A Case of DRESS/HLH Overlap syndrome

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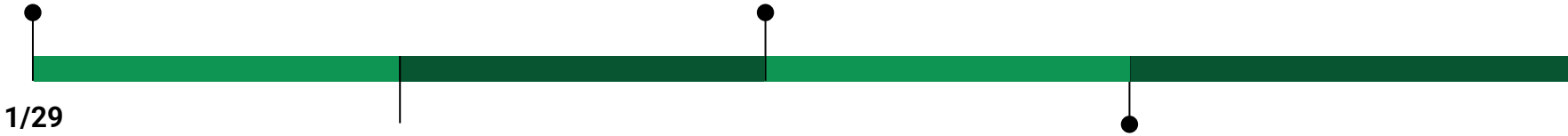
Patient Presentation

49 year old male diagnosed with seronegative rheumatoid arthritis, started on sulfasalazine and prednisone



1/29

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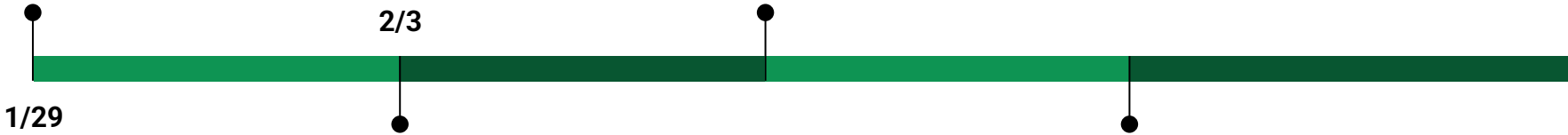

ED visit - fevers, malaise, HA, cough, abd pain, diarrhea.
CT C/A/P - no acute findings
Labs - ferritin 719, CRP 51, LFTs wnl
Dx: CAP
Tx: cefdinir and doxycycline

Patient Presentation

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1/29

2/3

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2/20

ED visit - persistent symptoms
Labs - ferritin 550, CRP 54, LDH 900, AST 108, ALT 84
Dx: Suspected Covid PNA
Tx: none

Patient Presentation

1/29

49 year old male diagnosed with seronegative rheumatoid arthritis, started on sulfasalazine and prednisone

2/3

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2/20

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2/27

ED visit - persistent symptoms
CT A/P - splenomegaly, lymphadenopathy
Labs - ferritin 3870, CRP 185, LDH 4155, AST 510, ALT 526
Admitted to OSH

Patient Presentation

PMH:

- HTN
- Seronegative RA

PSH:

- None

Allergies:

- Allopurinol - facial edema
- Febuxostat - facial edema

Medications:

- Sulfasalazine and Prednisone

Social History:

- Denies cigarette smoking or illicit drug use
- Stopped alcohol use several months ago
- Lives with nephew
- Currently unemployed, previously worked as an aerospace mechanic
- No recent travel or exposure to animals

Family History:

- No significant family history

Patient Presentation

Physical Exam:

•**Vitals:** Temp 37.3, BP 144/91, HR 114, RR 18, SpO2 100%

•**General:** Well-developed male; **appears tired and uncomfortable**

•**HEENT:** Sclera anicteric, oropharynx without erythema, exudates, or ulcers; no cervical lymphadenopathy

•**CV:** **Tachycardic**, normal S1 and S2; no murmurs

•**Pulm:** CTAB; no wheezes or crackles

•**Abdomen:** Soft, non-distended; no rebound or guarding; **mild discomfort to RUQ palpation, palpable splenomegaly**

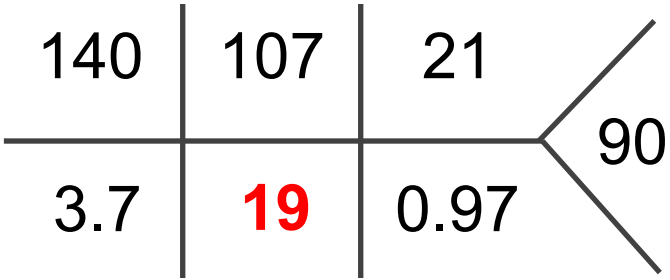
•**Extremities:** Warm and well perfused x4, no peripheral edema, radial and pedal pulses 2+

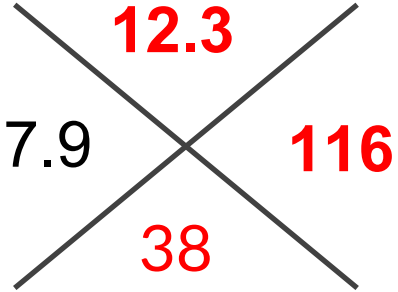
•**Neuro:** CN III-XII grossly intact; no focal deficits

•**Skin:** **Poorly demarcated erythematous rash of face and anterior chest**

Patient Presentation

Labs





Alk Phos - 182
ALT - 434
AST - 345
Total bili - 3.8

INR - 1.4
PTT - 37

Abs Eosinophils - 110

Labs

Triglycerides - 226

CRP - 19.1

ESR - 28

LDH - 1317

Ferritin - 6883

Haptoglobin - 194

Soluble IL-2 receptor - 7252

Other workup for autoimmune, rheumatologic, infectious (viral, bacterial, and fungal), hepatitis, and malignancies, including lymphoma were negative

Imaging/Pathology

CT Chest/Abdomen/Pelvis -
Mild enlargement axillary lymph nodes, splenomegaly with scattered periportal, portacaval and prominent iliac and inguinal lymph nodes

Imaging/Pathology

PET CT - Hypermetabolic lymph nodes throughout the neck, chest, abdomen, and pelvis with enlarged and abnormally avid spleen

Imaging/Pathology

Bone marrow biopsy - Cellular marrow with trilineage hematopoiesis, increased megakaryocytes, blasts, and small aggregates of T-cells consistent with reactive process. There are rare macrophages showing hemophagocytosis

Imaging/Pathology

Skin biopsy - Spongiotic and lichenoid dermatitis with mixed inflammation consistent with a reaction to a medication

Hemophagocytic Lymphohistiocytosis

- Inflammatory endpoint for a variety of conditions
  - Autoimmune diseases
  - Malignancies
  - Infections
  - Few case reports of drug induced HLH
- High morbidity and mortality, estimated rates 20-40%
- Retrospective cohort study on HLH patients
  - Infection (41.1%)
  - Malignancy (28.8%)
  - Autoimmune disease (6.8%)
  - Transplant (2.7%)
  - Idiopathic (17.8%)

Hemophagocytic Lymphohistiocytosis

Diagnostic criteria (at least five of the following):

- Fever ≥ 38.5° C
- Splenomegaly
- Cytopenia, with at least 2 of the following
  - Hemoglobin <9 g/dL
  - Platelets <100,000/microL
  - Absolute neutrophil count <1000/microL
- Hypertriglyceridemia (fasting triglycerides >265mg/dL) and/or hypofibrinogenemia (<150 mg/dL)
- Hemophagocytosis in bone marrow, spleen, lymph node, or liver
- Low or absent NK cell activity
- Ferritin >500 ng/mL
- Elevated soluble IL-2 receptor alpha (CD25)
- Elevated CXCL9

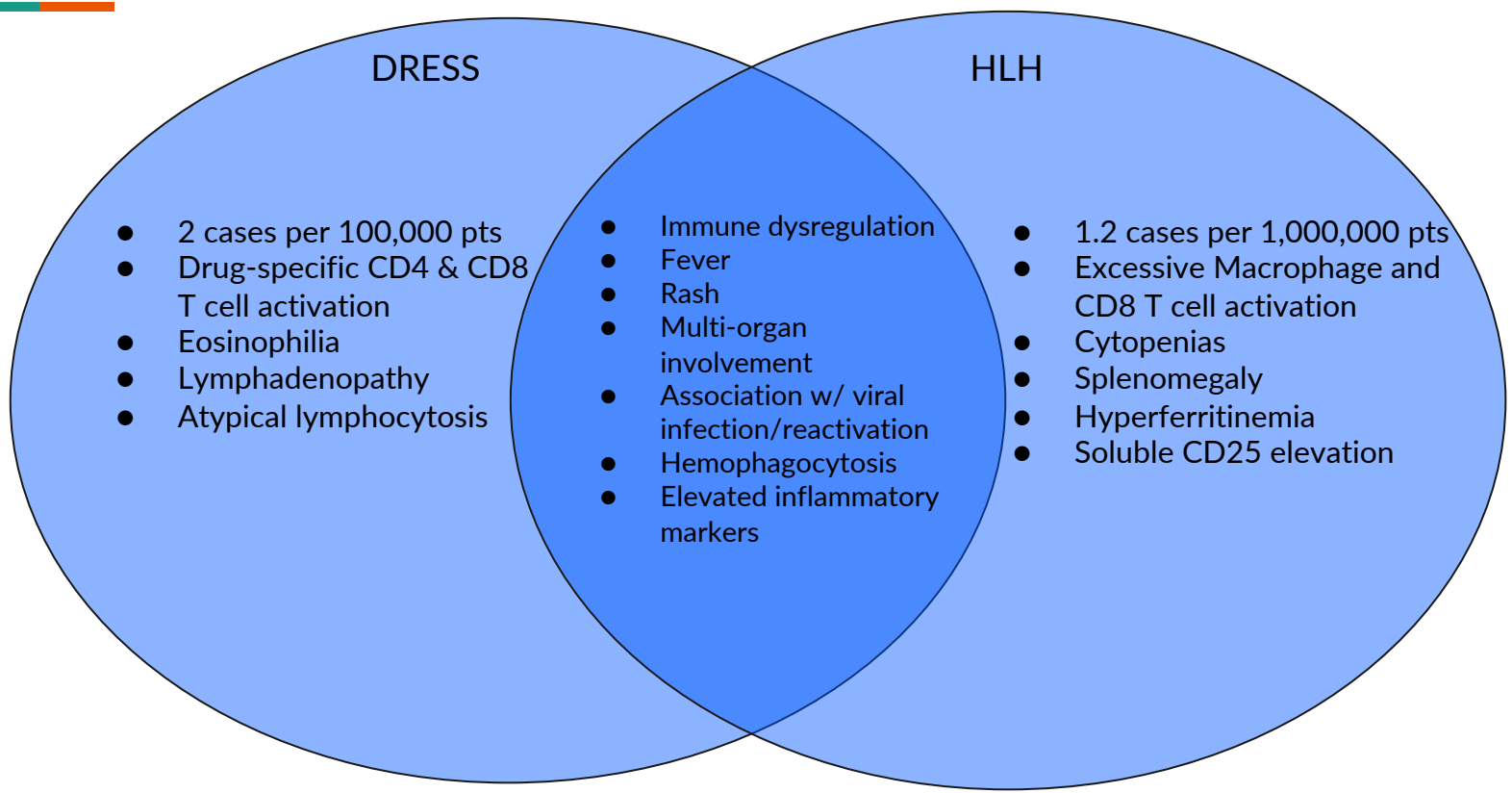
Hemophagocytosis

- Hemophagocytosis not a pathognomonic feature of HLH
- Seen in other hyperinflammatory conditions
- Unclear role in HLH

DRESS

- Drug induced induced hypersensitivity reaction characterized by a cutaneous eruption
- Registry of Severe Cutaneous Adverse Reactions scoring system (RegiSCAR)
  - Fever ≥ 38.5° C
  - Enlarged lymph nodes in at least two different body areas
  - Eosinophilia
  - Atypical lymphocytes
  - Skin involvement
    - Rash/biopsy suggestive of DRESS
    - Extent ≥ 50% BSA
  - Organ involvement
  - Resolution>15 days
  - Exclusion of other causes (If HAV, HBV, HCV, mycoplasma, chlamydia, ANA, blood cultures neg)

DRESS/HLH Overlap Syndrome



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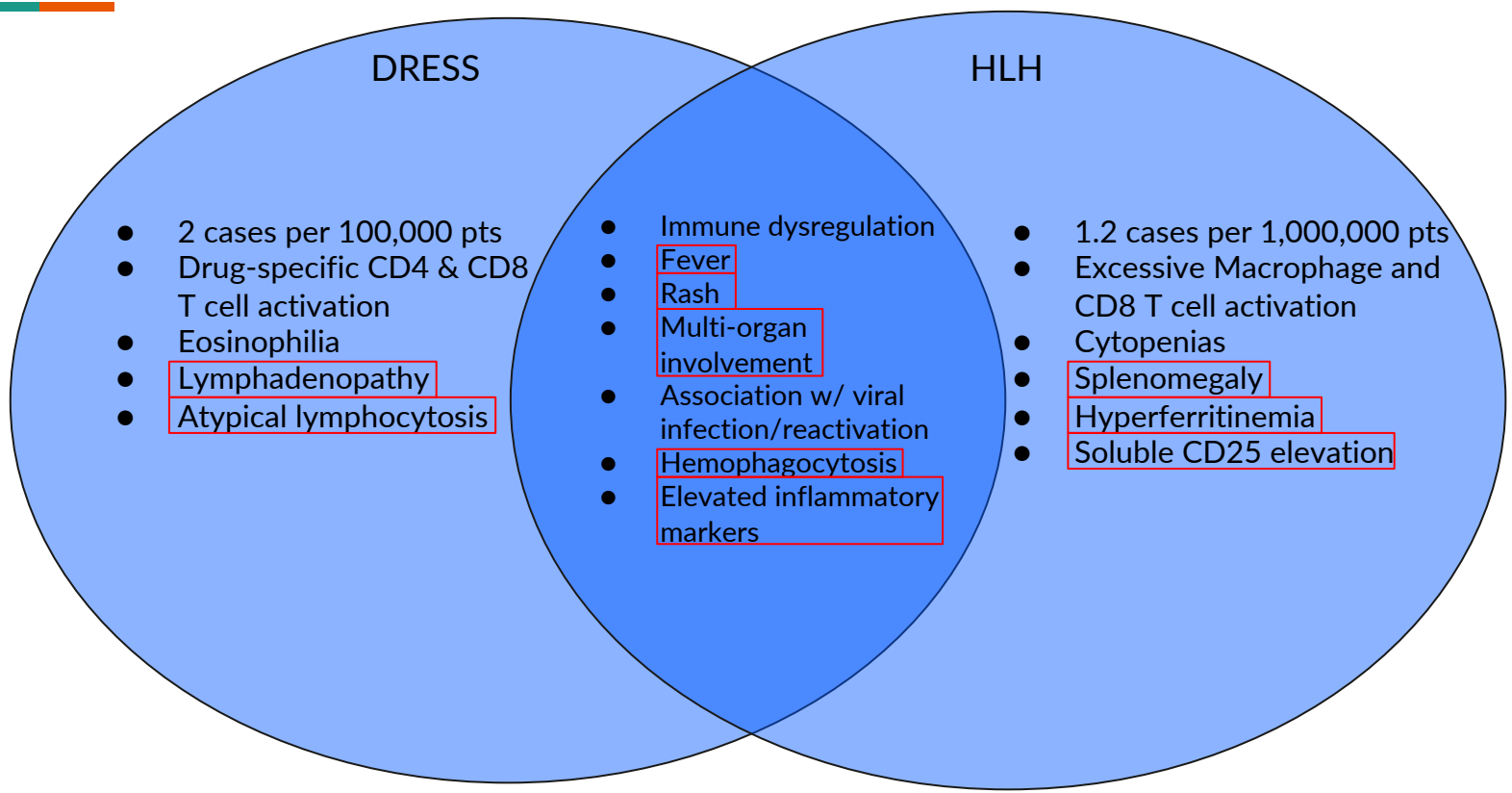

DRESS/HLH Overlap Syndrome

- Literature review over the last decade shows a small number of documented DRESS/HLH Overlap syndromes, with 21 cases
  - 11/21 cases involved infection/reactivation of herpesviridae
  - 10/21 without such features suggesting prolonged period of immune dysregulation with DRESS or HLH could induce the other

Acknowledgements

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