ECP NICE 2019: Haematopathology Short Course
Advances in extranodal lymphomas
“LYMPHOMAS IN THE SKIN”

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WHO 2017: MATURE B-, T- AND NK-CELL DISORDERS PRESENTING PRIMARILY IN SKIN

**B-cell**
- Primary cutaneous DLBCL, leg type
- Primary cutaneous follicle center lymphoma
- Extranodal marginal zone lymphoma of MALT (skin as a site)

**EBV+ mucocutaneous ulcer* (skin as a site)**

**T/NK cell**
- Hydroa-vacciniforme-like lymphoproliferative disorder
- Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides (and variants)

**Primary cutaneous CD30+ T-cell LPD**
  - Lymphomatoid papulosis
  - Primary cutaneous anaplastic large cell lymphoma
- Primary cutaneous γδ T-cell lymphoma

**Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma**

**Primary cutaneous acral CD8+ T-cell lymphoma***

**Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder***

- **New entities**
- **New genetic information**
- **Conceptual changes with revised nomenclature**
- **Provisional entities in italics**
Update on cutaneous lymphoma

New entities:
• EBV+ mucocutaneous ulcer (skin as a site)
• Primary cutaneous acral CD8+ T-cell lymphoma

New genetic information in primary cutaneous CD30+ LPD:
• Lymphomatosus papulosus with \textit{DUSP22} rearrangement
• Primary cutaneous ALCL with \textit{DUSP22} rearrangement

Conceptual changes resulting in revised terminology
• Primary cutaneous CD4+ T-cell LPD
• Hydroa vacciniforme-like LPD
NEW ENTITIES (i)

EBV-POSITIVE MUCOCUTANEOUS ULCER
1. EPSTEIN-BARR VIRUS POSITIVE MUCOCUTANEOUS ULCER

EBV Positive Mucocutaneous Ulcer—A Study of 26 Cases Associated With Various Sources of Immunosuppression

Stefan D. Dojcino, MD, FRCPath,* Girish Venkataraman, MD,†
Mark Raffeld, MD,† Stefania Pittaluga, MD, PhD,† and Elaine S. Jaffe, MD†

(Reports of lesions that are probably EBV-MCU present in contemporaneous and historical literature, particularly in associated with methotrexate)

Localized development of slowly evolving well defined indurated ulcers at mucosal or cutaneous sites

Arises in patients with some form of immune suppression:

• Elderly
• Patients undergoing therapeutic immunosuppression for CT disease
  • Most frequently methotrexate
• Post-transplant; solid organ > BMTx

**PATHOGENESIS**

- Speculated that immune surveillance is reduced to a level that is only just sufficient to maintain the EBV in a dormant state systemically
  - Age-related immune senescence
  - Iatrogenic immunosuppression

- Exposure to an additional site restricted immune modulating factor tips balance towards a localised EBV driven lymphoproliferation

- Sites at which EBV-infected cells are prevalent (e.g. Waldeyer’s ring) may be particularly prone to this disruption in equilibrium
CLINICAL FEATURES

- Well circumscribed, often painful, ulcerating lesions at mucosal or cutaneous sites
- Oropharyngeal mucosa is the most frequent site of presentation
- Cutaneous involvement often peri-oral
- Gastro-intestinal tract
  - Any part may be involved
- No mass lesion is detectable on clinical examination or imaging
- No systemic lymphadenopathy and/or splenomegaly
- EBV-DNA is typically undetectable in peripheral blood, even in post-transplant cases, in contrast to many other types of EBV-associated lymphoproliferative disorders

PATHOLOGICAL FEATURES:

Shallow sharply circumscribed ulcers

Large transformed lymphoid cells
  • Immunoblasts
  • Reed-Sternberg-like cells
  • B-cells: CD30+, EBV+

Polymorphous infiltrate in background
  • Lymphocytes – small lymphocytes concentrated at ulcer base
  • Plasma cells
  • Eosinophils
  • Histiocytes

Angioinvasion
  • Present in 6/26 cases in original series
  • Large lesional cells infiltrating medium sized arteries
  • Surrounding necrosis
CLINICAL HISTORY

• M72
• Liver transplant 14 years previously
• Recent excision of minimally invasive SCC left retromolar region
• Subsequently developed ulcer at site of operation
• Biopsied
PCR studies

- Monoclonal IG gene rearrangement in 7/18 (40%)
- Monoclonal TCR gene rearrangement in 6/16 (37.6%)
- Oligoclonal TCR gene rearrangement in 5/16 (31.2%)
  - T-cell response = restricted but reactive
  - Reflects reduced T-cell repertoire

Dojcinov SD et al, Am J Surg Pathol 2010
TREATMENT / OUTCOME

• Indolent course although response to treatment may be variable
• Spontaneous regression in a proportion
• For some patients surgical resection sufficient
• Withdrawal of MTx / Azothoprine or reduction in immunosuppression may be required
• Single agent Rituximab probably the most ‘aggressive’ therapy necessary
• Patients who have persisting lesion and/or run a relapsing and remitting course do not seem to progress to more widespread disease
D/Dx EBV+ MUCOCUTANEOUS ULCER FROM OTHER EBV+ B-CELL LPDs:

Mononuclear cell infiltrate
- Large CD30+ blasts
- EBV+
- Background small T-cells
- Vascular infiltration

Post Transplant LPD:
- EBV+ DLBCL
- Polymorphic B-LPD

Iatrogenic immunosuppression associated LPD:
- EBV+ DLBCL
- Polymorphic B-LPD

Lymphomatoid granulomatosis

EBV+ Diffuse Large B-cell Lymphoma

Classic Hodgkin lymphoma
**D/Dx EBV+ MUCOCUTANEOUS ULCER FROM OTHER EBV+ B-CELL LPDs:**

**CIRCUMSCRIPTION IS IMPORTANT PART OF DIAGNOSIS**

**SH2015-0072: Dr Dhesi**  
University of Michigan

**SH2015-0169: Dr Nicolae**  
National Institute of Health

**CLINICAL CORRELATION ESSENTIAL**
- Solitary lesion without mass
- No lymphadenopathy or organomegaly
- Peripheral blood EBV DNA negative
NEW ENTITY (ii)

PRIMARY CUTANEOUS ACRAL CD8+ T-CELL LYMPHOMA
PRIMARY CUTANEOUS ACRAL CD8+ T-CELL LYMPHOMA

Clonal proliferation of CD8+ T-cells

- Histologically high grade
- Clinically indolent

➢ 1st described on the ear

Indolent CD8-positive Lymphoid Proliferation of the Ear
A Distinct Primary Cutaneous T-cell Lymphoma?
Petrella T et al, AJSP 2007

➢ Spectrum expanded to include similar lesions on face

Indolent CD8-positive lymphoid proliferation on the face: part of the spectrum of primary cutaneous small-/medium-sized pleomorphic T-cell lymphoma or a distinct entity?
Suchak R et al, J Cutan Pathol 2009

➢ Involvement of acral sites also included

Indolent CD8+ lymphoid proliferation of acral sites: a clinicopathologic study of six patients with some atypical features
Greenblatt D et al, J Cutan Pathol 2013
Clinical
Middle age – elderly adults: (range = 29-89)

Slow growing plaques or nodules
- >50% reported cases on ears
- May occur elsewhere on face; particularly nose
- Also reported on hands and feet

Usually solitary; rarely bilateral

Clinical images courtesy of Werner Kempf

Diffuse monotonous infiltrate of medium-sized T-cells

- Dispersed nuclear chromatin and small nucleoli ("blast-like")
- Cytotoxic phenotype: CD8/TIA-1+, CD4-
- May show loss of normal T-cell antigens (CD2, CD5, CD7)
- CD30, CD56 and EBV-
- Low proliferation fraction (usually <10%)
- Monoclonal TCR gene rearrangement
Female aged 52 years; Solitary lesion on tip of nose
FOLLOW-UP

• Staging studies negative

• Lesion excised but no further treatment

• Alive, no evidence of disease at 12 months
CD68 expression is a discriminative feature of indolent cutaneous CD8-positive lymphoid proliferation and distinguishes this lymphoma subtype from other CD8-positive cutaneous lymphomas

M. Wobser, S. Roth, T. Reinartz, A. Rosenwald, M. Goebeler and E. Geissinger

1Department of Dermatology, Comprehensive Cancer Center Mainfranken, University Hospital Wuerzburg, Josef-Schneider-Str. 2, Wuerzburg 97080, Germany
2Institute of Pathology, Comprehensive Cancer Center Mainfranken, University of Wuerzburg, Wuerzburg, Germany

5 cases indolent CD8+ LPD
• All showed “Golgi dot” pattern of staining for CD68

39 other CD8+ cutaneous lymphomas
• All negative for CD68
TREATMENT AND OUTCOME

Indolent disease: aggressive therapy not necessary

25 cases in 7 publications with median FU of 14 months (3 – 156)

- XRT (n=13)
- Surgical excision (n=10)
- Biopsy only (n=2)

Response to treatment

- All achieved CR except 1 case that was only biopsied
- 5 cases relapsed: XRT = 3, excision = 2

Outcome

- 20 alive and disease free
- 1 died of unrelated causes with no evidence of disease
- 3 alive with stable disease
- 1 patient with no follow-up

APPROACH TO DIAGNOSIS AND MANAGEMENT

• Suspect as possible diagnosis if encountering a CD8+ LPD presenting at an acral site

• Phenotype distinguishes from
  • γδ T-cell lymphoma
  • ENKTCL

• Dermal involvement means not SPTCL

• Utility of anti-CD68?

• Importance of low Ki67 index?

• Make sure localized

• Initial conservative management
NEW INFORMATION

PRIMARY CUTANEOUS CD30+ LPD WITH DUSP22 REARRANGEMENT

• Lymphomatoid papulosis
• Primary cutaneous anaplastic large cell lymphoma
LYMPHOMATOID PAPULOSIS WITH *DUSP22* REARRANGEMENT

Chromosomal Rearrangements of 6p25.3 Define a New Subtype of Lymphomatoid Papulosis

Laszlo J. Karai, MD,*† Marshall E. Kadin, MD,‡ Eric D. Hsi, MD,§ Jason C. Sluzevich, MD,¶ Rhett P. Ketterling, MD,¶ Ryan A. Knudson, BS,¶ and Andrew L. Feldman, MD¶

• Elderly patients (67-88 years); 9M:2F
• Localized skin lesions
  • 1-multiple eruptive paulonodular lesions 0.3-1 cm diam
  • Often mistaken clinically for
    • Inflammatory dermatosis
    • Infection
    • Low grade epithelial skin tumour
• Untreated skin lesions spontaneously regress
• All cases have translocation involving 6p25.3 (*IRF4-DUSP22* locus)

### Pathology: Biphasic Appearance

**Morphology**

- Cohesive nodular dermal infiltrate
  - Medium – large cells
  - Abundant finely granular cytoplasm
  - “hallmark” cells

- Pagetoid reticulosis/MF-like infiltration of overlying dermis
  - Small – medium lymphocytes
  - Irregular, often cerebriform nuclei

**Phenotype**

- $\alpha/\beta$ T-cells
  - Majority CD4-/CD8- or CD4-/CD8+
  - All = TIA-1 negative

- CD30+
  - Strong staining in dermal nodules
  - Weak staining in epidermis
• Ill-defined nodular lymphoid aggregates in dermis

• Linear basal epidermotropism in overlying and adjacent epidermis
• Ill-defined nodular lymphoid aggregates in dermis

• Linear basal epidermotropism in overlying and adjacent dermis
Infiltrate consists of T-cells
Biphasic pattern of staining for CD30
  • Large cells in dermal nodules strongly positive
  • Smaller cells in dermis and epidermis weakly positive
**DUSP22-IRF4 FISH**

*DUSP22/IRF4 break apart probe*

Around 50% the cells show a clear break

*FISH reveals DUSP22 rearrangement*
**IS DUSP22 REARRANGEMENT SPECIFIC FOR LYP?**

Historical FISH studies find *DUSP22* rearrangements predominantly in pcALCL

<table>
<thead>
<tr>
<th></th>
<th>Wada et al</th>
<th>Pham-Ledard et al</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>pcALCL</td>
<td>9/45</td>
<td>6/23</td>
<td>15/68</td>
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<tr>
<td>LyP</td>
<td>1/32</td>
<td>0/7</td>
<td>1/39</td>
</tr>
<tr>
<td>Mycosis fungoides / Sezary syndrome</td>
<td>0/31</td>
<td>0/13</td>
<td>0/44</td>
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<tr>
<td>Transformed mycosis fungoides</td>
<td>0/13</td>
<td>2/11*</td>
<td>2/24</td>
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</tbody>
</table>
PRIMARY CUTANEOUS ANAPLASTIC LARGE CELL LYMPHOMA WITH

**DUSP22 REARRANGEMENT**

*DUSP22* rearrangement also described in cases of pcALCL

Some of these cases also display biphasic morphology:
EAHP18-LYWS-103
Arantza Onaindia, Santander

- 69-year-old woman
- Nodular lesion left cheek
- pcALCL
- Surgically excised
- No evidence of disease at 7 months

- 69-year-old woman
- Nodular lesion left cheek
- pcALCL
- Surgically excised
- No evidence of disease at 7 months
<table>
<thead>
<tr>
<th>Author</th>
<th>Cases with <em>DUSP22</em> rearrangement</th>
<th>Histological features</th>
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</thead>
<tbody>
<tr>
<td>Feldman, Leukemia 2009</td>
<td>8/14 pcALCL</td>
<td>No epidermotropism or specific features</td>
</tr>
<tr>
<td>Pham-Ledard, JID 2010</td>
<td>6/14 pcALCL 0/7 LyP</td>
<td>No epidermotropism or specific features</td>
</tr>
<tr>
<td>Wada, Mod Pathol 2011</td>
<td>9/45 pcALCL 1/32 LyP</td>
<td>No epidermotropism or specific features</td>
</tr>
</tbody>
</table>
**DUSP22 rearrangement also found in subset of systemic ALK- ALCL (20-30%):**

Predicts for favourable outcome

Prognosis for DUSP22+ ALCL equal to that for ALK+ ALCL
Prognosis for TP63+ ALCL worse than DUSP22+, ALK+ and triple negative ALCL

Outcomes in patients with ALCL based on genetic subtype. (B) OS rates in patients with ALCL, stratified by rearrangements of ALK (N = 29), DUSP22 (N = 21), and TP63 (N = 6). "−/−/−", triple-negative cases lacking all 3 rearrangements (N = 40).

<table>
<thead>
<tr>
<th>Translocation</th>
<th>5-year OS</th>
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<tbody>
<tr>
<td>ALK</td>
<td>85%</td>
</tr>
<tr>
<td>DUSP22</td>
<td>90%</td>
</tr>
<tr>
<td>None</td>
<td>42%</td>
</tr>
<tr>
<td>TP63</td>
<td>17%</td>
</tr>
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</table>

*Parilla Castellar ER et al, Blood 2014;124:1473*
**DUSP22** rearrangement in ALK- ALCL also reported to be associated with characteristic morphology........

*King RL et al, Mod Pathol 2016, Parilla Castellar ER et al, Blood 2014*

- Monotonous appearance
- Sheets of hallmark cells
- Typically lack cytotoxic molecules
  - Granzyme B
  - TIA1
  - Perforin
SUMMARY: *DUSP22* REARRANGEMENTS IN CD30+ LPDs

1. *DUSP22* rearrangements are found most frequently in pcALCL and systemic ALK- ALCL

2. *DUSP22* rearrangements found in a small percentage of LyP

3. Presence or absence of rearrangement does not help differentiate primary cutaneous CD30+ LPDs from systemic ALK- ALCL, but predicts favourable outcome in latter

4. In cutaneous CD30+ LPDs, presence of *DUSP22* rearrangement may correlate with characteristic ‘biphasic’ pathology

5. Absence of ‘biphasic’ morphology does not predict for absence of rearrangement
CONCEPTUAL CHANGES / CHANGES IN NOMENCLATURE

1. PRIMARY CUTANEOUS CD4+ SMALL/MEDIUM T-CELL LYMPHOPROLIFERATIVE DISORDER
PRIMARY CUTANEOUS CD4+ SMALL/MEDIUM T-CELL LYMPHOPROLIFERATIVE DISORDER

WHO 2008:

*Primary cutaneous CD4+ small/medium T-cell lymphoma*

WHO 2017:

*Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder*
PRIMARY CUTANEOUS CD4+ SMALL/MEDIUM T-CELL LYMPHOPROLIFERATIVE DISORDER

Most cases adults but reported in paediatric age group
  • Median age at presentation = 50-60 years
  • Range = 3-90 years

Most cases present with solitary or localized lesions
  • Papules/plaques/nodules
  • Usually of small size (<3 cm)
  • Patches of MF not present

Reported series contain variable proportion of cases with multifocal lesions
  • 13% in one recent review of literature

Leinweber B et al, Dermatology 2009; Rodriguez-Pinelli S et al, AJSP 2009; Baum CL et al, JAAD 2011)
**PATHOLOGY**

- **Clonal** proliferations of CD4+ T-cells that express one or more T-follicular helper cell markers:
  - $\text{PD1} > \text{CXCL13} > \text{CD10}$
- Rarely show loss of pan-T-cell antigens
  - $\text{CD7} >> \text{CD2}$

- Small - medium lymphocytes
  - Variable amounts of pale cytoplasm
  - Hyperchromatic, irregular nuclei

- <30% large cells by definition

- Epidermotropism absent or very minimal

**Significant component of reactive cells**
- Lymphocytes (incl B-blasts; often numerous small B-cells)
- Neutrophils & eosinophils
- Plasma cells
- Histiocytes

Significant reactive component always present
Treatment/Outcome

Majority of lesions respond well to local therapy
  • Excision +/- or XRT

Complete remission the norm
  • Rare cutaneous relapses
  • Quoted 5 year survivals of 60-80% but possibly dependent on inclusion criteria:
    • Series with few/no patients with multifocal lesions have excellent outcomes

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Median age at presentation in years (range)</th>
<th>No patients with FU (median duration)</th>
<th>Solitary or localised vs multifocal</th>
<th>Survival at end of FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grogg et al</td>
<td>15</td>
<td>56 (14-74)</td>
<td>11 (9 months)</td>
<td>93%;7%</td>
<td>100%</td>
</tr>
<tr>
<td>Garcia-Herrera et al</td>
<td>24</td>
<td>58 (28-85)</td>
<td>24 (24 months)</td>
<td>83%;17%</td>
<td>79%</td>
</tr>
<tr>
<td>Beltraminelli et al</td>
<td>136</td>
<td>53 (3-90)</td>
<td>45 (63 months)</td>
<td>98%;2%</td>
<td>100%</td>
</tr>
<tr>
<td>Leinweber et al</td>
<td>26</td>
<td>51 (6-80)</td>
<td>26 (79.7 moths)</td>
<td>100%;0%</td>
<td>100%</td>
</tr>
<tr>
<td>Rodriguez-Pinella et al</td>
<td>16</td>
<td>52 (23-67)</td>
<td>16 (10 months)</td>
<td>94%;6%</td>
<td>100%</td>
</tr>
<tr>
<td>Baum et al</td>
<td>10</td>
<td>38 (6-85)</td>
<td>10 (24.5 months)</td>
<td>80%;10%</td>
<td>100%</td>
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</tbody>
</table>
NEITHER CLONALITY OR THE NUMBER OF PD.1+ CELLS DISCRIMINATES BETWEEN CD4+ SMTCL AND CUTANEOUS T-CELL PSEUDOLYMPHOMA

Expression of Programmed Death-1 in Primary Cutaneous CD4-Positive Small/Medium-Sized Pleomorphic T-Cell Lymphoma, Cutaneous Pseudo-T-Cell Lymphoma, and Other Types of Cutaneous T-Cell Lymphoma

Fatma Çetinözman, MD,* Patty M. Jansen, MD, PhD,† and Rein Willemze, MD, PhD*


Are ‘localized’ primary cutaneous CD4+ SMTCL and cutaneous T-cell pseudolymphoma one and the same?

WHO 2008:
Primary cutaneous CD4+ small/medium T-cell lymphoma

WHO 2017:
Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder
Peripheral T-cell lymphoma presenting in skin, including some with TFH phenotype, may have poor outcome

- 86-year old male
- Presented with large nodule on forearm/elbow
- No other skin lesions, staging studies negative
Polymorphous: Lymphoid cells, histiocytes, plasma cells, occasional eosinophils

- High content of neoplastic cells expressing TFH markers; few reactive lymphocytes/other cells
- Patient died of lymphoma within 6 months
Take home message: Manage the patient appropriately

Small solitary lesions showing features of CD4+ SMPTCL
- Manage conservatively in the first instance
- Complete excision is probably sufficient

Caution required when
- Lesions large, rapidly growing or multiple
- Pathology is not typical of CD4+ SMPTCL
  - The following are present
    - Loss of CD2, CD3, CD5
    - Few CD8+ T-cells
    - Few CD20+ B-cells
    - High proliferation index
      - (predominance of neoplastic cells)
HYDROA VACCINIFORME-LIKE LYMPHOPROLIFERATIVE DISORDER

WHO 2008:

*Hydroa vacciniforme-like lymphoma*

WHO 2017:

*Hydroa vacciniforme-like lymphoproliferative disorder*
HYDROA VACCINIFORME-LIKE LPD: BACKGROUND (i)

Chronic active Epstein Barr virus infection of T/NK cell type
Displays broad spectrum of clinical manifestations
  • Indolent, localised, self-limiting proliferations
  • Aggressive and often fatal systemic disease characterised by
    • Fever
    • Hepatosplenomegaly
    • Lymphadenopathy

A proportion of cases within this group, at both ends of the clinical spectrum, show a predilection for the skin

Previously described under a variety of different names
  • Hydroa vacciniforme
  • Hydroa vacciniforme-like lymphoma
  • Edematous scarring vasculitic panniculitis
“Hydroa vacciniforme (HV)”

- Historically defined in Western countries
- Rare photosensitivity disorder of childhood characterised by
  - Papules and vesicles on sun-exposed skin
  - Lesions evolve to crusts that heal leaving varicelliform scars
  - Symptoms usually develop in childhood and resolve during early adult life
  - No associated systemic symptoms
“Hydroa vacciniforme-like lymphoma”

• Name given to a syndrome clinically very similar to HV but with a more aggressive clinical course in children from:
  • East Asia
  • Latin America
  • Mexico
HYDROA VACCINIFORME-LIKE LPD: BACKGROUND (iv)

“Hydroa vacciniforme-like lymphoma” (WHO 2008)

Characterised by:

- Marked facial oedema
- Recurring vesiculopapular rashes with large ulcers and crusts
- Severe scarring and disfigurement
- Develop on sun exposed and non-sun exposed skin

Systemic symptoms usually present

- Fever
- Weight loss
- Hepatosplenomegaly
- Lymphadenopathy

Frequent association with severe mosquito bite hypersensitivity

Prognosis is often poor with a fatal outcome

- Recognised as an entity in 2008 WHO classification
- Considered separate from classical HV
Considerable clinical and pathological overlap between cases originally designated “classical HV” and “HV-like lymphoma”

Lack of reproducible morphological, immunophenotypic and molecular findings to allow the distinction of these two putative entities

Proposed that there is a spectrum of EBV-associated of T/NK-cell lymphoproliferations with HV like cutaneous manifestations:

• Classic, self resolving HV at one end
• HV-like lymphoma with an aggressive clinical course at the other
Current approach is to include all HV-like lymphoproliferations under one heading

“Hydroa vacciniforme-like lymphoproliferative disorder (LPD)”

Recommended nomenclature used in the 2016 Update of the WHO classification

Blood 2016;127:2375-2390
PATHOLOGY

Perivascular and periadnexal infiltrate of varying density

Varied cytology of lymphocytes:
  • Bland, reactive appearing
  • Marked lymphocyte atypia
    • Large irregular nuclei
    • Prominent nucleoli
    • Abundant clear cytoplasm

May be associated
  • Angiodestruction
  • Extension into subcutaneous fat
  • Spongiotic vesicles +/- ulceration

Little/no epidermotropism

Abnormal lymphocytes typically only account for 10-40% lymphocytes in infiltrate; remainder reactive
PHENOTYPE

EBV+ by definition
  • EBER+
  • LMP1 usually –

T-cell phenotype in 60-70% of cases
  • αβ or γδ
  • Clonal TCR gene rearrangement

NK-cell phenotype in 30-40%
  • More often associated with
    • Mosquito-bite hypersensitivity
    • Prominent eosinophil infiltrate
    • Involvement of subcutaneous fat
TREATMENT / OUTCOME

Cases that behave aggressively:

- Severe symptoms at presentation
- Fatalities due to
  - Progression to T- or NK-cell lymphoma/leukaemia
  - Hepatic failure
  - Complication of treatment

No standard treatment

- Multiagent chemotherapy and radiotherapy offer little benefit
  - Only transient effect
  - Increase chances of sepsis or liver failure

- Immunomodulatory therapies may offer temporary remission / improvement of symptoms
  - Prednisolone
  - Interferon α
  - Chloroquine
  - Thalidomide

Quintanilla-Martinez L et al, Blood 2013
• Male aged 18 years
• History of intermittent fever for previous four years
• More recently developed hepatosplenomegaly and skin lesions
**PHENOTYPE**

**Positive:**
- CD2
- cCD3
- CD7
- CD56
- EBV (EBER)

**Negative:**
- CD4
- CD5
- CD8
- TCR-βF1
# 20th Meeting of the European Association for Haematopathology

Overlaps, borderlines and mimics

Dubrovnik, Croatia
11-16 September 2020

## Call for Abstracts
- Submission starts: 13 Sep 2019
- Submission deadline: 1 Apr 2020
- Notification of acceptance: 29 May 2020

## Call for Cases
- Submission starts: 13 Sep 2019
- Submission deadline: 15 Dec 2019
- Notification of acceptance: 20 May 2020

THANK YOU