

HYPERINFLAMMATION IN A PREGNANT PATIENT AFTER IMMUNIZATION: A DIAGNOSTIC & THERAPEUTIC CHALLENGE

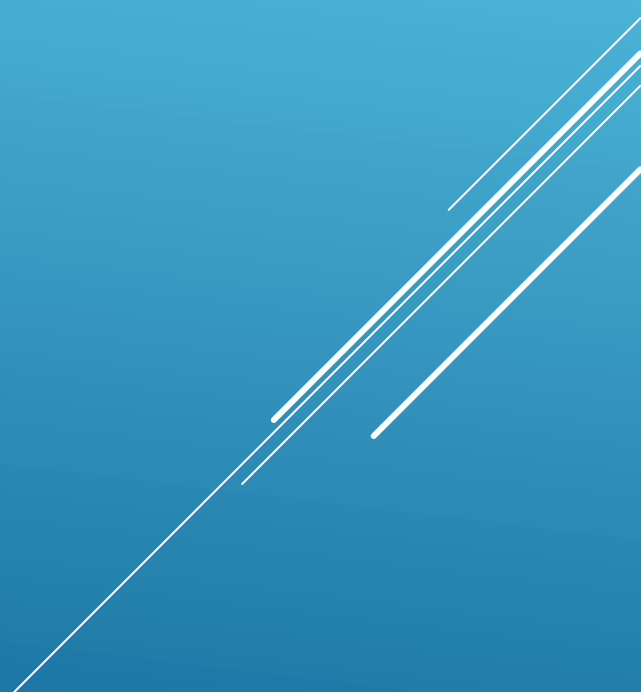
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DISCLOSURES

None



41F G2A1 @ 25⁺⁵ WEEKS GESTATION

- ▶ Diffuse rash, polyarthralgia, and myalgia x 2 wks
 - Pain constant and progressive, no clear morning stiffness
- ▶ Symptoms started 5-6 h after 6th COVID & annual Influenza vaccines
- ▶ Also had sore throat, pleuritic chest pain, and dyspnea
- ▶ ROS: Otherwise unremarkable, incl. no fevers or preceding infection
- ▶ PMHx: Obesity, HTN, T2DM
- ▶ Meds: ASA, labetalol, metformin, acetaminophen 1 g PO q4h
- ▶ SocHx and FamHx: Non-contributory, no recent travel

OBJECTIVE FINDINGS

- ▶ Vitals: T_{max} 38.4 °C (101.1 °F), otherwise within normal limits
- ▶ Physical exam:
 - Migratory pruritic maculopapular rash affecting trunk and limbs
 - Diffuse joint tenderness w/ swelling of L MCP3, R MCP1, R knee, R ankle
 - Doppler signal on POCUS
 - Cardiorespiratory, abdominal, and neurologic exam were unremarkable



INVESTIGATIONS SUMMARY

- ▶ WBC 22.8, ANC 20.8, Hgb 92, MCV 77, Plt 276
- ▶ Cr 46 $\mu\text{mol/L}$ (0.52 mg/dL), eGFR 118, urinalysis bland
- ▶ ALT 140, AST 183, GGT 152, ALP 115
- ▶ CRP >200, peak ferritin 5196
- ▶ RF 21 (N <20); negative CCP, ANA, ANCA, HLA-B27, APS Ab
- ▶ ECG: diffuse ST elevation & PR depression with ST depression in aVR
- ▶ TTE: Normal, no pericardial effusion
- ▶ XR/CTA chest: Normal
- ▶ Nasopharyngoscopy: generalized upper airway inflammation from nasal cavities to vocal cords
- ▶ Extensive infectious work-up negative

CASE SUMMARY

- ▶ 41-year-old gravid woman with oligoarthritis, waxing and waning rash, sore throat, pericarditis, neutrophilic leukocytosis, mixed liver enzyme elevation, and persistent systemic inflammation following COVID & Influenza vaccination.
- ▶ **What do you think is the diagnosis?**
 - A. Adult-Onset Still's Disease
 - B. Seronegative inflammatory arthritis
 - C. ANCA-negative vasculitis
 - D. Post-viral arthritis



CASE SUMMARY

- ▶ 41-year-old gravid woman with oligoarthritis, waxing and waning rash, sore throat, pericarditis, neutrophilic leukocytosis, mixed liver enzyme elevation, and persistent systemic inflammation following COVID & Influenza vaccination.
- ▶ **What additional information would you like to aid in your diagnosis?**
 - A. sIL-18
 - B. Skin biopsy
 - C. Liver biopsy
 - D. PET-CT scan

CASE DIAGNOSIS

- ▶ Skin biopsy: Scattered dyskeratotic keratinocytes in the epidermis, distinctive and most suggestive of Adult-onset Still's disease.
- ▶ Final diagnosis: Adult-Onset Still's disease, presumed vaccine-related
 - ? Masking of fevers with acetaminophen

1992 Yamaguchi criteria*		2002 Fautrel criteria	
Two major criteria and at least five total criteria		Four or more major criteria or three major criteria + two minor criteria	
Major criteria	Minor criteria	Major criteria	Minor criteria
Fever $\geq 39^{\circ}\text{C}$, ≥ 1 week	Sore throat	Spiking fever $\geq 39^{\circ}\text{C}$	Maculopapular rash
Arthralgias or arthritis ≥ 2 weeks	Lymphadenopathy	Arthralgia	Leukocytes $\geq 10,000/\text{mm}^3$
Typical rash	Hepatomegaly or splenomegaly	Transient erythema	
Leukocytosis $\geq 10,000/\text{mm}^3$ with $\geq 80\%$ granulocytes	Abnormal liver function studies	Pharyngitis	
	Negative ANA and RF	PMN $\geq 80\%$	
		Glycosylated ferritin $\leq 20\%$	
Notes: *Absence of infection, malignancy, or other rheumatologic disorders known to mimic AOSD.			
Abbreviations: AOSD, adult-onset Still's disease; ANA, antinuclear antibody; RF, rheumatoid factor; PMN, polymorphonuclear leukocyte.			

COVID VACCINE-INDUCED AUTOIMMUNE DISEASE

- ▶ COVID-19 immunization has been associated with the development of some autoimmune and autoinflammatory diseases
- ▶ Most common new onset rheumatologic diseases in a systematic review of 756 cases (Rodriguez 2022):
 - Leukocytoclastic vasculitis – 16 cases (2.1%)
 - Systemic lupus erythematosus - 15 cases (2.0%)
 - Polymyalgia rheumatica - 13 cases (1.7%)
 - **Adult-onset Still's disease - 12 cases (1.6%)**
- ▶ Proposed mechanisms include molecular mimicry, bystander activation, and epitope spreading

CHARACTERISTICS OF COVID VACCINE-INDUCED ADULT-ONSET STILL'S DISEASE

Literature review
& analyses of
pharmacovigilance
databases (N=159):
- 136 new (85.5%)
- 23 flares (14.5%)

(Palassin 2023)

Median age at onset ~43 years

Majority were mRNA-based COVID vaccines

Most occurred after 1st dose, w/in 3 weeks post-vaccine

Hyperferritinemia present in >80%

Generally treatable; few reported fatal outcomes

Steroid-sparing therapy required in >50% of cases

CASE RESOLUTION

- ▶ Started prednisone 20 mg PO BID and colchicine 0.6 mg PO BID with gradual improvement
- ▶ Initially required opioids for pain but eventually weaned off
- ▶ Prednisone tapered off over 4 mo
- ▶ Colchicine tapered off after 1 yr
- ▶ Delivered a healthy baby boy via Caesarean section
- ▶ No recurrence now >1 year after prednisone discontinuation



TAKE HOME POINTS

- ▶ COVID-19 vaccination can rarely induce new onset autoimmune and autoinflammatory diseases, including AOSD, PMR, SLE, and LCV
- ▶ AOSD induced by the COVID-19 vaccine usually presents after the 1st or 2nd dose, generally within 3 weeks post-vaccine
- ▶ The benefits of COVID-19 vaccination *still* outweigh these miniscule risks, especially as prognosis is generally favourable
- ▶ Consider AOSD in patients with prolonged fevers and/or hyperinflammation following COVID-19 vaccination
- ▶ Skin biopsy may be a helpful part of the diagnosis of AOSD

REFERENCES

Jung SW, Jeon JJ, Kim, YH, et al. Long-term risk of autoimmune diseases after mRNA-based SARS-CoV2 vaccination in a Korean, nationwide, population-based cohort study. *Nat Commun* 15, 6181 (2024). <https://doi.org/10.1038/s41467-024-50656-8>

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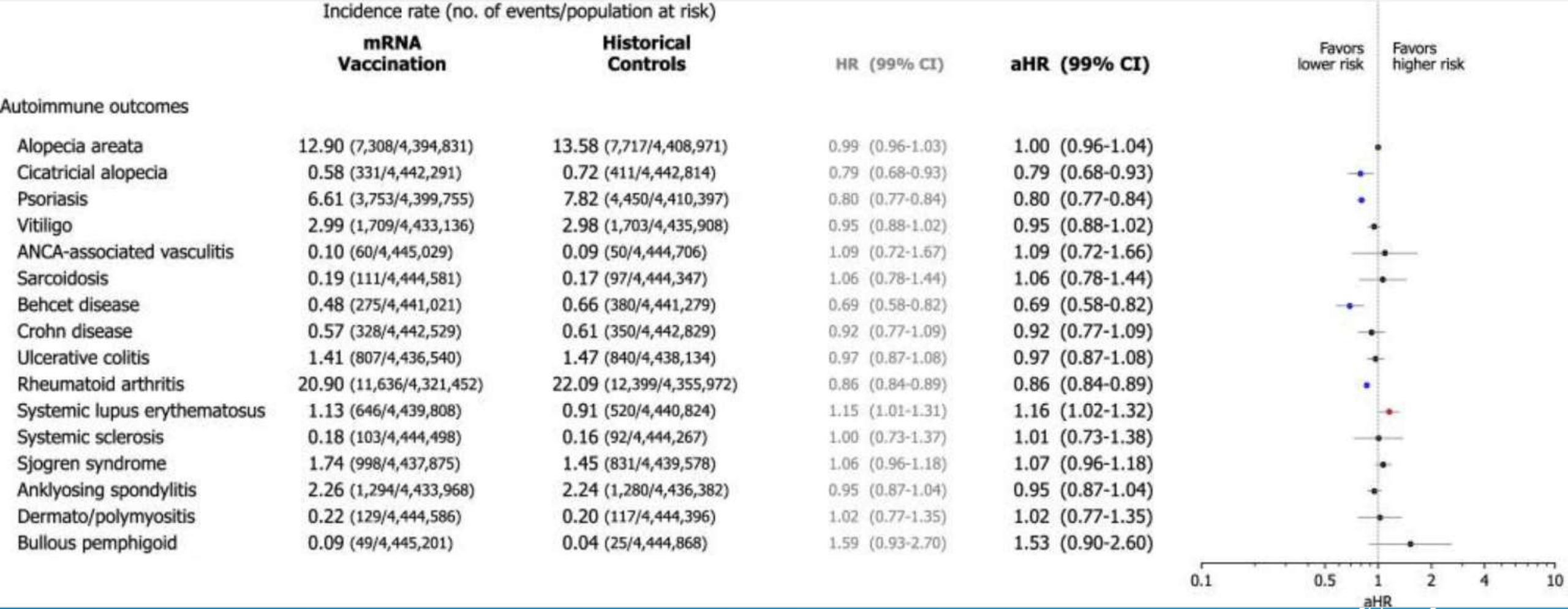
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Rodríguez Y, Rojas M, Beltrán S, et al. Autoimmune and autoinflammatory conditions after COVID-19 vaccination. New case reports and updated literature review. *Journal of Autoimmunity*. 2022;132:102898. doi:10.1016/j.jaut.2022.102898.

QUESTIONS ARE WELCOME 😊

Thank you for listening!





Korean population-based cohort (N=9.3 million) (Jung 2024): COVID-19 mRNA vaccination was associated with a modest increase in SLE risk (HR 1.16) compared to historical controls