of the follicle with resultant foreign body or suppurative granuloma is seen in late lesions of follicular occlusion tetrad (hidradenitis suppurativa, pilonidal sinus, dissecting cellulitis of scalp and acne keloidalis).

When an infundibular or pilar cyst or steatocystoma ruptures, the sequestered antigens of keratinocytes elicit an intense dermal inflammation, which culminates in a suppurative granulomatous inflammation. Presence of remnants of cyst walls helps in diagnosis. Demonstration of bacteria within the follicular infundibulum helps to differentiate nodulocystic acne from ruptured follicular cyst. However, it is not possible to find the bacteria always and then clinicopathologic correlation becomes essential. Presence of leukocytoclastic vasculitis with suppurative granuloma is suggestive of sterile neutrophilic folliculitis with perifollicular vasculopathy.

Palisaded granulomas occur in rheumatoid nodule and palisaded neutrophilic and granulomatous dermatitis (PNGD). In both instances, the center of the granuloma contains degenerated, thickened collagen bundles; neutrophils and nuclear dust surrounded by palisade of histiocytes, epithelioid cells with or without Langhan's giant cells. However, the central degenerated collagen is red due to fibrinoid degeneration in the rheumatoid nodule in contrast to basophilic degeneration of collagen in PNGD. Basophilic degeneration occurs due to the enzymes released by the neutrophils in the infiltrate. Also, the presence of thick fibrin cuff separating the vessel from the surrounding tissue and sparsity of extravasated red blood cells in spite of presence of leukocytoclastic vasculitis is characteristic of PNGD and helps to differentiate it from rheumatoid nodule.

## **NEUTROPHILIC INFILTRATE PREDOMINANTLY PERIVASCULAR**

Superficial sparse perivascular infiltrate of neutrophils is one of the earliest signs of prurigo pigmentosa. But similar features are seen also in some cases of urticaria (chronic, cold and cholinergic), bullous SLE and dermatitis herpetiformis. This is largely a very transitory histological pattern occurring in the early course of the disease and hence, perivascular pattern of infiltrate does not have much diagnostic significance. Prominent perivascular neutrophilic infiltrate and papillary dermal edema with or without subepidermal abscess and vasculitis are features of bowel-associated dermatosis-arthritis syndrome.

## **PREDOMINANTLY APPENDAGEAL NEUTROPHILIC INFILTRATE**

### *Neutrophilic infiltrate predominantly follicular*

Sterile folliculitis occurs in early lesion of pyoderma gangrenosum and sterile neutrophilic folliculitis with perivascular vasculopathy. However, the latter is also characterized by the presence of frank leukocytoclastic vasculitis or infiltration of vessel wall by neutrophils without evidence of fibrin deposition around the follicle. Follicular pustules may occur in acute generalized exanthematous pustulosis but is rather due to a generalized phenomenon involving follicles.

In pseudofolliculitis though, the inflammation is the result of hair shaft piercing the epithelium and hence coming in direct contact with the dermis. The intense inflammation gives rise to a parafollicular pustule.

## **NEUTROPHILIC INFILTRATE PREDOMINANTLY ECCRINAL**

Neutrophilic infiltrate with leukocytoclasia predominantly around the secretory coils of eccrine glands is observed in neutrophilic eccrine hidradenitis. Occasionally, it is associated with necrosis of secretory epithelium. Preferential involvement of the eccrine duct and lack of syringo-squamous metaplasia differentiates palmoplantar hidradenitis from the former.

## **Atypical features of various neutrophilic dermatoses [Table 2]**

### *Sweet's syndrome*

The classical Sweet's syndrome exhibits a diffuse dermal neutrophilic infiltrate with or without neutrophilic spongiosis.



**Table 2: Summary of atypical findings in various neutrophilic dermatoses**

Neutrophilic dermatosis	Atypical features
Sweet's syndrome	<ol style="list-style-type: none"> <li>1. Presence or absence of neutrophilic spongiosis</li> <li>2. Diffuse, lichenoid, perivascular or combination of these patterns of infiltrate</li> <li>3. Presence of vasculitis<sup>[18]</sup></li> <li>4. Destruction of elastic fibers</li> <li>5. Presence of myeloid or lymphoid precursor / atypical cells</li> <li>6. Histiocytoid (immature myeloid cells)<sup>[19]</sup></li> </ol>
Pyoderma gangrenosum	<ol style="list-style-type: none"> <li>1. Presence of myeloid or lymphoid precursor / atypical cells</li> <li>2. Vasculitis</li> </ol>
Bullous SLE	<ol style="list-style-type: none"> <li>1. Dermatitis herpetiformis-like pattern<sup>[22]</sup></li> </ol>
Bowel-associated dermatosis-arthritis syndrome	<ol style="list-style-type: none"> <li>1. Pustular folliculitis</li> <li>2. Septal panniculitis in erythema nodosum-like lesion</li> </ol>
Rheumatoid neutrophilic dermatosis	<ol style="list-style-type: none"> <li>1. Neutrophilic spongiosis<sup>[23]</sup></li> <li>2. Transepidermal elimination of fibrinoid material<sup>[24]</sup></li> <li>3. Fibrinoid degeneration of collagen<sup>[25]</sup></li> <li>4. Vasculitis<sup>[26]</sup></li> <li>5. Subepidermal vesicle<sup>[27]</sup></li> </ol>
Rheumatoid nodule <sup>[28]</sup>	<ol style="list-style-type: none"> <li>1. Mixed cellular infiltrate of lymphocytes and histiocytes<sup>[29]</sup></li> <li>2. Ulceration<sup>[30]</sup></li> <li>3. Pauci-inflammatory vascular thrombosis</li> <li>4. Glomeruloid neovascularization</li> <li>5. Vasculitis: leukocytoclastic, lymphocytic or granulomatous</li> <li>6. Occlusive intravascular histiocytic foci "RA-associated intravascular histiocytopathy"</li> </ol>
Behcet's disease	<ol style="list-style-type: none"> <li>1. Lobular panniculitis with polyp-like lipophages protruding into the fat cysts</li> <li>2. Superficial and deep perivascular mononuclear cell infiltration</li> <li>3. Intraepidermal pustules</li> <li>4. Lymphocytic or leukocytoclastic vasculitis<sup>[31]</sup></li> </ol>
Erythema elevatum diutinum	<ol style="list-style-type: none"> <li>1. Bulla<sup>[32]</sup></li> <li>2. Neutrophilic microabscesses in tips of dermal papilla similar to dermatitis herpetiformis</li> <li>3. Necrotizing granuloma</li> <li>4. Lipids and lipophages between collagen bundles</li> </ol>
Epidermolysis bullosa acquisita	<ol style="list-style-type: none"> <li>1. Bullous pemphigoid-like with perivascular lymphocytes, neutrophils and few eosinophils</li> </ol>
Acute generalized exanthematous pustulosis	<ol style="list-style-type: none"> <li>1. Leukocytoclastic vasculitis<sup>[33]</sup></li> </ol>
Granuloma faciale	<ol style="list-style-type: none"> <li>1. Toxic hyaline around vessels</li> <li>2. Foam cells and foreign body giant cells</li> </ol>

However, the infiltrate can be diffuse, band-like or perivascular or a combination of any of those patterns.<sup>[18]</sup> Vasculitis is usually an epiphenomena rather than a primary event in SS and is the result of vessel wall damage secondary to release of inflammatory mediators from the neutrophils. Malone *et al.*, have demonstrated that the presence of vasculitis correlates with the duration of the lesion biopsied.

Requena *et al.*,<sup>[19]</sup> have demonstrated the presence of histiocyte-like cells in the infiltrate rather than classical neutrophilic-rich infiltrate in 41 patients with Sweet's syndrome (six of them had associated malignancy). Based on the presence of strong immunoreactivity for myeloperoxidase, presence of pan-histiocytic markers viz. CD 68, MAC 386 and absence of genetic abnormalities (*bcr/abl* gene fusion), these cells were concluded to be immature myeloid cells. In addition to this, they could not find any variation in the type of inflammatory infiltrate cells with the duration of the lesion. This contrasts with observations of Jordaan, 1989 who demonstrated three phases in the evolution of Sweet's syndrome (initially lymphocytic, then neutrophilic and later histiocytic-rich infiltrate).<sup>[20]</sup> In chronic Sweet's syndrome, Vignon-Pennamen *et al.*, 2006 have demonstrated an initial

lymphocytic stage and later classical neutrophil-rich infiltrate and propose that the lymphocytic stage is a harbinger of cutaneous involvement in patients with myelodysplasia.<sup>[21]</sup>

Lesions histologically classical of Sweet's syndrome but with the presence of leukocytoclastic vasculitis and morphologically present on dorsal hands were referred to as "pustular vasculitis of hands". As some of these lesions lacked vasculitis, now this entity has been referred to as "neutrophilic dermatosis of dorsal hands" and is considered as a subset of Sweet's syndrome. The term 'pustular vasculitis' has also been used to denote conditions with pustules that show features of vasculitis. It may occur as an isolated dermatosis or can be seen in various diseases viz. systemic lupus erythematosus or primary biliary cirrhosis due to intense perivascular inflammation.

Because of the similar histological pattern in most of the neutrophilic dermatoses, additional investigations are required to differentiate each of these. The characteristic pattern of the antibodies is summarized in Table 3. However, occasionally the immunofluorescence pattern is identical and then the diagnosis depends on antigen mapping.

**Table 3: Immunofluorescence pattern in various neutrophilic dermatoses**

Condition	Type of staining pattern	Antibody	Antigen
<b>Epidermal</b>			
Pemphigus foliaceus	Intercellular deposits involving entire epidermis or only upper part of epidermis	IgG	Desmoglein 1
IgA pemphigus, subcorneal pustular dermatosis type	Only upper part of epidermis in subcorneal pustular dermatosis type	IgA	Desmocollin 1
IgA pemphigus, intraepidermal neutrophilic dermatosis type	Intercellular deposits involving entire epidermis in intraepidermal neutrophilic dermatosis type	IgA	Desmoglein 1 and 3
Subcorneal pustular dermatosis	Intercellular deposits	IgA	-
<b>Subepidermal, linear</b>			
Linear IgA dermatosis, lamina lucida type	Linear deposits in N-serrated pattern <sup>[34]</sup>	IgA1> IgA2, C3, rarely also, IgG	97kD and 120 kD protein present in extracellular part of 180kD BPAG2
Linear IgA dermatosis, Sublamina densa type	Linear deposits in N-serrated pattern <sup>[34]</sup>	IgA1> IgA2, C3, rarely also, IgG	Unknown Occasionally, NC-1 domain of Type VII collagen
Drug-induced Linear IgA dermatosis	1. Linear deposit 2. Linear deposits in sublamina densa <sup>[35]</sup> 3. Granular, linear deposits along dermoepidermal junction <sup>[36]</sup>	1. IgA and C3 2. IgA1 <sup>[35]</sup> 3. IgA and C3 <sup>[36]</sup>	180-kD polypeptide of keratinocytes
<b>Subepidermal, granular</b>			
Dermatitis herpetiformis	Granular deposits at the summit of dermal papilla	IgA	Reticulin, smooth muscle endomycium, gluten, β-lactoglobulin, bovine serum albumin
Bullous systemic lupus erythematosus	Ribbon-like / tubular pattern (50%) or granular band-like (25%) along the basement membrane	IgG, C3	290kD or 145kD protein component of Type VII collagen
Epidermolysis bullosa acquisita	Linear deposits in u-serrated staining pattern <sup>[34]</sup>	1. IgG 2. IgA 3. IgG and IgA* 4. IgG and C3 <sup>[37]</sup>	1. Globular carboxyl terminus of Type VII collagen 2. Plectin 3. Dermal side of Type IV collagen

\*Linear deposits of both IgA as well as IgG have been reported in a case with blisters and immunoblotting revealed antibodies reacting with NC1 domain of Type VII collagen, suggestive of EBA as well as with the 120-kDa linear IgA bullous dermatosis antigen, LAD-1.<sup>[38]</sup>

As the lesions evolve, the histological features too change accordingly and hence, there cannot be rigid characterization of features. This change can be,

1. *Change in the pattern of inflammation:* Palisaded neutrophilic and granulomatous dermatitis has predominance of leukocytoclastic vasculitis in the early stage, later becomes more granulomatous and in final stages, fibrosis sets in.
2. *Change in the type of inflammatory cells in infiltrate:* Early lesions of Behcet's disease reveal a predominantly neutrophilic infiltrate typical of neutrophilic dermatosis. However, with evolution of disease, the infiltrate becomes more lymphohistiocytic rather than neutrophilic.

While newer neutrophilic dermatoses might be identified in future, the approach and classification mentioned in this article should help pin most diagnoses.

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### Multiple choice questions

1. Neutrophilic epidermal abscess occurs in
  - a. Acropustulosis of infancy
  - b. Halogenoderma
  - c. Erythema toxicum neonatorum
  - d. Acute generalized exanthematous pustulosis
2. Granulomatous inflammation occurs in all except
  - a. Crohn's disease
  - b. Granuloma faciale
  - c. Behcet's disease
  - d. All of the above
3. Grenz zone is seen in
  - a. Granuloma faciale
  - b. Erythema elevatum diutinum
  - c. Sweet's syndrome



- d. Amicrobial pustulosis associated with autoimmune diseases
- 4. Sparing of hair follicle is seen in
  - a. IgA pemphigus
  - b. Hydroa vacciniformae
  - c. Pemphigus foliaceus
  - d. None of the above
- 5. Following does not qualify as a neutrophilic dermatosis except
  - a. Miliaria pustulosa
  - b. Pustular psoriasis
  - c. Pyostomatitis vegetans
  - d. Pyoderma faciale
- 6. Transepidermal elimination of fibrinoid material occurs in
  - a. Rheumatoid neutrophilic dermatosis
  - b. Behcet's disease
  - c. Epidermolysis bullosa acquisita
  - d. Bullous SLE
- 7. Intercellular deposits of IgA are found in
  - a. Bullous SLE
  - b. Subcorneal pustular dermatosis
  - c. Pemphigus foliaceus
  - d. Bullous rheumatoid neutrophilic dermatosis
- 8. Fat cysts are seen in
  - a. Bowel-associated arthritis-dermatosis syndrome
  - b. Behcet's disease
  - c. Acute generalized exanthematous pustulosis
  - d. Sweet's syndrome
- 9. Neutrophilic abscesses are seen in all except
  - a. Sweet's syndrome
  - b. Sneddon-Wilkinson disease
  - c. Cholinergic urticaria
  - d. Keratoacanthoma
- 10. Papillomatosis is seen with,
  - a. Psoriasis
  - b. Prurigo pigmentosa
  - c. Transient neonatal pustular melanosis
  - d. Halogenoderma

Answer: 1) a 2) b 3) a 4) b 5) c 6) a 7) b 8) b 9) c 10) d