

Case Study

Immune Reconstitution Inflammatory Syndrome (IRIS) Presenting As Bilateral Severe Granulomatous Sclerouveitis In A HIV-Infected Patient With Mycobacterium Tuberculosis Infection: A Case Report

ABSTRACT

Aim: To report a case of Tuberculosis associated immune reconstitution inflammatory syndrome (IRIS) presenting as rapid progressive bilateral severe granulomatous sclerouveitis

Presentation of Case: A 26-year-old HIV-infected male who was on antiretroviral therapy (ART) 3 months prior to presentation complained of left acute painful red eye with blurring of vision and floaters. There was bilateral eyes severe granulomatous uveitis with left eye necrotizing scleritis. There was also cervical neck swelling that was positive for *Mycobacterium tuberculosis*. He initially responded well to antituberculosis therapy together with topical steroids and antibiotics, oral NSAIDs and antiretroviral therapy. His vision deteriorated after 6 weeks of treatment. He developed bilateral severe sclerouveitis and marked sclera thinning with self-sealed perforation on the left eye. A diagnosis of IRIS was made and systemic steroid was added. Ocular inflammation was controlled but his left vision remained poor due to perforated extensive necrotizing scleritis, seclusio pupillae and cataract.

Discussion: Intraocular TB may be presented with aggressive rapid progression of the disease in HIV –infected patients. ART-associated TB is seen in HIV patients who developed TB after initiation of ART. Subset of ART-associated TB could be due to unmasking IRIS. Patients who were treated for opportunistic infection after ART may develop paradoxical IRIS.

Conclusion: Bilateral severe granulomatous uveitis with necrotizing scleritis is a rare manifestation of TB-related IRIS in a HIV patient. It is a potential sight threatening condition.

A close monitoring for development of IRIS during treatment of HIV is essential to minimize the morbidity.

Keywords: *Immune reconstitution inflammatory syndrome, Tuberculosis, granulomatous uveitis, necrotizing scleritis*

1. INTRODUCTION

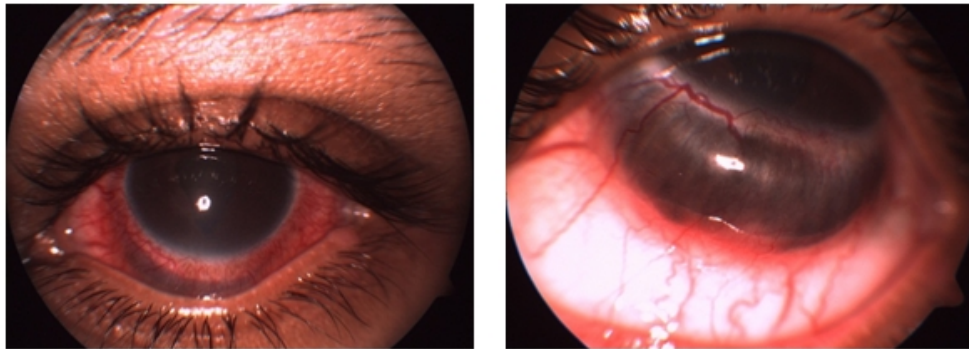
Immune reconstitution inflammatory syndrome (IRIS) is an important complication following the management of HIV infected patients on highly active antiretroviral therapy (ART) [1-2]. Infections from bacteria, virus and fungi, autoimmune disease and malignancy are associated with IRIS [1-4]. Tuberculosis (TB) is commonly associated with IRIS in HIV patients. The incidence ranges from 11 to 45% and is associated with extrapulmonary involvement [5-9]. Ocular manifestation of IRIS is rare. Most of the reported ocular cases were immune restoration uveitis or vitritis associated with cytomegalovirus infection [10, 11]. We report a rare case of IRIS associated with TB presenting as bilateral severe necrotizing granulomatous sclerouveitis.

2. CASE REPORT

A 26-year-old HIV infected man who was recently started on 3 months duration of antiretroviral therapy (ART), presented with sudden left painful red eye for 2 weeks. It was associated with blurring of vision and floaters. However, there were no flashes of light. He denied any history of headache, nausea and vomiting. He had no history suggestive of tuberculosis infection prior to ART. He had recently been treated for herpes varicella infection. His latest CD4 count prior to ART was 104/ul.

On examination, the best corrected right vision was 6/9 and left eye was counting fingers. Both eyes were congested and inflamed. Anterior segment examination of both eyes showed presence of mutton-fat keratic precipitates, extensive posterior synechiae and anterior chamber cells, which was more severe in left eye. There was active necrotizing anterior scleritis involving the inferonasal quadrant of the left eye (Figure 1). Both lenses were clear. There was mild vitreous inflammation in right eye. Left eye vitritis was more severe causing poor visualization of fundus. Intraocular pressures were normal in both eyes. Right funduscopy showed hyperemic optic disc with presence of choroiditis, but there was no evidence of choroidal tubercle. B scan of the left eye revealed moderate vitreous opacities. Fundus fluorescein angiogram of the right eye showed an inflamed optic disc, vasculitis, choroiditis and cystoid macular edema.

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52 Figure 1: Severe granulomatous sclerouveitis with inferior thinning in left eye

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54 He was initially diagnosed with bilateral granulomatous panuveitis secondary to herpetic
 55 infection due to negative TB workout. Intravenous acyclovir was started but there was no
 56 clinical improvement after 2 weeks of treatment. A cervical lymph node was found and was
 57 proven positive for *Mycobacterium tuberculosis* following biopsy. Mantoux test was then
 58 performed which was positive and the erythrocyte sedimentation rate (ESR) was raised at
 59 98mm/hour. The diagnosis was revised as presumed intraocular TB. Systemic
 60 antituberculous therapy was initiated together with topical steroids, topical antibiotics and
 61 oral NSAIDS. ART was continued.

62

63 There was remarkable improvement in the ocular inflammation. However, upon review 6
 64 weeks later the ocular condition had deteriorated drastically. He claimed to have maintained
 65 compliance to the treatment. His right eye vision was reduced to counting fingers and left
 66 eye was only perceptive to light. There was worsening of necrotizing scleritis with scleral
 67 thinning in both eyes. There was also intense intraocular inflammation of both eyes with the
 68 presence of fibrin. There was marked scleral thinning with a self-sealed perforation on the
 69 left eye (Figure 2). The anterior chamber was shallower with seclusio pupillae on the left eye.
 70 Both corneas were edematous and hazy with raised intraocular pressures. There was no
 71 view of the fundi. Systemic examination revealed a new lymph node enlargement which was
 72 negative for *Mycobacterium tuberculosis* based on biopsy. Other septic workout was
 73 negative, and there was no evidence suggestive of toxicity to antituberculous therapy.

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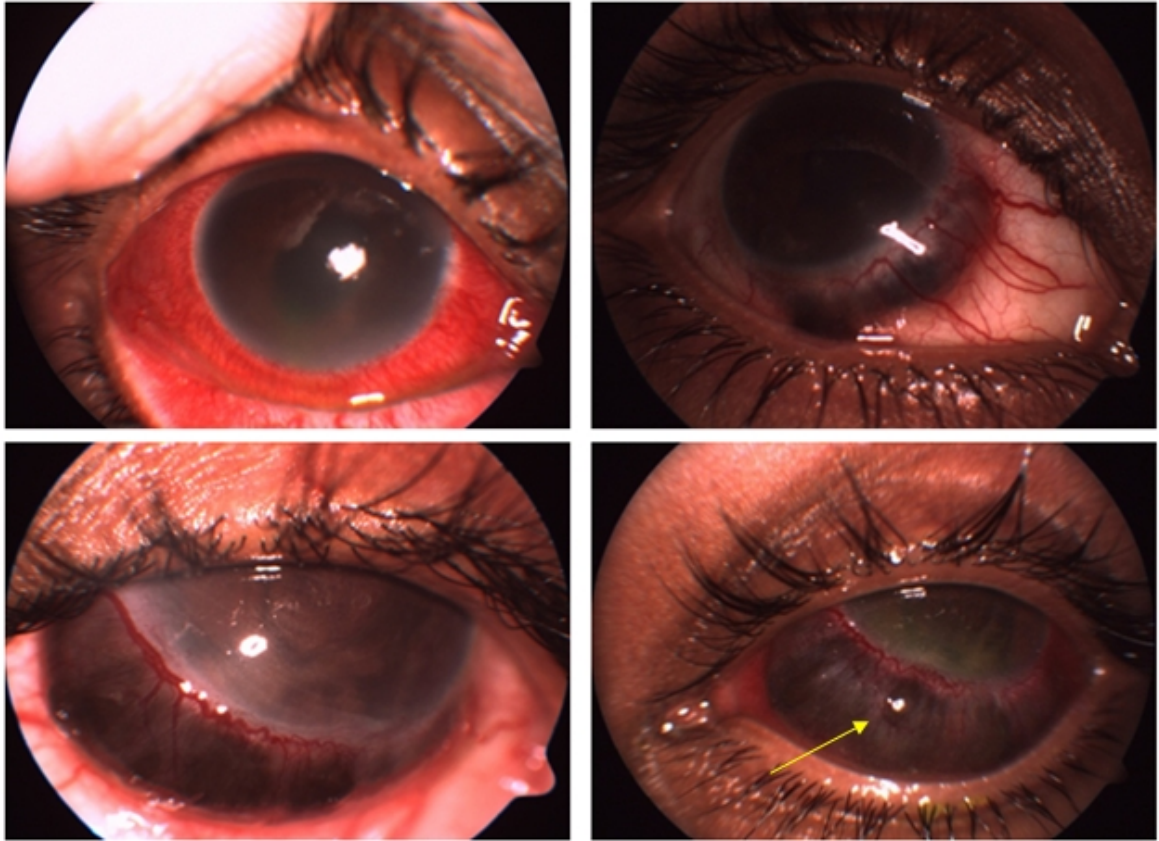
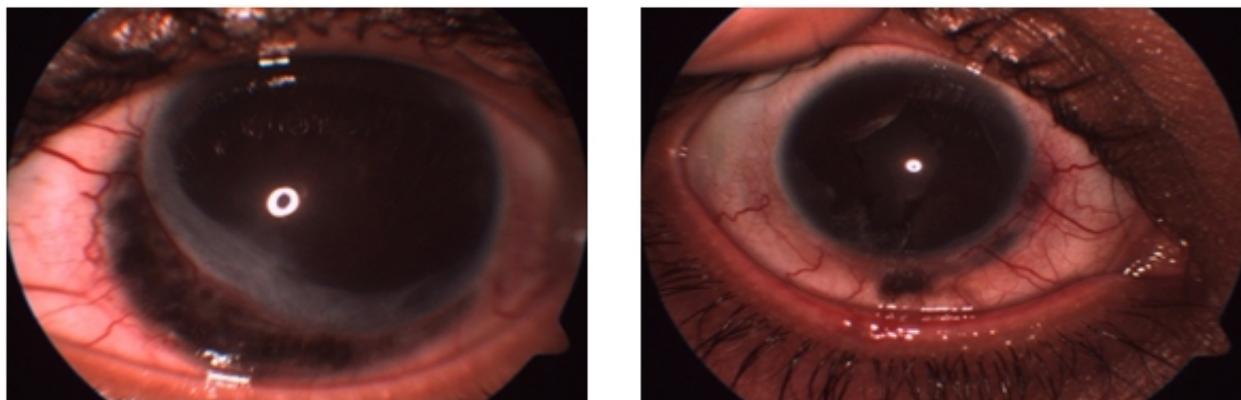


Figure 2: Worsening of granulomatous sclerouveitis with inferior thinning of bilateral eyes. Upper panels: Right eye. Lower: Left eye with self-sealed perforation and seclusio pupillae.

In view of the paradoxical worsening of the ocular inflammation, a diagnosis of IRIS was made. Systemic steroids were immediately commenced together with continuation of antiretroviral, antituberculosis and topical medications. His visual acuity of the right eye improved to 6/9 after six months of treatment. However, the left vision remained hand movements even with well controlled ocular inflammation (Figure 3). The left eye anterior chamber remained shallow with presence of seclusio pupillae. There was presence of cataractous lens in the left eye.



89 Figure 3: Improved ocular inflammation after 6 months of follow up. Left: Left eye; Right: Right eye

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91 3. DISCUSSION

92 Antiretroviral therapy (ART)-associated TB is term used to define HIV patients who are
 93 diagnosed with TB infection after initiation of ART [9]. It is believed to be due to on-going
 94 persistent immunodeficiency or due to rapid restoration of immune response against TB after
 95 commencement of antiretroviral therapy [9]. Clinical presentation of intraocular TB varies
 96 widely from anterior and posterior segment involvement even to neurophthalmic involvement
 97 [12, 13]. It is often misdiagnosed due to lack of uniformity of diagnosis criteria, and difficulty
 98 in retrieving ocular samples [14]. It is even more challenging in HIV patient as in this case
 99 [15, 16]. The presence of history of herpetic varicella infection masked the potential of
 100 intraocular TB. Lack of laboratory evidences further complicates the matters initially.

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102 Moreover, herpetic and TB sclerouveitis are both responsible for granulomatous type of
 103 intraocular inflammation. The differentiation of the clinical presentation was further
 104 complicated by poor fundus visualization. Patients with HIV infection may present with
 105 aggressive ocular TB infection despite previous adequate antituberculosis therapy [15].
 106 However, in this case there was no history of previous tuberculosis infection. Negative
 107 Mantoux test is not surprising in HIV patients. It is reported smear positivity rates in HIV
 108 infected patients are poor [16, 17]. During the treatment of ART, the rapid restoration of
 109 immune system leads to increase immune responses to specific antigen that may cause
 110 positivity in Mantoux test [17].

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112 The rapid aggressive presentation of ocular inflammation after the commencement of anti-
 113 TB treatment and ART in the present case leads to the diagnosis of IRIS. To the best of our
 114 knowledge, this is the first case of severe granulomatous uveitis and necrotising scleritis in

115 IRIS. IRIS is postulated to result from rapid restoration of the immune response towards the
 116 pathogen and presents with a paradoxical clinical presentation following initiation of
 117 antiretroviral therapy [1, 2, 9]. It can either present as “unmasking” of an occult opportunistic
 118 infection, or “paradoxical” worsening of the symptoms, which can present at the original site
 119 or new body site [6, 9]. The presence of tubercular lymphadenitis increases the index of
 120 suspicious of IRIS. Extrapulmonary TB, for example tubercular lymphadenitis is reported as
 121 one of the risk factors of developing IRIS [8, 9, 18]. In this patient, the latest CD4 count at
 122 initiation of ART was slightly more than 100/ μ l. IRIS is reported to develop in cases with
 123 CD4 less than 100/ μ l [1, 2, 18, 19]. This patient had received ART at the age of 26. Ratnam
 124 et al reported the major predictor for IRIS development were younger age at initiation of ART
 125 [20]. This is due to the greater restoration of immune system in younger patients. This
 126 patient developed “unmasking” TB-associated IRIS 3 months post initiation of ART. TB
 127 therapy was then started at 3 months of ART. Early period of ART and short interval
 128 between ART and treatment of opportunistic infection as seen in this patients are another
 129 recognized risk factors for IRIS development [18-20].

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131 Rapid aggressive ocular presentation with impending ocular perforation is really alarming in
 132 this patient. High index of suspicious is important to initiate appropriate treatment and arrest
 133 further morbidity for this young HIV patient. Until now, there is no prospective consensus in
 134 managing IRIS [1, 2, 7]. In severe cases, systemic immunosuppressive corticosteroid is
 135 recommended with continuation of treatment for opportunistic infection and HAART therapy
 136 [2, 7]. Vision is important to improve quality of life even in HIV patients.

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138 **4. CONCLUSION**

139 Detection and management of TB associated IRIS is challenging. The dramatic sight-
 140 threatening complications of IRIS may pose a challenge in the management of intraocular
 141 TB. High index of suspicion is warranted to minimize the morbidity and mortality due to TB
 142 associated IRIS.

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144 **COMPETING INTERESTS**

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146 Authors have declared that no competing interests exist.

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149 **CONSENT**

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151 All authors declare that 'written informed consent was obtained from the patient for
152 publication of this case report and accompanying images.

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154 **ETHICAL APPROVAL**

155

156 Non applicable

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