Disseminated herpes zoster: What is it?

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Kindly put yr mobiles on silent mode to avoid this...

"I HAVE TO HANG UP NOW. I'M CRASHING!"
Varicella (chicken pox) and herpes zoster (shingles) are distinct clinical entities caused by the varicella zoster virus (VZV).
VARICELLA

**Epidemiology**
- Occurs most often in children
- Is the result of primary infection of susceptible individual

**Clinical features**
- Rash begins on face → trunk
- Rose colored macules → papules → vesicles → pustules → crusts

**Complications**
- Normal children: serious complications rare
- Adults, compromised: complications
Epidemiology of Zoster

- No seasonal prevalence
- Incidence depends on factors that affect host-virus relationship
- Old age
- Cellular immune dysfunction
- HIV, leukemia & lymphoma, bone marrow transplant, cancer chemotherapy, steroids
Epidemiology of Zoster

Patients less contagious than varicella (one-third)

Uncomplicated cases - spread by direct contact with lesions

Disseminated zoster - transmit in aerosols

Exposure to children, contact with varicella → confers protection
About the virus

- VZV - member of the herpes virus family
- Other members: HSV-1, HSV-2, EBV, CMV, HHV-8
- Morphologically similar
- Capacity to establish latent infection that persist throughout life
- Only one VZV serotype
PATHOGENESIS
Course of typical spinal nerve

A typical spinal nerve.
Trigeminal nerve
31 pairs of spinal nerves
• 8 cervical (C1-C8) nerves emerge from the cervical spine;
• 12 thoracic (T1-T12) nerves
• 5 lumbar (L1-L5) nerves emerge from the lumbar spine;
• 5 sacral (S1-S5) nerves emerge from the sacral bone;
• 1 coccygeal nerve emerge from the coccygeal bone;

Each spinal nerve is attached to the spinal cord by two roots: a dorsal (back, posterior) sensory root and a ventral (front, anterior) motor root. The nerves carry messages to and from the skin of specific body regions called dermatomes.
Pathogenesis of Herpes Zoster

Varicella-Zoster Virus
Non-immune individual (commonly a child)

Virus in a dorsal spinal ganglion

Varicella

Latent phase

Reactivation

Herpes Zoster

Dermatome
Factors involved in re-activation

- Immuno-suppression
- Emotional stress
- Irradiation of spinal column
- Tumor involvement of cord, dorsal root ganglion
- Local trauma

Most important: decline in VZV-specific cellular immunity that occurs with age
Clinical Findings

PRODROME OF ZOSTER

• Pain and paresthesia in the involved dermatome preceding the eruption by several days

• Common in elderly

• *Zoster sine herpete*: acute segmental neuralgia without eruption
RASH OF ZOSTER

- Always **U/L**
- Limited to area of skin innervated by single sensory ganglion
- **MC**: trigeminal nerve, trunk (1/2 of cases)
Clinical Findings

Erythematous macules, papules

- 12-24 hrs

Vesicles

- 3rd day

Pustules

- 7-10 days

Crusts

Persist for 2-3 weeks

- New lesions continue to appear for 1-4 days
- Older people → most severe, lasts longest
- Children → least severe, shortest duration
Complications

Post herpetic neuralgia
- Constant pain
- Intermittent pain
- Allodynia

Pain elicited by stimuli that are usually not painful

Immunocompromised
- Skin necrosis, scarring
- Cutaneous dissemination
- Visceral dissemination

HIV
- Severe, disseminated
- Multiple recurrences
- Chronic verrucous, hyperkeratotic, ecthymatous lesions
- Acyclovir resistant
Complications

- **cutaneous**
  - Bacterial superinfection
  - Scarring
  - Zoster gangrenosum
  - Cutaneous dissemination

- **visceral**
  - Pneumonitis
  - Hepatitis
  - Oesophagitis, gastritis
  - Pericarditis
  - Arthritis

- **neurologic**
  - PHN
  - Meningoencephalitis
  - Transverse myelitis
  - Nerve palsies
  - Deafness ocular
Disseminated herpes zoster: What is it?
Presenting Complaints

63 year old female

- **Segmental** grouped vesicles and pus filled lesions over right side of chest x 3 days
- **Pain** in the lesions x 3 days
- Reddish lesions over abdomen, back, thigh x 1 day
History of Present Illness

• No H/O constitutional symptoms
• No H/O fever
• No H/O headache/neck stiffness

• No H/O trauma/ emotional stress
Past History

• Post menopausal

• No H/O DM/HT/TB
• H/O chickenpox during childhood

• No H/O prolonged fever in the past
• No H/O weight loss/diarrhoea
• No H/O lump in the body/abdominal pain/prolonged bleeding from any site/chronic cough

• Family history: unremarkable
Examination

Segmental grouped vesicles and pustules with erythematous base over right side of chest
Examination

Multiple pin-point vesicles over back
Examination
Examination

• **Mucosae**: normal
• **Hair, nails**: normal
• **No LAP**
• **Cardiac**: normal S1/S2
• **Respiratory**: normal breath sounds
• **P/A**: no organomegaly
• **CNS**: normal
Differential Diagnosis

• Disseminated Herpes Zoster in an immunocompetent host

• Disseminated Herpes Zoster in an immunocompromised host  ? Occult malignancy  ? HIV
Investigations

Tzanck smear:
multinucleated giant cells (MNGCs)
Investigations

• **HIV Serology**: Non-Reactive

• **Blood Sugar (Fasting)**: 80 mg/dL

• **Blood Sugar (Post-prandial)**: 108 mg/dL

• **Chest X-Ray (PA view)**: Normal
# Investigations

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<th>Result</th>
<th>Reference Range</th>
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<td>Hb</td>
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<td>(11.50-15.00)</td>
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<tr>
<td>PCV</td>
<td>35.50%</td>
<td>(36.0-46.0)</td>
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<tr>
<td>RBC count</td>
<td>3.57 mil/mm³</td>
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<td>MCV</td>
<td>99.50 fL</td>
<td>(80-100)</td>
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<tr>
<td>MCH</td>
<td>31.70 pg</td>
<td>(27.0-32.0)</td>
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<td>MCHC</td>
<td>31.80 g/Dl</td>
<td>(32.0-35.0)</td>
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<td>RDW</td>
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# Investigations

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<tr>
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<td>Basophils</td>
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<td>0.01-0.10</td>
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<td>Platelet count</td>
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<td>ESR</td>
<td>28</td>
<td>0-30</td>
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Investigations

PERIPHERAL BLOOD SMEAR

• Anisocytosis ++
• Predominantly normocytic normochromic RBCs
• Leucocytosis with increase in lymphoid series of cells along with smudge cells and prolymphocytes
• Platelets are adequate

Suggestive of a chronic lymphocytic disorder
## Investigations

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<td>ALT (SGPT)</td>
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<td>GGTP</td>
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<td>Urea</td>
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<td>223</td>
<td>(&lt;247)</td>
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<td>Electrolytes (Na, K, Cl, Ca, Po)</td>
<td>WNL</td>
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USG Abdomen

Normal
No organomegaly
# Flow Cytometry

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<tr>
<th>Marker</th>
<th>Result</th>
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<td>CD3</td>
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</tr>
<tr>
<td>CD7</td>
<td>-</td>
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<tr>
<td><strong>B cell markers</strong></td>
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<td>CD20</td>
<td>+</td>
</tr>
<tr>
<td>CD79b</td>
<td>+</td>
</tr>
<tr>
<td>Ig M</td>
<td>+</td>
</tr>
<tr>
<td>Kappa</td>
<td>+</td>
</tr>
<tr>
<td>Lamda</td>
<td>-</td>
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<tr>
<td><strong>CD5 &amp; CD 19 co-expression</strong></td>
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# Flow Cytometry

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<td>CD23</td>
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<td>CD103</td>
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</tr>
<tr>
<td>FMC7</td>
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<tr>
<td>ZAP70</td>
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Final Diagnosis

Disseminated Herpes zoster with B-cell chronic lymphocytic leukemia
Treatment given

ANTIVIRAL
• Acyclovir 10mg/kg 8 hourly

ANTIBIOTIC
• Amox-Clav 1 g BD X 5 days
• Mupirocin ointment LA BD

ANALGESICS
• Pregabalin+ methylcobalamin BD
• Tramadol + acetaminophen

Acyclovir injections: 25 mg/ml
Vials: 20 ml
Monitor KFT
Response to treatment

New lesions stopped appearing 2 days after starting i.v acyclovir

Patient started on oral valacyclovir, discharged with the following treatment

1. Tab Valacyclovir 1 g TDS
2. Tab Amox-Clav 1 g BD
3. Tab Pregabalin+methylcobalamin BD
4. Mupirocin ointment LABD
5. Tab Tramadol-PCM BD
Response to treatment

- F/U at 7 days
- F/U at 14 days
- F/U at 21 days

6 weeks - complete healing of lesions with scarring and hypopigmentation
Discussion

• Most serious complications of herpes zoster occur in immunocompromised persons.

• Incidence of complications in immunocompromised persons is as high as 25-50%.

• 10% of patients with cutaneous dissemination also manifest widespread, visceral dissemination (lungs, liver, spleen).
Herpes Zoster in HIV +

All Three Divisions of 5th Cranial Nerve
Herpes Zoster in HIV +
Disseminated herpes zoster

more than 20 small widespread vesicles resembling varicella outside the area of the primary and adjacent dermatomes, and may or may not involve visceral organs.

elderly or persons with immunosuppression due to HIV infection, hematologic malignancy, or chemotherapy;

in otherwise healthy individuals it is very rarely reported

2-10% of patients with immunologic defects

Route: Hematogenous dissemination
QUERIES

• Role of Tzanck smear?

• Role of skin biopsy?
  (atypical skin lesions, prevesicular stage)

• Role of serology?
MANAGEMENT
Goals of Treatment

- Shorten the clinical course
- Provide analgesia
- Prevent complications
- Decrease the incidence of PHN
Antivirals

- Decreases the length of time for new lesion formation
  - Should be started within 72 hours of rash onset (ophthalmic zoster & new lesion formation)

- Decreases the number of days to attain complete crusting

- Decreases the days of acute discomfort

- Valacyclovir and famciclovir may be superior to acyclovir in resolving pain & accelerating healing
Antiviral Therapy

Non-immunocompromised patient

- **Age<50 yrs**
  - Symptomatic treatment only
  - **Acyclovir** 800 mg 5 times/day x 7 days

- **Age>50 yrs, or with ophthalmic involvement**
  - **Acyclovir** 800 mg 5 times/day x 7 days
  - **Valacyclovir** 1 g TDS/day x 7 days
  - **Famciclovir** 500mg TDSx7 days
Immunocompromised patient

Mild compromise/ HIV

- Acyclovir 800mg 5 times/day x 7-10 days
- Valacyclovir
- Famciclovir

Severe compromise

- Acyclovir 10 mg/kg IV 8 hourly x 7-10 days

Acyclovir resistant

- Foscarnet 40 mg/kg IV 8 hourly until healed
Disseminated Zoster

**Acyclovir 10mg/kg 8 hourly** till new lesions stop appearing

Can be shifted to **oral antivirals**

Antiviral therapy has been demonstrated to halt progression & dissemination of acute herpes zoster even when initiated more than 72 hours after rash onset

**Continued till lesions resolve**
Role of Steroids???

To reduce acute pain of herpes zoster (neuronal inflammation)

• Does not change the incidence of chronic pain

Studies: conflicting results

• Not recommended (especially in older patient, potential for adverse effects, viral dissemination)

May improve motor outcomes and acute pain in VZV induced facial paralysis & cranial polyneuritis- may be used
Analgesics

Greater severity of acute pain → contributes to central sensitization & genesis of chronic pain

Non-opiate or opiate analgesics

Regional/local anaesthetic nerve blocks

Efficacy of anticonvulsants & TCAs when administered during acute phase in reducing the incidence, duration, or severity of PHN is not known
Post Herpetic Neuralgia

Pain in the affected region 90-120 days after rash onset
Precautions

• **Contact precautions**: avoid direct skin contact esp with immunocompromised persons, pregnant women and individuals with no H/O chicken pox

• **Airborne precautions**: for disseminated zoster
Take Home Message

Patients with disseminated herpes zoster with no known co-factors deserve a complete work-up to elucidate any underlying malignancy or immunodeficiency.

Our case also depicts how skin findings act as a mirror for internal disease. Disseminated herpes zoster, in this patient, acted as a presenting sign for CLL.
FINAL WORDS…

• Time flies.

• Thanks for listening.

Contact me at: drpoojamrig@gmail.com
Any Questions........???
WAIT!
THERE’S MORE COMING...!!!

Thank you for your patience...

Cheer Up Today will be over soon!
What’s your diagnosis?
10 year old boy with fever, sore throat, rash x 2 days
10 year old boy with fever, sore throat, rash x 2 days
SCARLET FEVER

Prodrome:
- headache, vomiting, pharyngitis, abd pain

12 hrs-5 days after exposure

1-2 days
- Rash
  - Neck → trunk → extremities
  - Coarse, sandpaper like. Blanches with pressure

Few days
- Rash becomes more intense around skin folds
- Pastia’s lines (petechiae) can be seen

Pastia’s lines (petechiae) can be seen 12 hrs - 5 days after exposure.

Rash becomes more intense around skin folds a few days after exposure.
Oral Findings

- Oedematous erythematous tonsils
- Forschheimer’s Spots (petechiae on soft palate and uvula)
- White strawberry tongue (first 2 days)
- Red strawberry tongue

Tender anterior cervical LAP, flushed face with circumoral pallor
30 year old truck driver with asymptomatic lesions on face
Molluscum contagiosum in HIV
Mucocutaneous disorders as indications for HIV sero testing

Highly indicative of HIV infection
1 Exanthem of acute retroviral syndrome
2 Proximal subungual onychomycosis
3 Chronic herpetic ulcers
4 Oral hairy leukoplakia
5 Kaposi’s sarcoma
6 Eosinophilic folliculitis
7 Multiple facial molluscum contagiosum in adults

Strongly associated with HIV infection
1 Any sexually transmitted disease
2 Herpes zoster
3 Signs of injected drug abuse
4 Oropharyngeal or recurrent VVC

May be associated with HIV infection
1 Generalized lymphadenopathy
2 Extensive, refractory seborrheic dermatitis
3 Recurrent, refractory aphthous ulcers
65 year old female
• No H/O allergies
• No family H/O scabies
• No H/O drug intake
• No H/O systemic disease

• LFT/KFT/TSH/Hemogram: Normal (except eosinophilia)
Papuloprupruritic eruption of HIV

- Multiple, pruritic, skin-colored papules on the face, trunk, and arms.
- The mucous membranes (mouth, nostrils, eyes, genitals), palms, and web spaces are spared.
- Diagnosis of exclusion
- Nonspecific histologic picture,
- Eosinophil counts were significantly increased
- IL-5 involved (Th 2 response)
- Resistant to treatment
3 year old female (product of consanguineous marriage)

Sparse hair

Dry skin
Delayed dentition with peg shaped teeth

Normal nails
**Hypohidrotic ectodermal dysplasia**

- Group of inherited disorders characterized by development abnormalities in two or more ectodermal structures (hair, teeth, nails, sebaceous, sweat glands)

- Affected males present at birth with collodion membrane or marked scaling of skin

- Scalp hair: sparse, fine and blonde
  - Ability to sweat is compromised—heat intolerance

- Nails normal

- Periorbital wrinkling and hyperpigmentation
Hypohidrotic ectodermal dysplasia

**Delayed dentition, peg shaped teeth**

- **ENT:** recurrent URT, decreased saliva, hoarse voice

**Frontal bossing, depressed midface, saddle nose**

- **GIT:** GER, failure to thrive in infancy

**HPE:** eccrine glands absent/ incompletely developed

Reduced sebaceous glands and hair follicles
• 60 year old man, chronic smoker with asymptomatic pigmentation over face

• Admitted in medicine ward for work up of chronic cough (prov diagnosed as TB)
Ectopic ACTH secretion from small round cell tumor of lung

100X10 MAGNIFICATION SHOWING SMALL ROUND CELL TUMOR OF LUNG NEGATIVE FOR LEUCOCYTE COMMON ANTIGEN
Most relevant question

WHICH ONE WILL YOU OPEN FIRST..?
QUIZ
Question 1

• Number of cutaneous lesions required for diagnosis of disseminated herpes zoster
  a. 10-20
  b. >20
  c. >30
  d. >40
Question 2

- Which one of the following is not indicated in treatment of uncomplicated herpes zoster
  
a. Antivirals
b. Analgesics
c. Anticonvulsants
d. Glucocorticoids
Question 3

Most common dermatome involved by herpes zoster

A Ophthalmic and thoracic
B coccygeal
C Lumbar
D sacral
10 year old child presents with herpes zoster at T2 dermatome associated with mild burning sensation for the past 5 days. What is the best treatment?

A. acyclovir
B. Valacyclovir
C. Famciclovir
D. symptomatic treatment
E. either of a or b or c
Question 5

70 year old man presents with herpes zoster in ophthalmic division of trigeminal nerve, duration 5 days.

Associated with severe pain and redness in the eyes. Best treatment

a. Acyclovir + gabapentin
b. Analgesics
C. Antibiotics
D. b & c
Question 6

Zoster sine herpete is

a. Dermatomal pain not followed by rash
b. Multidermatomal zoster
c. Visceral involvement by VZV
d. None of the above
Disseminated herpes zoster is due to
A re-infection with VZV
B reactivation of VZV
C relapse of VZV
D resistance to VZV
A 70 year old man presents with unilateral segmental vesicles over trunk, along with multiple vesicles over body (generalized distribution).

The work-up will involve all except:

a. HIV serology
b. Hemogram
c. FNAC from enlarged lymph node
d. Skin biopsy
Final question

IF OLIVE OIL IS MADE OF OLIVES...THEN....

...BABY OIL IS MADE OF...
Sometimes the questions are complicated and the answers are simple.
Just enjoy your books when u are at it
Cutaneous findings in chronic lymphocytic leukaemia

K.L. Agnew, R. Ruchlemer,
D. Catovsky, E. Matutes,
C.B. Bunker

• **Summary**
• **Background** Chronic lymphocytic leukaemia (CLL) is a malignancy characterized by clonal expansion of B lymphocytes with distinct morphology and immunophenotype. The dermatological literature relating to CLL is sparse. A global descriptive survey of a large number of CLL patients has not previously been published.
• **Objectives** To report the spectrum of dermatological conditions seen in a large series of CLL patients.
• **Methods** Skin complications in patients with established CLL were identified retrospectively from clinical and photographic records, principally a database of over 750 consecutive cases. These events were classified, enumerated and compared.
• **Results** Forty patients with 125 skin manifestations were identified and studied. Forty-one manifestations had documented clinical or histological atypia. In 21 of these 41 complications there had been no prior immunosuppressive therapy. We observed that cutaneous malignancies frequently presented atypically both clinically and histologically. There were 18 patients with 56 instances of basal cell carcinoma (BCC) or squamous cell carcinoma (SCC), and clinical atypia was more common with SCC than with BCC. Other cutaneous findings included varicella zoster \( (n = 6) \), leukaemia cutis \( (n = 3) \), acute graft-versus-host disease \( (n = 5) \), cutaneous drug eruptions \( (n = 9) \), multiple warts \( (n = 3) \), herpes simplex \( (n = 3) \), cutaneous T-cell lymphoma \( (n = 2) \), eosinophilic folliculitis \( (n = 2) \), malignant melanoma \( (n = 2) \) and Merkel cell tumour \( (n = 2) \).
• **Conclusions** We have identified a range of dermatological conditions in CLL patients, with a tendency to atypical presentations. The atypia was independent of prior chemotherapy.