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Kaposi's sarcoma-associated immune reconstitution inflammatory syndrome (KS-IRIS) in Africa: initial findings from a prospective evaluation

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Background

Immune reconstitution inflammatory syndrome (IRIS) is a set of conditions, characterized by findings of inflammation, which occur in HIV-infected patients after initiation of antiretroviral therapy (ART). It is believed to result from an overly exuberant response to residual opportunistic pathogens by the newly reconstituted immune system. Specific manifestations of IRIS depend upon the pathogen being targeted, but among the variants of IRIS, Kaposi's sarcoma-associated IRIS (KS-IRIS) is one of the least understood – especially in resource-limited settings where KS is epidemic. Now that ART is becoming available in sub-Saharan Africa, we have hypothesized that KS-IRIS is likely to be most relevant in this region. This is because of the high prevalence of AIDS-related KS in sub-Saharan Africa (i.e., large number of patients with AIDS-KS initiating ART) and because of factors that theoretically may predispose to KS-IRIS, specifically higher KS lesion burden and lower pre-ART CD4+ T cell count.

Methods

In Kampala, Uganda, we studied the incidence and spectrum of KS-IRIS in a randomized trial for the initial therapy of AIDS-related KS. Participants without indications for chemotherapy were randomized to one of two different ART regimens and then evaluated every 4 weeks for 48 weeks with a questionnaire, physical examination, and digital photography to record signs and symptoms compatible with KS-IRIS. KS-IRIS was defined as development of a) any of the following in pre-existing KS lesions: swelling, pain or tenderness, paresthesia, erythema, or warmth; or b) not otherwise explained subcutaneous nodules, node enlargement, edema, or pleural effusion.

Results

Of the first 30 subjects evaluated, 17 (57%) exhibited ≥ 1 sign or symptom compatible with KS-IRIS. The most common finding was lesion swelling (43%), and there were several instances of dramatic lesion enlargement followed by spontaneous reduction (see Figures 1 and 2 from two subjects). Other manifestations included lesion pain or pares-thesia (33%), warmth or erythema (23%), femoral or inguinal node enlargement with scrotal swelling (n =

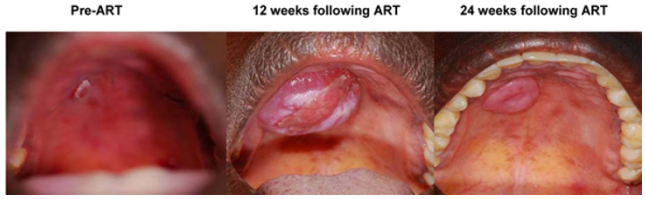

Figure 1

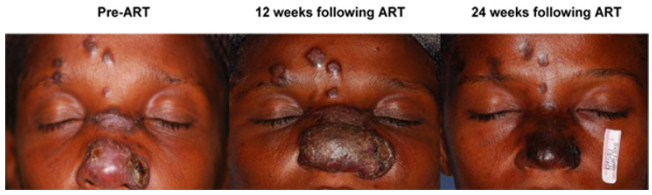

Figure 2

1), and pleural effusion (n = 1). The most fulminant KS-IRIS case featured diffuse lesion swelling and new diffuse subcutaneous nodules; death ensued but the causative role of KS-IRIS is unknown. Of the three participants with KS-IRIS that did not resolve spontaneously and who were given chemotherapy, two had a good response to liposomal doxorubicin.

Conclusion

In sub-Saharan Africa, KS-IRIS occurs at a clinically relevant frequency with a wide spectrum of manifestations. Many of the findings are difficult to distinguish in real time from natural KS progression, and even some of the most dramatic cases can be self-limiting. This, coupled with the general lack of effective chemotherapy for KS in resource-limited settings, makes patient management complicated when KS-IRIS is suspected. In this setting, diagnostic tests are thus urgently needed to distinguish IRIS-based disease from natural progression of KS.