Atypical Presentation of Adult-Onset Still's Disease

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LEARNING OBJECTIVES

1. Discuss the challenges and the **delays in diagnosing** Adult-Onset Still's Disease (AOSD) in a patient with significant travel history to an endemic country.
2. Describe the **unusual neurological presentations** associated with AOSD.

CASE PRESENTATION

- A 49-year-old man who **returned from Brazil** a month ago had multiple hospitalizations and emergency department (ED) visits for **fevers and rash**, considered secondary to a viral infection or a potential tick-borne illness. By the time of presentation to our ED, he had been treated with doxycycline and low-dose steroids **without improvement** and had had extensive infectious disease workup, which was negative.
- At the time of admission, he was found to have fever, associated **severe dysphagia and odynophagia**, an evanescent, nonpruritic, blanchable, diffuse maculopapular rash, mostly on his trunk and proximal extremities (Figure 1), submandibular swelling, **asymmetric quadriparesis** with preserved reflexes, and **bilateral facial weakness**.
- Laboratory studies were pertinent for **neutrophilic leukocytosis**; elevated erythrocyte sedimentation rate, C-reactive protein, fibrinogen, and lactate dehydrogenase levels; a **ferritin level >16,500 µg/L** (normal range, 10 to 200); and elevated liver enzymes. In addition to reviewing the infectious workup with an infectious diseases specialist, we completed an autoimmune, hematologic, and malignancy workup. All new testing, including the skin biopsy to exclude vasculitis or dermatomyositis, **returned negative**.
- While testing was in process, the patient started experiencing **bulbar palsy** causing severe dysphagia, episodes of choking, and acute hypoxia requiring supplemental oxygen. Treatment with **high-dose intravenous methylprednisolone** was started, and his **symptoms improved markedly within 48 hours**.
- The clinical picture and laboratory findings were considered consistent with **7/8 criteria of AOSD**. At a follow-up visit 3 weeks later, he reported **feeling much stronger**, but remained on high-dose steroids, which is why *Pneumocystis* prophylaxis with trimethoprim-sulfamethoxazole was started.

Yamaguchi Criteria for AOSD[1]
Diagnosis requires ≥5 criteria, including ≥2 major criteria

Type	Clinical Feature	Our Patient
Major	**Fever ≥39°C** (≥1 week)	–
	Arthralgia or Arthritis (≥2 weeks)	+
	Salmon-pink macular rash (non-itchy)	+
	Leukocytosis ≥10,000/mm³ (≥80% PMNs)	+
Minor	**Sore throat**	+
	Lymphadenopathy / Splenomegaly	+
	Abnormal liver function tests	+
	Negative ANA and RF	+
Rule out: Infections, Malignancies, Rheumatic diseases		+

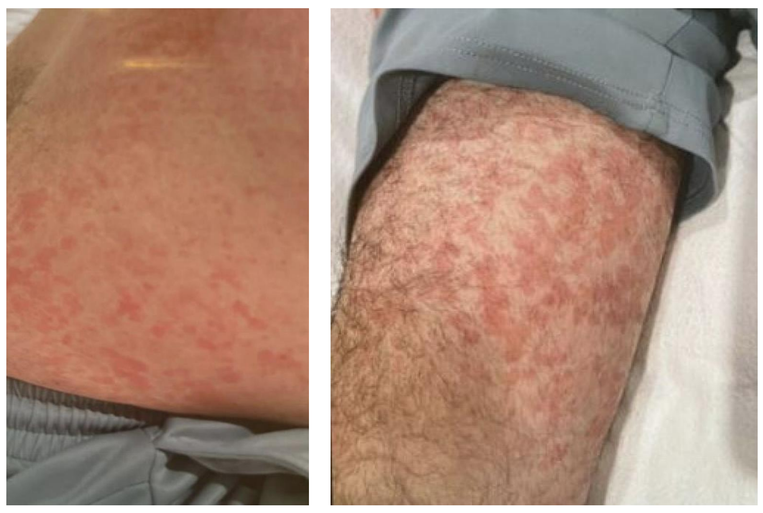


Figure 1. Salmon-pink, nonpruritic maculopapular rash involving the trunk (left) and proximal lower extremity (right)

Infectious Workup	Results
Viral Hepatitis & HIV	**Negative:** HIV-1/2 Ag/Ab, Hep A (IgM), Hep B (sAg, core IgM), Hep C (Ab)
Tick-Borne Pathogens	**Negative:** Lyme, *Babesia*, *Anaplasma*, *Ehrlichia*, *Rickettsia*, *B. miyamotoi*
Tropical / Arboviruses	**Negative:** Dengue (IgM/IgG), Zika (IgM), Chikungunya (IgM/IgG), Malaria smear
Cultures & PCR Panels	**Negative:** CSF, Stool Pathogens, *C. diff*, Enterovirus, Respiratory Panel, *Brucella*, *Legionella*
Other Viral Serologies	**Past Infection:** Parvovirus B19, EBV; **Indeterminate:** CMV PCR (low level: 189 IU/mL)

Immunologic & Rheumatologic Workup	Results
Core Rheumatologic	**Negative:** ANA, Rheumatoid Factor (RF), Anti-CCP, Anti-dsDNA
ENA Panel	**Negative:** Anti-Sm, Anti-RNP, Anti-SSA (Ro), Anti-SSB (La), Scl-70, Jo-1
Vasculitis & Myopathy	**Negative:** ANCA (MPO, PR3), Myositis Panel (including MDA-5, Jo-1, TIF1-γ)
Antiphospholipid	**Negative:** Cardiolipin, Antiphospholipid Abs; **Positive:** Lupus Anticoagulant
Acute Phase / Other	**Elevated:** C3 (193 mg/dL), C4 (41 mg/dL); Skin Biopsy: No dermatitis/inflammation **Normal:** Creatine Kinase

Hematologic & Oncologic Workup	Results
Flow Cytometry (Peripheral)	**Negative:** No immunophenotypic evidence of a clonal hematologic malignancy (leukemia/lymphoma)
Peripheral Smear	**Abnormal:** Leukocytosis with absolute neutrophilia and mild left shift (band forms). **Negative:** No blasts, no hemolysis, no intra-erythrocytic parasites.
Hyperinflammation Markers	**Elevated:** Soluble Interleukin-2 Receptor (sIL-2R / CD25): 4261.6 U/mL

DISCUSSION

- AOSD is a **rare autoinflammatory disorder** (prevalence 1–10 per million[1]) defined by fever, rash, and arthritis. With no specific biomarker, it is a **diagnosis of exclusion**, usually made with the Yamaguchi criteria.[1]
- Recent travel to Brazil kept endemic infections on the differential and **delayed the diagnosis**. Steroids, started for bulbar palsy while infection was being excluded with infectious diseases, worked within 48 hours.
- **Neurological involvement** occurs in 7–12% of patients, mostly as aseptic meningitis, and carries higher rates of macrophage activation syndrome (MAS).[2,3] Our patient had **severe quadriparesis and bulbar palsy**, yet MAS was unlikely (HScore 136, cutoff 169; high fibrinogen).
- Internists should consider AOSD even in atypical presentations, because **timely corticosteroid therapy is critical**. Mortality is low overall (2.6%[5]) but reaches 10–22% with MAS and about 90% with untreated thrombotic thrombocytopenic purpura.[4]

CONCLUSION

AOSD should remain on the differential for systemic inflammation with severe neurological deficits, despite confounders like tropical travel. Once competing infectious etiologies are excluded, **timely recognition and initiation of corticosteroid therapy** may result in rapid clinical improvement.

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