CAS-075

The Paradox of Healing: Adult-Onset Still's Disease in the era of Human Immunodeficiency Virus treatment

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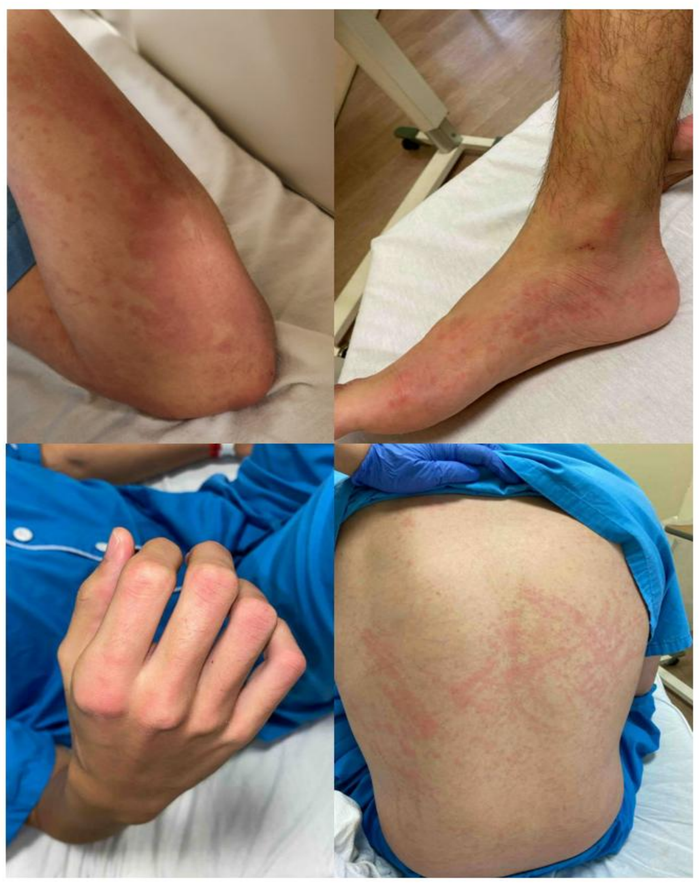
Case Vignette

- A 21-year-old Chinese male with recently diagnosed HIV presented with daily fevers for three months, accompanied by significant weight loss, migratory polyarthritis, and urticated plaques over the limbs and trunk.
- There were no focal infective symptoms, mucocutaneous ulcers, or recent exposures. He had no personal or family history of autoimmune disease or tuberculosis. Antiretroviral therapy (bictegravir, emtricitabine, tenofovir alafenamide) had been initiated six months earlier, resulting in an undetectable viral load and increased CD4 count (from 346 to 534 cells/μL) prior to symptom onset.
- Examination revealed urticated plaques and symmetric arthritis of large and small joints. Investigations showed neutrophilic leukocytosis, elevated inflammatory markers, transaminitis, and negative autoimmune and infectious screens. Imaging was unremarkable.
- Adult-onset Still's Disease was diagnosed based on Yamaguchi criteria and he responded well to corticosteroids and NSAIDs.



Discussion / Learning Points

- **AoSD: A disease at the crossroads:** Straddles autoinflammation (innate immune activation, cytokine storm: IL-1, IL-6, IL-18, TNF-α) and autoimmunity (T-cell dysregulation, adaptive immunity involvement)[1,2]. Classic triad of daily fevers, arthritis, evanescent salmon rash; Typically, seronegative for autoantibodies.
- **Immunological Overlap with HIV:** This dual immune involvement mirrors the pathophysiology of HIV, where T-cell dysfunction drives systemic immune changes. Such overlap raises the possibility of an immunological link between HIV and the development of AoSD.
- **IRIS as a Trigger:** In patients starting antiretroviral therapy (ART), immune reconstitution inflammatory syndrome (IRIS) can paradoxically trigger hyperinflammatory states[3]. IRIS occurs in 10–40% of patients, driven by rapid CD4 recovery, restoration of effector function, and a surge of cytokines such as IL-1, IL-6, and TNF-α. While typically manifesting within 8 weeks of ART, delayed onset up to 6 months—as seen in our patient—can occur. IRIS may therefore unmask autoimmune or autoinflammatory conditions such as AoSD.
- **Risk Factors and Clinical Implications:** Key risk factors for IRIS include low baseline CD4 counts with rapid recovery, high viral load, latent infections, and genetic predisposition to autoimmunity[4,5]. Clinically, IRIS represents a double-edged sword: ART is lifesaving, yet immune recovery can trigger severe inflammation. Management of AoSD in this context generally requires immunomodulation with NSAIDs, corticosteroids, or immunosuppressive agents, while ART should be continued to maintain viral suppression.
- **Looking Forward:** Recognition of AoSD as a possible IRIS-mediated complication highlights the need for heightened vigilance among clinicians. Further research into the immunological interplay between HIV, immune reconstitution, and autoinflammatory/autoimmune disorders is essential to guide prevention and optimize treatment strategies.

Mechanism	Role in HIV immune reconstitution and Adult-onset Still's disease
CD4 T cell recovery	Triggers exaggerated immune response (IRIS)
Cytokine surge	IL-1, IL-6, IL-18 which are key in both IRIS and AoSD
Macrophage activation	Macrophage activation syndrome can occur due to overactivated innate immunity
Toll-like receptors dysregulation	Triggers inflammatory cascades mimicking AoSD

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