Management of Rheumatologic Disease in the Setting of the COVID-19 Pandemic

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ANTHC Rheumatology
Rural Provider Lecture Series
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Objectives

• Understand unique characteristics of patients with rheumatologic disease that increase their risk of infection

• Discuss changes in clinical management that may help to reduce risk of exposure to COVID-19

• Review Guidelines from the American College of Rheumatology for the management of rheumatic diseases in the setting of the COVID-19 pandemic

• Review recent data on COVID-19 infection in patients with rheumatic disease
High Risk Population

• Immunosuppressed due to medications
• Immunosuppressed due to underlying disease
  • Dysregulated innate and adaptive immune systems
• Stress shown to increase risk of flare of autoimmune disease
  • Global pandemic = Stress!
• More likely to require travel for medical treatment
  • clinic, pharmacy, infusion center
• Elderly
• Multiple co-morbidities (CVD, HTN, DM)
Treatment Goals:

• Prevent exposure to/infection with COVID-19
  • Patient
  • Provider/Health Care System

• Achieve or maintain low disease activity or remission

• Prevent flares
  • Flares increase:
    • Risk of infection
    • Requirement for steroids
    • Dose of DMARD/Biologic
    • Need for clinic visit or hospitalization
Prevention: Patient

- Patients should follow all CDC and Alaska State Department of Health Guidelines

- As Alaska “re-opens”, our patients should adopt these new measures slowly
  - Continue social/physical distancing
  - Limit public outings
  - Wear a mask in public
  - Work from home if possible
Prevention: Provider

• Provide patient education
  • Disease state, medications, signs/symptoms of flare
  • Online patient resources (ACR, Creaky Joints)

• Avoid disruption in treatment
  • Continue routine follow-up appointments via telemedicine
  • Ensure adequate refills of all chronic medications
  • Utilize medication mail-out systems
  • Reduce frequency of lab monitoring

• Discuss behavioral health concerns
  • Increased anxiety about risk of infection
  • Depression from lack of social interaction, financial stress
  • Substance abuse, physical abuse

• Treat co-morbidities
Lab monitoring

• When possible, routine lab monitoring (CBC, CMP) for high risk DMARDs, including methotrexate and leflunomide, should be continued in local clinics every 3 months.

• For patients who are unable to travel or when flight restrictions prevent lab processing, we recommend continuation of methotrexate and leflunomide for up to 4-5 months, but not more than 6 months, without lab monitoring in those who have had stable labs on these drugs for at least a year.

• Patients on infused biologics can have labs drawn in coordination with infusion appointments.
American College of Rheumatology
COVID-19 Clinical Guidance for Adult Patients with Rheumatic Diseases

• Developed March 26, 2020. Updated April 14, 2020
• Expert Opinion
  • Virtual panel of Rheumatologists and Infectious Disease Specialists
• Guidelines contain only statements that received a moderate (M) or high (H) level of consensus among panel members
• Guidelines are highly disease-, patient-, geography- and time-specific
• Not intended to replace clinical judgement
• Subject to change as new developments arise
Clinical Scenarios

1. Treatment of stable disease - no COVID
2. Treatment of stable disease - asymptomatic COVID exposure
3. Treatment of new or active disease – no COVID
4. Treatment of disease in the setting of confirmed COVID infection
Treatment of Stable Disease

• In the absence of known COVID-19 infection, continue current medication therapy:
  • NSAIDs
  • DMARDs
  • Biologics
  • Janus Kinase Inhibitors
  • Immunosuppressants
  • Corticosteroids
NSAIDs

• Conflicting data on the impact of Ibuprofen on COVID-19 disease severity related to ACE2 receptor upregulation. There is limited data on other NSAIDs.

• Patients who are on chronic NSAIDs may continue therapy.
  • NSAIDs are not associated with an increased risk of other infections and are safer to use for arthritis flares than steroids.

• Patients who are acutely ill should stop NSAIDs due to risk of gastritis and renal insufficiency.

• In COVID patients with severe respiratory symptoms, NSAIDs should be stopped (M)
Conventional Synthetic Disease Modifying Anti-Rheumatic Drugs (DMARDs)

- Hydroxychloroquine (Plaquenil)
- Sulfasalazine
- Methotrexate
- Leflunomide (Arava)
Hydroxychloroquine

• Standard arthritis dose: 200mg-400mg daily (5mg/kg or less)

• COVID-19 dose: **400mg BID on day 1**, then 200mg BID for 4 days

• NOT proven to prevent or treat COVID-19
  • Avoid false sense of security!

• Toxicity is dose dependent
  • Most patients on a stable arthritis dose of HCQ have a low risk of cardiac toxicity
  • Use caution in patients on other QTc prolonging drugs
  • Avoid in patients with prolonged QTc

West, 2019
Biologics

- Proteins derived from living cells
- Specifically target cytokines and cell surface proteins involved in the pathogenesis of autoimmune disease

West, 2019
Cytokine Targeted Biologics

- **Anti-TNF**
  - Etanercept (Enbrel)
  - Adalimumab (Humira)
  - Infliximab* (Remicade)
  - Certolizumab (Cimzia)
  - Golimumab

- **IL-1 Inhibitors**
  - Anakinra (Kineret)
  - Rilonacept
  - Canakinumab

- **IL-6 Inhibitors**
  - Tocilizumab (Actemra)
  - Sarilumab

- **Anti IL-12/IL-23**
  - Ustekinumab (Stelara)

- **Anti IL-17A**
  - Secukinumab (Cosentyx)
  - Ixekizumab

- **Anti IL-17 receptor**
  - Brodalumab

*Biosimilar (Renflexis) available at ANMC*
Cell Targeted Biologics

**B-Cell**
- Anti-CD20
  - *Rituximab* (*Rituxan*)
- B-Cell Growth Factor Inhibitor (Anti-Blys)
  - *Belimumab* (*Benlysta*)

**T-Cell**
- Co-stimulatory Molecule Inhibitor
  - *Abatacept* (*Orencia*)
Janus Kinase (JAK) Inhibitors

- JAK- intracellular protein that associates with and binds to cytokine and growth factor receptors
- **Tofacitinib (Xeljanz) and Baracitinib (Olumiant)**

sourced from Wikimedia “Jakstat pathway”, diagram created by Peter Znamenkiy
Immunosuppressants

- Azathioprine
- Cyclosporine
- Cyclophosphamide
- Mycophenolate mofetile
- Tacrolimus
Corticosteroids

• Intra-articular steroids favored over systemic steroids in the setting of monoarticular flare

• Prednisone doses >6mg-10mg/day and especially at doses >20mg/day increase risk of infection and should be avoided if possible in RA, spondyloarthritis, psoriatic arthritis, and gout.

• Severe flares of lupus, vasculitis (including giant cell arteritis), myositis, interstitial lung disease and others may require high dose steroids and management should be directed by the patient’s rheumatologist.

• Critically ill patients who are on chronic steroids (>5mg for 30+days or 20mg for 5+ days) will need stress dose steroids
1. Treatment of Stable Disease – No COVID

• In the absence of known COVID-19 infection, continue current medication therapy:
  • NSAIDs
  • DMARDs
  • Biologics
  • Janus Kinase Inhibitors
  • Immunosuppressants
  • Corticosteroids
2. Treatment of Stable Disease – asymptomatic COVID exposure

- In patients with stable rheumatic disease who are asymptomatic, but have been exposed to COVID-19:
  - HCQ, SSZ and NSAIDs may be continued (M/H)
  - Immunosuppressants, non-IL-6 biologics and Jak inhibitors should be stopped temporarily until COVID-19 testing is negative or after 14 day symptom-free period (M)
    - Uncertainty among panel members regarding temporary hold of MTX and leflunomide
  - In certain circumstances, IL-6 inhibitors may be continued (M)
3. Treatment of Active or New disease

• Inflammatory Arthritis:
  • For patients with active or newly diagnosed disease, conventional DMARDs may be started or switched. (M)
  • For patients with moderate to high disease activity despite conventional DMARD therapy, biologics may be started (H)
    • Uncertainty about JAK inhibitors
  • If indicated, low-dose glucocorticoids (10mg or less prednisone equivalent) or NSAIDs may be started. (M/H)

• Other Rheumatic Diseases:
  • In patients with systemic inflammatory or vital organ-threatening disease (ie. Lupus nephritis, vasculitis), high dose glucocorticoids or immunosuppressants may be initiated (M)
4. Active COVID-19 infection:

**CONTINUE**
- Hydroxychloroquine (Plaquenil) (M/H)
- Corticosteroids
- IL-6 inhibitors (select circumstances) (M)

**STOP (M/H)**
- Sulfasalazine, leflunomide, methotrexate
- Immunosuppressants
- Biologics
- Janus Kinase (JAK) inhibitors
- NSAIDs (in severe respiratory disease) (M)
Covid-19 in Immune-Mediated Inflammatory Diseases- Case Series from New York
Haberman, et al. 29 April 2020. NEJM

- Prospective Case Series, March 3- April 3, 2020
- 86 patients at NYU Langone Health Center, New York City.
  - 59 confirmed COVID, 27 highly suspicious for disease
  - RA, Psoriasis, Psoriatic Arthritis, Ankylosing Spondylitis, IBD, or related diseases
  - 76% on biologic or Jak inhibitor therapy
- 16% of patients required admission
  - Older age
  - Rheumatoid Arthritis
  - More co-morbidities (HTN, DM, COPD)
  - 79% were discharged, 2 still hospitalized, 1 required mechanical ventilation
  - One death
- Infection rate similar to general NYC population
- Patients on biologics do not have a worse outcome
COVID-19 Global Rheumatology Alliance

**Our Mission:**
- Our mission is to collect, analyze and disseminate information about COVID-19 and rheumatology to patients, physicians and other relevant groups to improve the care of patients with rheumatic disease.

**Our Vision:**
- Bringing together the global rheumatology community to curate and disseminate accurate and comprehensive knowledge to advance rheumatology care in the COVID-19 pandemic.

**https://rheum-covid.org/**

- Secure, de-identified, international case reporting registry of patients with rheumatic disease who contract the COVID-19 virus

- Certain organizations and Tribal Councils may restrict enrollment of patients. Know your local rules before enrolling patients!
COVID Testing

• Testing should be conducted based on state and local recommendations and test availability

• We are not currently preferentially testing asymptomatic patients on immunosuppressive therapy

• Patients on immunosuppressive therapy are still at high risk for OTHER infections that can be life threatening! Don’t ignore symptoms if COVID-19 testing is negative.
Online Rheumatology Resources

  • Patient handout with summary of Recommendations

• American College of Rheumatology: https://www.rheumatology.org/
  • Clinical Guidelines
  • Disease and Treatment handouts for patients

• CreakyJoints: https://creakyjoints.org/
  • COVID-19 support program for chronic disease patients and their families
Rheumatology Consults

• Tiger Text:
  • “ANMC Rheumatology Consult”
  • Coverage from 8am-4:30pm

• Phone:
  • Internal Medicine Clinic (907) 729-1500
  • Rheumatology RN Case Manager (907) 729-2071

• Cerner, AFHCAN referrals
References


THANK YOU!!