A Delayed Diagnosis: Adult Onset Still's Disease

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Introduction

Objective: To highlight the diagnostic difficulties associated with Adult Onset Still's Disease (AOSD), and clinical confounders that cause this to be an elusive diagnosis.

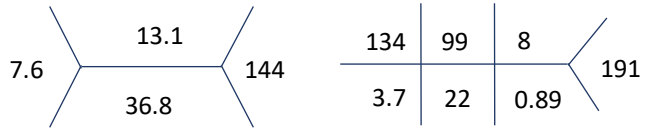
- AOSD is a systemic inflammatory disease presenting as a quotidian fever, evolving into an arthralgia and rash.
- Many cases of AOSD go unrecognized; approximately one third of cases self-resolve. Intermittent presentations may be frequently confused with other rheumatologic syndromes due to lack of definitive diagnostic testing.

Case Presentation

1. **History of Present Illness:**
   - 41-year-old Caucasian male
   - CC: Fever for 1 day, hematuria of 2 days (resolved), and improving 'gouty' bilateral knee and elbow joint pain ongoing for one year
   - PMH: Gout, & uric acid nephrolithiasis
   - Home medications: Prednisone as needed for joint pain, taking approximately 3 x per week, last taken on day of admission, and Febuxostat 80 mg daily

2. **Physical Examination:**
   - Tachycardia.
   - Febrile, Tmax 102.4F
   - Minimal swelling in elbow, ankles and knees, otherwise unremarkable examination

3. **Diagnostic Laboratory Results:**



Initially admitted with a *working diagnosis of pyelonephritis* on broad spectrum antibiotics prior to admitting details about joint pains or rash…

Pathology & Further Investigations

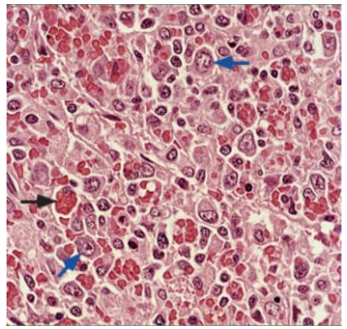


Figure 1: Reactive hemophagocytosis. The red pulp of the spleen diffusely permeated by large lymphoma cells (blue arrows) & histiocytes showing erythophagocytosis (black arrow). [3]

Hospital Day #4, new onset maculopapular rash over the trunk with elbow joint swelling, progressive anemia and high fevers:

1. Further Laboratory Results:
   - CRP = 356.1
   - Ferritin = 3,875
   - Triglycerides = 389
   - Mild transaminitis.
   - Hemoglobin: 10.8, Platelets: 77
   - Negative CBC Path
   - ANA: 1:320 with negative reflex assay
2. Imaging:
   - CT Abdomen/pelvis: retroperitoneal lymphadenopathy, splenomegaly, & nonspecific perinephric fat stranding.
3. Infectious disease & rheumatology consultations.
   1. Further history obtained revealed history of similar arthralgia & rash that improved after Prednisone use.
   2. Negative infectious work-up

Diagnostic Criteria for AOSD

Yamaguchi Diagnostic Criteria

5 or more criteria, at least 2 Major

Major:
1. Fever >39 C for >7 days.
2. Arthralgia >2 weeks.
3. Leukocytosis, >80% granulocytes.
4. Non-pruritic macular skin rash during febrile episodes.

Minor:
1. Sore throat
2. Lymphadenopathy
3. Hepatomegaly / Splenomegaly
4. Abnormal liver function studies.
5. Negative antinuclear antibody & rheumatoid factor.

Sensitivity: 96%. Specificity: 92%

HLH Diagnostic Criteria

Requires 5 out of 8

1. Fever >38.5 C.
2. Splenomegaly
3. Peripheral blood cytopenia.
4. Hypertriglyceridemia +/- hypofibrinogenemia.
5. Hemophagocytosis in bone marrow, spleen, liver, or lymph node.
6. Low NK cell activity.
7. Ferritin >500 ng/mL
8. Elevated soluble CD25.

Sensitivity: 97.5%. Specificity: 96%

Defining the Diagnoses

- Patient started on high dose steroid therapy after negative infectious work up
- Rash and joint pain improved in 24 hours
- Thrombocytosis occurred and anemia resolved in 72 hours

Given overlap of symptoms between AOSD and HLH (*highlighted in the bottom middle*), work-up initiated to rule out HLH as alternative etiology in the outpatient setting.

- Several cases of rheumatologic conditions, such as AOSD, triggering HLH have been reported.
- Negative outpatient work-up for malignancy suggests patient presented with a hybrid of both syndromes.

Conclusions

- A thorough patient history should always be obtained.
- Patients utilizing steroids on an 'as needed' basis should be closely followed to ensure appropriate use.
- This case highlights a unique presentation of two prognostically dissimilar pathologies (AOSD and HLH) sharing a significant diagnostic overlap.
- There is a need for improved diagnostic modalities for AOSD to minimize long-term adverse consequences and patient quality of life.

References

1. Andrei Brateanu. (2018, January 23). *Adult Onset Still's Disease: Early Diagnosis and Treatment Increases Likelihood of Recovery*. Cleveland Clinic QD.
2. Çalik. (2011, June). *Hemophagocytic Syndrome in a Patient with Adult-onset Still's Disease*. Archives of Rheumatology.
3. *Warnke RA, Weiss LM, Chan JK, et al. Tumors of the lymph nodes and spleen. Atlas of tumor pathology (electronic fascicle), Third series, fascicle 14, 1995, Washington, DC. Armed Forces Institute of Pathology.*