LYMPHOHISTIOCYTOSIS
MASQUERADING AS DRESS

ASEEM SOOD
MD
HISTORY OF PRESENT ILLNESS

27-YEAR OLD FEMALE IN ART SCHOOL

PAST MEDICAL HISTORY OF ANXIETY AND TEMPORAL LOBE EPILEPSY, DIAGNOSED TWO WEEKS EARLIER BY ELECTROENCEPHALOGRAM AND STARTED ON LAMOTRIGINE.
HISTORY OF PRESENT ILLNESS

One week before presenting to the ED:
flu like symptoms,
headache she described as worst of her life,
nausea & vomiting,
photophobia,
joint pains.
HISTORY OF PRESENT ILLNESS

Few days before presenting to the ED:
Developed persistent fevers up to 39.9°C,

Maculopapular rash, began on hands and spread rapidly to trunk
HISTORY OF PRESENT ILLNESS

Travelled to Japan few months earlier

No known sick contacts

Childhood vaccinations up to date,

No recent vaccinations
No Known Drug Allergies

Home Medications: Duloxetine & Lamotrigine

Drinks occasionally. No illicit drug use
PHYSICAL EXAM

Vitals: T 39.7°C, HR 100, BP 95/52, RR 24, SpO2 92%

Gen: Young, anxious diaphoretic female in mild distress from pain. Alert and oriented x3.

HENT: Neck stiffness. Oral mucosa moist; no erythema or exudates.
PHYSICAL EXAM

MSK: Limited ROM BL wrists, shoulders, knees, and ankles due to pain.

Skin: Erythematous, confluent, blanchable diffuse maculopapular rash
LABORATORY RESULTS

**Granulocytes:** >90%
**Lymphocytes:** 7.7%
**Monocytes:** <1%
**Basophils:** 0%
**Eosinophils:** 0.3%

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<th>136</th>
<th>100</th>
<th>14</th>
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<tr>
<td>3.2</td>
<td>23</td>
<td>0.94</td>
<td>9.2</td>
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<td>28.5</td>
<td>80</td>
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**AST:** 528; **ALT:** 658
**ALP:** 954
**RHEUMATOLOGIC**
+ANA; anti-DsDNA

**Fasting Lipid Profile:**
**Chol:** 116; **LDL:** 120, **HDL:** 18, **TG:** 292
IMAGING STUDIES

**Head CT**
No acute intracranial abnormalities

**CXR**
No acute intrathoracic abnormalities
WORKING DIAGNOSIS

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome

Often occurs 2-6 weeks after initiation

Estimated 10% mortality
Lamotrigine is the third most common drug associated with DRESS. Temporal relation of symptom onset with lamotrigine supported diagnosis of DRESS. Lamotrigine was stopped on admission. Broad antimicrobials started.
Lumbar Puncture: Clear.
Glucose: 76, Protein: 290
WBC 520 [93% PMN]
Gram Stain: PMN, no bacteria
HSV 1&2 DNA (-)

Microbiology:
Pharyngeal Group A streptococcus (+)
Rapid Influenza A & B: (-)
EBV qualitative DNA PCR (+)
Clinical Deterioration
Altered mental status, bilateral pulmonary edema, worsening liver function and urine output.

Coagulation tests:
PT: 22.0
PTT: 79.9
Elevated D Dimer
Fibrinogen: 162 (low)
Challenging Our Working Diagnosis
Patient has pancytopenia rather than eosinophilia.

Minority of patients with DRESS can lack eosinophilia
The Suggestion of a Medicine Intern
FERRITIN: 18,154 ng/mL
History is fond of her grandchildren, for it offers them the marrow of the bones, which the previous generation had hurt its hands in breaking.
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<td>★ Fever ≥ 38.5°C</td>
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<td>★ 2. Splenomegaly</td>
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<td>★ Cytopenias (affecting at least 2 of 3 lineages in the peripheral blood)</td>
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<td>Hemoglobin &lt; 9 g/dL (in infants &lt; 4 weeks: hemoglobin &lt; 10 g/dL)</td>
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<td>Platelets &lt; 100 × 10³/mL</td>
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<td>Neutrophils &lt; 1 × 10³/mL</td>
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<td>★ Hypertriglyceridemia (fasting, &gt; 265 mg/dL) and/or hypofibrinogenemia</td>
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<td>(&lt; 150 mg/dL)</td>
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<td>★ Hemophagocytosis in bone marrow, spleen, lymph nodes, or liver</td>
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<td>★ 6. Low or absent NK-cell activity</td>
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<td>★ Ferritin &gt; 500 ng/mL‡</td>
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<tr>
<td>★ 8. Elevated sCD25 (α-chain of sIL-2 receptor)§</td>
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Ferritin level over 10,000 ng/mL was 90% sensitive and 96% specific for HLH.

Activated macrophages secrete ferritin.
Overlapping Features

HLH vs. DRESS

FEVER

RASH

Internal Organs involved

FEVER

RASH

Internal Organs involved
**Hemophagocytic Lymphohistiocytosis**

1.2 cases per 1 million individuals per year

Hyper-proliferation of tissue macrophages called histiocytes, leading to over activation of phagocytosis, cytokine storm, and multi-organ failure.
Estimated 70% of HLH occurs in pediatrics <1 year old

HLH in adults is much less studied.

Secondary (acquired) HLH can present at any age, triggered by infection or malignancy or vaccine.

Remarkably fatal.
Case Series: six month survival of 54% despite therapy.
Ferritin testing is crucial to identifying HLH, as molecular testing (soluble IL-2 receptor, NK cell activity) is only done at a few national labs and often treatment cannot be delayed awaiting those results.
Identifying HLH made it possible to achieve a fortunate outcome in the case of this young patient.

Body surface dosing IV dexamethasone initiated with gradual complete recovery and discharge home with her family the day before Christmas Eve.
ACKNOWLEDGEMENTS

My patient. For teaching us.
Drs. Raman & Archana Sood
Dr. Robert Dobbin Chow
The teaching faculty of
University of Maryland Medical Center Midtown Campus
References


8. Schram A, Berliner N. How I Treat Hemophagocytic Lymphohistiocytosis in