

Hydroxychloroquine Associated Retinal Toxicity

Adverse effect of HCQ - Retinal damage (macula) → Potentially irreversible vision loss

Mechanism: HCQ accumulation in the retinal pigment epithelium → photoreceptor damage

Risk factors: high dose (>5 mg/kg) and long treatment duration (>5 years) (<2% at 10 yrs | ~20% at 20 yrs)

Clinic: Often **asymptomatic**, may manifest with visual field defects and central vision loss

Screening: Ophthalmologic baseline examination (OCT, fundus autofluorescence); **annually after 5 yrs**

Management:

- **Drug discontinuation**
- Retinal damage may progress even after stopping HCQ

Rosenbaum et al. Arthritis & Rheumatology. 2021.

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Rhupus Syndrome – RA – SLE Overlap

Coexistence of clinical, serological, and radiological features of both RA and SLE in the same patient

First employed 1971 by Shur et al – still no classification criteria

Clinical findings available in the literature review.

Key features of Rhupus

- RA-like erosive, symmetric polyarthritis
- **Clinical features of SLE**
- Highly specific autoantibodies

Prevalence among SLE patients: **0.1 - 9.7%**

Sequential onset (2/3 RA diagnosed first)

Treatment extrapolated from RA and SLE guidelines

- Guided by dominant clinical phenotype

| | Results |
|---------------------------|-----------------|
| Number of patients | 287 |
| Polyarthritis | 88.2% (225/255) |
| Affecting hand | 82% (134/164) |
| Symmetric | 87% (206/237) |
| Erosions | 90% (251/278) |
| Rheumatoid nodules | 16% (43/262) |
| Skin lesions | 41% (118/287) |
| Oral ulcers | 23% (65/287) |
| Photosensitivity | 30% (87/287) |
| Alopecia | 17% (47/271) |
| Raynaud's | 9% (25/271) |
| Serositis | 26% (74/287) |
| Neurological involvement | 5% (14/287) |
| Renal involvement | 35% (100/287) |
| Pulmonary involvement | 6% (16/287) |
| Hematological involvement | 70% (202/287) |
| Vasculitis | 4% (12/287) |

Antonini et al. Rhupus: A Systematic Literature Review. Autoimmun Rev. 2020.

Frade-Sosa et al. A Comparative Study on Clinical and Serological Characteristics Between Patients With Rhupus and Those With Systemic Lupus Erythematosus and Rheumatoid Arthritis. Lupus 2020.

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| | Results |
|-----------------------|---------------|
| Number of patients | 287 |
| Low complement | 50% (78/157) |
| ANAs | 89% (255/287) |
| Anti-dsDNA antibodies | 74% (206/278) |
| Anti-Sm antibodies | 13% (37/278) |
| Anti-SSA antibodies | 25% (69/270) |
| Anti-SSB antibodies | 10% (27/270) |
| APL antibodies | 19% (51/272) |
| Rheumatoid factor | 84% (241/287) |
| Anti-CCP antibodies | 58% (126/218) |

ANA: Anti-nuclear antibodies; dsDNA: Double-stranded DNA;
APL: anti-phospholipid.

Antonini et al. Rhupus: A Systematic Literature Review. Autoimmun Rev. 2020.

Frade-Sosa et al. A Comparative Study on Clinical and Serological Characteristics Between Patients With Rhupus and Those With Systemic Lupus Erythematosus and Rheumatoid Arthritis. Lupus 2020.



Type III Hypersensitivity Reactions to Biologics

Anti-drug antibodies (IgG or IgM) → immune complexes → complement activation

Timing: Delayed, **typically 5–14 days** (earlier with re-exposure)

Clinic: Serum sickness–like reaction - **Fever, arthralgia/arthritis, rash** – rarely other organ manifestations

Risk factors: **Chimeric/humanized mAbs**, long dosing intervals, pre-existing autoimmune disease

Diagnosis: Clinical timing, ↑ CRP/ESR, anti-drug antibodies

Management

- Systemic corticosteroids, NSAIDS
- Consider drug discontinuation & switch to another biologic whenever possible
- Alternatively rechallenge using desensitization protocols

Khan et al. Drug allergy: A 2022 practice parameter update. J Allergy Clin Immunol. 2022.



Key Learnings

1. **Hydroxychloroquine can cause retinal damage (dose- and duration-dependent)**
2. **Flares of autoimmunity may occur after HCQ discontinuation, even after years of stable disease**
3. **Diagnostic reassessment is essential in refractory cases**
4. **Rhupus syndrome is characterized by erosive RA-like arthritis and SLE features**
5. **Type III Hypersensitivity is a delayed immune complex-mediated reaction**
 - Discontinuation and switch to an alternative biologic should be considered whenever feasible