CD$_{30}^{+}$ cells in benign inflammatory infiltrate of some dermatological diseases

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**Abstract**

**Background:** CD30 (cluster of differentiation) is a membrane antigen belonging to the so called activation antigen that are induced in lymphocytic cells following their activation.

**Objective:** Assessment of CD$_{30}^{+}$ cells status in benign inflammatory infiltrate of some dermatological diseases such as psoriasis, lichen planus and scabies in Nile Delta, Egypt.

**Patients & Methods:** This study conducted on 30 patients with three benign inflammatory skin diseases (psoriasis, lichen planus and scabies) and 10 normal volunteers as controls. Skin biopsies were taken from all patients and normal controls under local anesthia. All specimens were stained by hematoxylin and eosin for routine histopathological diagnosis. Each disease was classified into early and late well developed stage according to duration and pathological findings. Immunodetection of CD$_{30}^{+}$ cells was performed. In each biopsy specimen, the distribution and the number of CD$_{30}^{+}$ cells were evaluated as follows: isolated weak positive cells (+), small non-cohesive aggregates (3-5 cells) of positive cells (++) and large aggregates (> 5 cells) of strong positive cells (+++).

**Results:** Histopathologically, the skin lesions of the three diseases showed the classical pathological findings. It was found that two out of ten normal human specimens gave a weak positive (+) staining for CD30+ cells. All late cases of psoriasis (6 cases), lichen planus (4 cases), and scabies (7 cases) stained positive (+++) or strong positive (+++) for CD30.

**Conclusion:** CD30 antigen expression occurs in benign inflammatory infiltrate of some benign skin conditions such as psoriasis, lichen planus and scabies.

**Key words:** CD30 – Psoriasis – Lichen planus- Scabies.

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INTRODUCTION

CD30 antigen expression in skin infiltrate of large atypical cell has been considered a diagnostic feature and a hallmark of cutaneous CD30 lymphoid proliferations (lymphomatoid papulosis/cutaneous CD30+ lymphoma) (1). Nowadays, it became evident that CD30 antigen expression in large lymphoid cell can also be present within inflammatory infiltrate of some cutaneous benign disorders such as atopic dermatitis, several infectious and parasitic diseases, in peritumoral inflammatory reactive infiltrates and in some peculiar drug reactions (2).

The presence of isolated large atypical lymphoid cells has been occasionally been observed in inflammatory infiltrate of lesions of scabies, mainly the nodular form (3).

PATIENTS AND METHODS

Thirty patients (21 males and 9 females) of different inflammatory skin diseases (psoriasis, lichen planus and scabies) in addition 10 healthy normal volunteers were enrolled in this study. Their age ranged from 10 to 63 years. They were collected from outpatient clinic of Dermatology and Andrology, Benha university hospital and from Benha prison. All patients had been asked to stop receiving treatment for at least 3 weeks prior to biopsy taking.

All patients were subjected to full medical history and general examination. Local examination of the lesions was performed for individual lesion determination. The diagnosis of the diseases had been established on the basis of characteristic clinical features and confirmed by biopsy from the lesion for histopathological identification of the disease.

Classification:

1- Control group: 10 persons (2 females and 8 males) with normal skin neighbouring to excised benign skin tumors (seborrheic keratosis, and acrochordons).

2- Patients group: 30 patients (9 females and 21 males) classified into 3 inflammatory skin diseases. Each group included 10 patients; a-psoriasis (psoriasis vulgaris), b-lichen planus (actinic and hypertrophic) and c-scabies.

Methods

Following an informed consent 5mm punch biopsy specimens were obtained from patients with fully developed skin lesions and control persons under local anesthesia (2% xylocain). Biopsies were preserved in formosaline solution 10% then subjected to the following histopathological examinations:

1- Hematoxylin and eosin staining as a preliminary diagnostic tool.

2- Immunohistochemical staining used for detection and localization of CD30+ve cells.

Immunohistochemical staining

Paraffin embedded tissue sections, 4 micron thick, were mounted on positively charged slides and heated at 60°C for 30 minutes, then deparaffinized and rehydrated through a series of xyline and alcohol before staining.

After antigen retrieval with microwave treatment in citrate buffer, endogenous peroxidase was blocked with 3% hydrogen peroxide for 20 minutes, the sections were washed 3 times with cold 0.01 Phosphate Buffered Saline (PBS). After blocking with 10% normal rabbit serum, the sections were incubated with rabbit anticow polyclonal against CD30 protein.

The immunohistochemical stain was performed using the avidin-biotin peroxidase complex technique (ABC kit, vector laboratories, Burlingame, CA). The primary antibody was incubated for 1 hour for CD30 protein. The ABC reaction was developed in the presence of Diaminobenzedine supplement with hydrogen peroxide (DAB). Lastly, sections were counterstained with Mayer's hematoxylin (4).

The stained slides were microscopically examined by two observers using the following parameters and the semi
quantitative criteria for CD\textsubscript{30} according to the
distribution and the number of CD\textsubscript{30}\textsuperscript{+} cells as
follow:
- Isolated cells (+) (week positive).
- Small non-cohesive aggregates (3-5) of
  positive cells (+++) (positive).
- Large aggregates (> 5 cells) of positive
  cells (+++) (strong positive).

A perivascular, periadnexal, band like or
diffuse distribution of positive cells was also
defined. A correlation between the
histopathological and immunophenotypical
features, and specifically the CD\textsubscript{30} antigen
expression, with the clinical and evolutive
features of lesions was also performed.

RESULTS

The study group included 30 patients; 21
males (70%) and 9 females (30%). Their age
ranged from 10 to 63 years with mean age
39.33 ±13.6 years. They had the inflammatory
diseases for a period ranging from
one week (scabies) to 25 years (psoriasis).

A- Psoriasis group:

Ten patients (4 females and 6 males), their
age ranged from 24 to 63 years with mean of
42.3±15.7 years. They had psoriasis for a
period of 1 month to 25 years (mean: 7.3
±9.27 years).

Four cases had psoriasis for less than 6
months (Early lesions). Their age ranged from
24 years to 3 months (mean 2.2 ±24.8
months).

The other 6 cases had psoriasis for more
than 6 months (late lesions). Their age ranged
from 34 to 63 years with mean age of 27.5 ±2.06 years. They had psoriasis for a
period of 1 to 3 months (mean 27.5 ±2.06 years). They had psoriasis for a
period of 1 month to 25 years (mean: 7.3
±9.27 years).

B- Lichen planus group:

Ten patients (3 females and 7 males), their
age ranged from 29 to 61 (mean 32 ± 12.7
years). They had the infection for a
period ranging from 3 weeks to 4 months (mean 2.77
±1.56 months).

Three cases had lichen planus for less than 3
months (early lesions). Their age ranged from
10 to 27 years with mean of 17.6 ± 7.03 years. They had lichen planus for a period of one week to 3
weeks (mean 2.3 ± 0.94 weeks).

The other 7 cases had lichen planus for more
than 3 months (late lesions). Their age ranged
from 32 to 61 years with mean age of 38.1
±7.9 years. They had lichen planus for a period of 3
to 4 months (mean 3.7 ±0.45 months).

Histopathological examination:

I. Control group: normal histological picture
of skin. CD\textsubscript{30} is not expressed except in 2
cases. They showed isolated cells (+) week
positive within the dermis.

II. Psoriasis vulgaris:

- Early developing lesions examination
  revealed moderate acanthosis, thin or
  absent granular cell layer, mounds of
  parakeratosis with neutrophils, thin
  suprapapillary zone with focal spongiosis
  and presence of micro-abscesses, dilated,
  congested blood vessels in edematous
dermal papillae and perivascular infiltrate
of lymphocyte and few neutrophils.

- Late well-developed psoriatic lesions
  showed marked acanthosis, clubbing of
  rete ridges, thinning of supra papillary
  epidermis with occasional presence of a
  small spongiform pustule of Kogoj,
  diminished or absent granular layer,
confluent parakeratosis and the presence of munro micro-abscesses. The dermis showed elongated and edematous dermal papillae with dilated, tortuous capillaries (fig. 1).

Fig. (1): A case of late psoriasis showing marked hyperkeratosis, parakeratosis and edematous dermal papillae with congested dilated blood vessels. Munro micro abscess is seen in stratum corneum (H&E × 200).

- **CD30 staining:**

In all biopsies from 6 patients with late lesions (6 months or longer), CD30+ cells were identified. Large aggregates of CD30+ cells (strong positive) were demonstrated. Perinuclear and cell membrane CD30 antigen expression was detected on large atypical cells. Small perivascular groups (positive) of CD30+ cells were noted in the papillary and superficial reticular dermis (fig. 2).

All the early lesions (4 cases) did not show CD30+ cells (negative).

Fig. (2): Immunohistochemical staining of a case of late psoriasis showing strong positive reaction in papillary dermis represented by presence of large aggregates of CD30+ cells (CD30 ×400).

### III. Lichen planus

- **Early lesions:** They showed hyperkeratosis, hypergranulosis, increased epidermal eosinophilia, and irregular acanthosis with saw-toothed rete ridges. The basal cell layer showed hydropic degeneration & pigmentary incontinence. A band like mononuclear inflammatory infiltrate is noticed in the papillary dermis hugging the epidermis (fig. 3).

- **Late lesions:** The same picture as early lesions except for the basal cell layer which was completely wiped-out and had the appearance of flattened squamous cells.

- **CD30 staining**

Isolated (weak positive) or small non-cohesive aggregates (positive) of CD30+ cells were demonstrated in biopsy specimens from all 4 patients with late lesions (6 months or longer). Perinuclear and cell membrane CD30 antigen expression was detected on large atypical cells. All the early lesions (6 cases) did not show CD30+ cells (negative).

### IV. Scabies:

All biopsy specimens showed a perivascular dermal lymphocytic infiltrate. Occasional large atypical histocyte-like cells were observed.
Fig. (3): A case of early L.P showing hyperkeratosis and hydropic degeneration "civatte bodies" of basal cell layer with pigmentary incontinence. The dermis showed a band of mononuclear inflammatory cell infiltrate "lichenoid cell infiltrate" (H&E × 100).

The presence of abundant eosinophils within the inflammatory infiltrate was a constant feature. Sarcoptes scabiei were observed in histological preparations from all early lesions (less than 3 months).

**CD30 staining**

Large aggregates (strong positive) of CD30+ cells were demonstrated in 7 biopsy specimens from all late lesions. Perinuclear and cell membrane CD30 antigen expression was detected on large atypical cells. Small perivascular groups (positive) of CD30+ cells were also noted in the papillary and superficial reticular dermis. A perivascular, periadnexal, band like or diffuse distribution of positive cells was also defined. All the early lesions (3 cases) did not show CD30+ cells.

Fig. (4): Immunohistochemical staining of a late case of scabies showing strong positive reaction in papillary and superficial reticular dermis represented by aggregates of large CD30+ cells (CD30 × 400).

**Table (1): Mean age and disease duration in studied group:**

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Mean ± SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psoriasis</td>
<td>10</td>
<td>42.30 ± 15.72</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>10</td>
<td>43.70 ± 9.79</td>
<td></td>
</tr>
<tr>
<td>Scabies</td>
<td>10</td>
<td>32.00 ± 12.78</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>39.33 ± 13.61</td>
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<tr>
<td><strong>Duration (month)</strong></td>
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<td>&lt;0.05</td>
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<tr>
<td>Psoriasis</td>
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<td>87.90 ± 111.27</td>
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<tr>
<td>Lichen planus</td>
<td>10</td>
<td>6.25 ± 7.78</td>
<td></td>
</tr>
<tr>
<td>Scabies</td>
<td>10</td>
<td>2.77 ± 1.56</td>
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</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>32.30 ± 73.91</td>
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</table>

**Table (2): Study group according to presence of CD30 (+ve) cells**

<table>
<thead>
<tr>
<th>Disease</th>
<th>CD30</th>
<th>-ve</th>
<th>+ve</th>
<th>Total</th>
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<tr>
<td>Psoriasis</td>
<td>4</td>
<td>6</td>
<td>10</td>
<td></td>
<td>&gt;0.05</td>
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<tr>
<td>Lichen planus</td>
<td>6</td>
<td>4</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scabies</td>
<td>3</td>
<td>7</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>17</td>
<td>30</td>
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</table>
Table (3): Study of early and late lesions according to duration of the diseases

<table>
<thead>
<tr>
<th>Skin disease</th>
<th>No</th>
<th>Mean duration</th>
<th>± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early lesions</td>
<td>4</td>
<td>2.2 months</td>
<td>24.8</td>
</tr>
<tr>
<td>Late lesions</td>
<td>6</td>
<td>12 years</td>
<td>8.5</td>
</tr>
<tr>
<td>Lichen planus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early lesions</td>
<td>6</td>
<td>1.1 months</td>
<td>0.43</td>
</tr>
<tr>
<td>Late lesions</td>
<td>4</td>
<td>1.1 years</td>
<td>0.50</td>
</tr>
<tr>
<td>Scabies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early lesions</td>
<td>3</td>
<td>2.3 weeks</td>
<td>0.94</td>
</tr>
<tr>
<td>Late lesions</td>
<td>7</td>
<td>3.7 months</td>
<td>0.45</td>
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**DISCUSSION**

The current study tried to detect CD30 (+ve) cells in inflammatory infiltrates of some dermatological diseases such as psoriasis, lichen planus and scabies. Skin biopsies from patients had been subjected to Routine H&E staining for histopathological diagnosis and evaluation and Immunohistochemical staining for CD30.

The present study, disclosed the presence of large, atypical CD30 +ve lymphoid cells in cutaneous inflammatory infiltrates of long standing scabies and in inflammatory infiltrate of late cases of psoriasis and lichen planus. This is consistent with what had been found by Cebeda et al.\(^5\), as they reported the presence of CD30+ve cells in inflammatory infiltrates of many benign dermatological diseases such as lichen planus, atopic dermatitis, psoriasis, scabies and papilloma viral infection. In this series, CD30 +cells were an almost constant in long standing psoriasis, lichen planus and nodular scabies.

The presence of CD30+ve cells could not be related to an underlying immuno-suppression, or a concomitant treatment (as the treatments were stopped for 21 days).

In this study, scabies revealed histologically dense and deep perivascular and interstitial inflammatory cell infiltrates of lymphocytes, histocytes, plasma cell, numerous eosinophils, and a few atypical mononuclear cells. This histological picture was similar to what was described by Ploysangam et al.\(^6\).

Late developed cases of scabies (nodular scabies) showed strong expression of CD30 +ve cells while all early cases of scabies do not express CD30 +ve cells and this is in agreement with Werner et al.\(^7\) who found that CD30+ve cells expression in 72% of scabietic cases which are all corresponding to long lasting infestation more than 3 months.

Liu et al.\(^8\) considered that in nodular scabies, the lesions are thought to result from a persistent antigenic stimulation and to represent a delayed host response similar to that found following some arthropod bites.

McCalmont and LeBoit \(^9\) reported the presence of numerous, large, atypical CD30 +ve cells in a single case of recurrent scabies.

In psoriatic cases, they appear histologically by the presence of small multilocular pustules in the upper stratum malpighii within a sponge-like network made of flattened keratinocytes (spongiform pustules of Kogoj "diagnostic"). A moderate inflammatory infiltrate around blood vessels (perivascular) in the papillary dermis consisting of lymphocytes, macrophages, neutrophils and increased number of mast cells is also seen. This histological picture was similar to what was described by Jiaravuthisan et al.\(^10\)

In early developing lesions where acanthosis is less prominent, the expression of CD30 +ve cells was not detected. On the other hand, late developed lesions of psoriasis...
vulgaris which showed prominent acanthosis and parakeratosis, the expression of CD30 +ve cells was detected and this is in agreement with Nathan (11) who assessed the expression of CD30 on mast cells of the lesional skin of 10 psoriatic patients (late lesions) from 15 studied patients while early lesions don't express CD30.

Also, CD30 +ve cells are found in late developed lesions of LP only which appear histologically by the presence of liquefaction degeneration of basal cell layer with a band like dermal infiltrate that hugs the basal layer which appear wiped out. This result is similar to what Van der Putte et al. (12) had found, as they detected reactivity of Ki-1 antibody (monoclonal antibody of CD30) in the T cell infiltrates in patients with long standing lichen planus, while in early cases of LP, CD30 +ve cells were not detected.

Although the role of CD30 as a marker of Th2 cells is somewhat controversial, its expression is clearly associated with nodular scabies and in late cases of psoriasis and lichen planus as we detected in this study. This may explain a possible relationship between the evolution of the diseases and CD30 antigen expression as said by Ofilazoglu et al. (13)

Despite some authors postulating that CD30 expression may be useful tool to establish a reliable differential diagnosis between lymphomatoid papulosis and other skin conditions (14), the present study pointed out the observation of scattered CD30 positive cells in inflammatory infiltrate of some benign skin diseases.

On the basis of our results and those of other studies of CD30 antigen expression in non-neoplastic conditions, it seems obvious that the presence of scattered large atypical CD30+ positive cells in a cutaneous inflammatory infiltrates of the skin does not imply unequivocally the diagnosis of neoplastic skin diseases.

Finally, the role or the function of CD30 in these diseases is still unknown. Weed and Flope (15) found that it may be strictly linked to certain stage of lymphoid cell differentiation or may play a direct biological role in the clinical behavior of these diseases. Disregarding its function, now we have the contentment that not every skin disease expresses CD30+ve cells is necessary neoplastic one.

In conclusion, after discussing the presence of CD30+ve cells in neoplastic and non neoplastic skin diseases, the relation of expression of CD30 and the chronically of the diseases and its non obvious role it's sure that many other researches should be done to know more about the function of CD30 in tissues in benign diseases and how to make benefit of its usage.

The presence of scattered large atypical CD30+ positive cells in cutaneous infiltrate does not necessarily means a neoplasm. Such cells could be present within the infiltrate of chronic cases of many cutaneous disorders. The role of these cells in the evolution and chronicity or even recurrence of such disorders should be evaluated.

REFERENCES