Management of IRIS

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Table 2: Major and Minor Presentations of IRIS	
Underlying Opportunistic Infection	**IRIS Signs/Symptoms**
Major Presentations	
Tuberculosis (TB)	• Patients responding to TB treatment may have worsening of pulmonary symptoms, X-ray findings that suggest worsening of TB disease, enlarging lymph nodes causing airway obstruction, or meningeal symptoms. • Enlarging tuberculoma or pericardial effusions have been described. • TB-IRIS can also result in acute hepatitis, which may be difficult to distinguish from medication-induced toxicity. • Undiagnosed multidrug-resistant TB can mimic TB-IRIS and should be ruled out in patients whose symptoms worsen while receiving first-line TB treatment.
Mycobacterium avium complex (MAC)	• May present as pulmonary disease or systemic inflammation that is indistinguishable from active MAC. • Atypical presentations, such as localized lymphadenitis or endobronchial mass lesions, may occur; osteomyelitis is an atypical late manifestation. • Patients with MAC-IRIS may not be bacteremic and may have no known history of a MAC diagnosis.
Cryptococcal meningitis	Usually presents as worsening of meningitis symptoms, including possible rapid hearing and/or vision loss, ataxia, and/or elevated intracranial pressure.
Cytomegalovirus (CMV) retinitis	• Presents as retinitis, vitritis, or uveitis (variable timing, with median time to immune reconstitution vitritis 20 weeks after ART initiation in one study): – Retinitis is inflammation that is usually at the site of previous CMV retinitis lesions. – Uveitis and vitritis are the presence of inflammatory cells in the eye as a result of IRIS and may help to distinguish IRIS from active CMV retinitis. • CMV-IRIS in the eye can cause rapid and permanent vision loss.
Hepatitis B or C virus	• Transient elevations in transaminases may occur after initiation of ART with immune reconstitution and can be difficult to distinguish from drug-induced hepatitis. • Hepatic flares are usually mild and self-limited but can result in decompensation in someone with pre-existing cirrhosis.
Progressive multifocal leukoencephalopathy (PML)	PML lesions may be unmasked or worsen and could appear as new or worsening focal neurologic deficits or lesions on MRI.
Kaposi's sarcoma (KS)	• Presents as worsening of KS. • Cutaneous lesions are the most common presentation; other signs include lymphedema and oral, gastric, lung, genital, or conjunctival lesions. • Fatal cases of KS-IRIS have been reported.
Cerebral toxoplasmosis	May present as a cerebral abscess (also known as toxoplasmosis encephalitis) or, rarely, diffuse encephalitis or chorioretinitis.
Histoplasmosis	May present as mucocutaneous lesions, disseminated disease, or fever without localizing symptoms.
Autoimmune diseases	• Pre-existing sarcoidosis may be exacerbated. • Late presentations of Grave's disease have been reported 8 to 33 months after ART initiation.
Minor Presentations	
Herpes simplex virus (HSV) and varicella zoster virus (VZV)	• HSV and VZV can reactivate after initiation of ART, even in patients without previously diagnosed disease. • Presentations are usually similar to non-IRIS disease; however, IRIS may worsen a patient's symptoms.
Mpox	Several case reports have described worsening of previously crusted lesions, the appearance of new lesions, and necrosis after ART initiation.
Nonspecific dermatologic complications	A number of dermatologic manifestations, such as folliculitis and oral and genital warts, may appear or worsen during immune reconstitution.
Abbreviations: ART, antiretroviral therapy; IRIS, immune reconstitution inflammatory syndrome; MRI, magnetic resonance imaging.	