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Recurrent Giant Molluscum Contagiosum Immune Reconstitution Inflammatory Syndrome (IRIS) after Initiation of Antiretroviral Therapy in an HIV-infected South African Male

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Summary

We describe an HIV-infected South African male who experienced two distinct episodes of disseminated giant molluscum contagiosum (MC) immune reconstitution inflammatory syndrome (IRIS) over a 6-year period. The first episode of MC-IRIS occurred with rapid virologic suppression following antiretroviral therapy (ART) initiation. The second episode occurred during a rapid increase in CD4 cells following stable viral suppression with second-line ART. His MC lesions then completely resolved during a reduction in CD4 count, despite maintaining virologic suppression. Nearly one year after the resolution of his giant MC-IRIS lesions, he maintains an undetectable viral load, but his level of immune deficiency has not improved. In the absence of well-controlled therapeutic trials, MC-IRIS presents important management challenges.

Keywords

Molluscum contagiosum; HIV/AIDS, Immune reconstitution inflammatory syndrome (IRIS); antiretroviral therapy (ART); South Africa

INTRODUCTION

Molluscum contagiosum (MC) is a possible manifestation of immune reconstitution inflammatory syndrome (IRIS) following the initiation of antiretroviral therapy (ART) in HIV-infected persons.¹⁻³ ART alone is generally sufficient to resolve MC-IRIS lesions,⁴⁻⁶ but there is a paucity of information about the ideal management of MC-IRIS among those who do not demonstrate good immunologic recovery. We describe a case of recurrent giant

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MC-IRIS observed over a 6-year period in an HIV-infected male, which eventually resolved with sustained virologic suppression.

CASE

A 25-year-old South African male with a productive cough was diagnosed with HIV-1 (CD4 25/mm³) and sputum smear-positive pulmonary tuberculosis in April 2006. He received 4-drug anti-tubercular therapy (isoniazid, rifampin, ethambutol, pyrazinamide) for 6 months. One year later, his HIV-1 RNA was >100,000 copies/ml, and he initiated antiretroviral therapy with stavudine, lamivudine, and nevirapine. Within 6 months, he developed large nodular, umbilicated lesions on his face, trunk, extremities, and genitals, but sparing his back. His CD4 count was 8/mm³; HIV-1 RNA was <40 copies/ml (Figure 1). He was clinically diagnosed with unmasking cutaneous MC-IRIS, and started on topical salicylic acid and mupirocin ointment to prevent bacterial superinfection.

Over the next 2 years, virologic suppression was sustained, but his CD4 count remained low (range 5-22/mm³) and MC lesions persisted (Figure 2). He showed no response to a 12-month trial of topical imiquimod, during which topical salicylic acid and mupirocin were stopped. Surgery was deferred due to his low CD4 count and he declined photodynamic therapy due to cost. Since an initial skin biopsy was inconclusive, repeat skin biopsies were performed in April 2010 and confirmed MC.

In September 2010, he was switched to second-line ART with tenofovir, lamivudine, and ritonavir-boosted lopinavir for virologic failure. He regained virologic suppression (<150 copies/ml) within 4 months. Between June and September 2011, his MC lesions markedly worsened and his CD4 count peaked at 131 /mm³. In September 2011, he presented with fever and worsening verrucous papular lesions appearing significantly larger, pinker, and more numerous than before (Figure 2). Several lesions had malodorous discharge of pus and blood suggesting secondary bacterial infection. He had enlarged bilateral inguinal lymph nodes and non-tender hepatomegaly. He was admitted for antibiotic therapy and intravenous fluids. During hospitalization, a comprehensive infection work-up was unrevealing. He was discharged 2 weeks later with a diagnosis of exacerbated giant MC secondary to paradoxical recurrent IRIS.

Since hospital discharge, he has maintained virologic suppression on protease inhibitor (PI)-based ART, but has not achieved immunologic recovery (CD4 range 20-39 cells/mm³). Over a follow-up period of 10 months, his extensive MC lesions gradually and completely resolved, leaving post-inflammatory pigmentation and some scarring (Figure 2). By January 2013, he was in good health; his HIV-1 RNA was <150 copies/ml and CD4 count was 20 cells/mm³.

DISCUSSION

Several case reports of MC-IRIS exist,⁷⁻⁹ but none have described recurrent MC-IRIS from both virologic suppression and acute immunologic reconstitution, both unmasking and paradoxical IRIS, or the complete resolution of MC lesions without immunologic recovery. IRIS can occur any time after ART initiation, and cases are typically diagnosed during a

rising CD4 cell count.¹⁰ A rapidly falling HIV viral load also predicts development of IRIS, and this has assumed a more prominent role in some IRIS definitions.^{7,10-12} Two forms of IRIS are recognized; unmasking IRIS involves the emergence of a pathogen or process following ART and paradoxical IRIS involves the clinical worsening of an existing pathogen or process following ART.⁷ Our patient demonstrated both forms at different time points against the same pathogen, which has not been previously reported.

Our patient experienced resolution of his MC lesions following a decline in his CD4 count to pre-ART levels. This observation makes for interesting speculation. First, the transient increase in CD4 cell count following initiation of potent PI-containing ART generated an immune response that initially led to an exacerbation of lesions, followed by gradual clearing of the pathogen. The concomitant rise of his CD4 cell percentage after PI-based ART initiation (1.7% to 6.3%) supports the possibility that he generated immune-mediated clearance of the MC virus, which led to the eventual resolution of his lesions. Second, the reduction of CD4 cells may have removed the inflammatory signals that were propagating paradoxical MC-IRIS. Third, the acute rise in CD4 count may have been related to his bacterial superinfection and elevated white blood cell count ($15.2 \times 10^9/L$), and played little role in the resolution of his MC lesions, suggesting an alternate pathway or natural resolution.

Disseminated giant or verrucous MC lesions are more common among HIV-infected men with low CD4 counts, and usually resolves with immunologic recovery of CD4 count >200 cells/mm³ following ART initiation.¹³⁻¹⁵ Therapeutic options for refractory MC are limited and largely based on anecdotal case reports. These include topical 3% cidofovir cream, photodynamic therapy with 5-aminolevulinic acid, and topical imiquimod.¹⁶⁻²⁰ Options were restricted in the management of our patient. The absence of well-controlled clinical trials makes treatment of refractory MC challenging, and more research is needed on the epidemiology and therapy of MC-IRIS.

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Figure 1.

Patient's HIV Viral Load and CD4 Count Measures from HIV Diagnosis to Present.

Figure 2. Photographic Appearance and Evolution of Molluscum Contagiosum in HIV-Associated Immune Reconstitution Inflammatory Syndrome

[Images A and B taken Sept. 2009 (CD4 22/mm³; viral load <20 copies/ml); Images C-F taken Oct. 2011 (CD4 131/mm³; viral load <40 copies/ml); Images G and H taken May 2012 (CD4 28/mm³; viral load <40 copies/ml); Images I and J taken Sept. 2012 (CD4 25/mm³; viral load <150 copies/ml)].