Kaposi's Sarcoma in people living with HIV who are virally suppressed : A Case series

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Abstract

Background

Kaposi's sarcoma (KS) is an AIDS defining illness and, in most cases is related to immunosuppression, a low CD4 count and HIV viral replication. A decline in KS has been seen since the introduction and widespread use of effective antiretroviral therapy (ART). However KS is still a concern amongst people living with HIV (PLWH) who are fully virally suppressed and have a robust CD4 count ("Fully suppressed KS"). There are varying hypothesis for why this occurs including, chronic HHV8 antigen exposure, lower responses to HHV8 specific antigens and lower specific HHV8 CD8 T cells responses. A decrease in CD4/CD8 T cells has also been seen in these patients. Here we present a case series of three PLWH who developed KS while virally suppressed on antiretroviral therapy with robust CD4 counts.

Methods

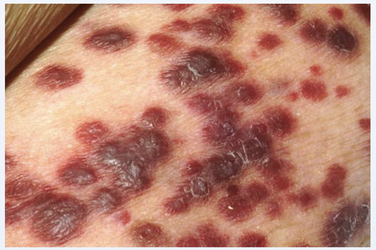
Approval was received from the research and innovation department in St James Hospital. Cases of KS were identified from the electronic patient record system (EPR). EPR was used to review the patients' records for year of HIV diagnosis, CD4 count at diagnosis, Year of KS diagnosis, CD4/CD8 ratio at KS diagnosis, ART regimens, viral suppression and medication adherence.

Results

Three patients within our cohort developed Kaposi sarcoma while virally suppressed. They all had robust CD4 counts between 800 – 1400 cell/mm3 , all patients had excellent adherence to ART and excellent viral control. All patients had cutaneous KS lesions, none had visceral involvement of KS. One patient had KS at diagnosis years earlier followed by 2 recurrences when virally suppressed. Two patients had a CD4/CD8 ratio >1 , one had a CD4/CD8 ratio <1.

Conclusion

KS in virally suppressed PLHIV is an emerging and important clinical entity. It is important to consider KS as a diagnosis even amongst virally suppressed patients. Further research and exploration of immunological pathways is important in learning more about this emerging clinical problem.



Aims

Kaposi sarcoma in virally suppressed individuals has recently been reported in the literature. More information is needed to assess the pathophysiology of KS in fully suppressed PLWH. Here we reviewed our cohort of patients to assess the number of patients with fully suppressed KS and to fully review their HIV history including previous and current antiretroviral therapy in order to add to the growing number of cases in the literature in the hope we will increase our understanding of this developing entity.

Methods

A list of patients with a diagnosis of Kaposi sarcoma was generated from the electronic patient record. A list of patients with HIV oncology issues was also reviewed. These cohorts were reviewed to find cases of "fully suppressed KS". EPR was then used to assess the year of HIV diagnosis, CD4 count at diagnosis, Year of KS diagnosis, CD4/CD8 ratio at KS diagnosis, ART regimens, viral suppression and medication adherence.

The research and innovation department in St James Hospital gave approval for the study to be carried out .

Results

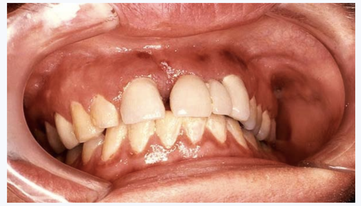
Out of a total of 76 charts reviewed 3 individuals were identified as having KS while fully suppressed on antiretroviral therapy. All were male.

Patient 1

Our first patient was diagnosed with HIV in 2006 and developed KS in 2014 at the age of 44. He identifies as MSM (men who have sex with men) and is from Central America.

His nadir CD4 count was 300 cell/mm3 and his CD4 count at KS diagnosis was 1365 cell/mm3 with a CD4/CD8 ratio of 1.05.

He was commenced on ART at diagnosis in 2006 with AZT/3TC/ABC and remained on this until he transferred his care out of our clinic in 2015.



He had cutaneous lesions only, no visceral involvement. He was treated with excision of the KS lesions.

He was noted to have excellent viral control across all of his clinic visits

Patient 2

The second patient was diagnosed with HIV in 2008 at which point he was also diagnosed with KS. However he again developed KS, despite viral suppression, in 2018 and 2021. He also identifies as MSM and is from South America. He was 45 and 47 years old at these diagnoses respectively.

His CD4 count at KS diagnosis in 2018 was 1262 cell/mm3 and in 2021 was 1022 cell/mm3 . His CD4/CD8 ratio in 2018 was 0.81 and in 2021 was 0.88.

He was commenced on ART at diagnosis in 2008 with AZT/3TC//LPVrit. He was subsequently switched to TDF/FTC/DTG in 2015 followed by a switch to TAF/FTC/DTG.

He also had cutaneous lesions only that were treated by excision (2018) and radiotherapy (2021).

He was also noted to have excellent viral control over the years

Patient 3

The third patient was diagnosed with HIV in 2008 and developed KS in 2020 at the age of 48. He identifies as MSM.

His nadir CD4 count was 423 cell/mm3 (15%) and his CD4 count at KS diagnosis was 811 cell/mm3 with a CD4/CD8 ratio of 1.45.

He had been commenced on ART at diagnosis in 2008 with TDF/FTC/EFV and has remained on this since.

He had cutaneous lesions only which were treated with radiotherapy.

Again he was noted to have excellent viral control at clinic visits.

Discussion

The overall incidence of KS has reduced with the widespread use of ART, however there are emerging reports of KS in patients with fully suppressed HIV.

There are varying hypothesis of why KS occurs in virally suppressed individuals; including chronic HHV8 exposure, leading to persistence of immune activation (1) . A loss of immune control by NK cells and T cells has also been suggested (1).

It is further postulated that T cells active against HHV8 undergo immune exhaustion (1). HHV8 associated CD8 T cells responses have been shown to be lower in patients with HHV8 associated KS and HIV than in those with asymptomatic HHV8 carriage (1) (2)

A decrease in CD4/CD8 ratio has been observed in patients with fully suppressed KS , however this has only been observed with 1 of our patients in this case series. A low CD4/CD8 ratio has been linked to T cell activation which would further add to the theory of immune exhaustion

Clinical forms of KS in these circumstances appear less aggressive than in those patients who are viraemic with low CD4 counts (1).This was seen in our case series, with patients having cutaneous lesions only and no visceral involvement. While initiation of ART has always been the first line treatment for KS, in patients with fully suppressed KS this leads to a therapeutic 'dead end' in patients already fully adherent to effective therapy(2).

Despite previous use of boosted protease inhibitor based treatment for KS, Lajuanie et al found there is no increased risk of KS in patients switched off a PI based regime to a non PI containing regime (3). In patients with KS, non PI based regimes have not shown to be inferior to PI based regimes (4).

In contrast to this there have been case reports of patients developing KS after switching from a PI based regimen to a integrase regimen. (6) (7)

Conclusions

KS remains the most common AIDS associated malignancy since the beginning of the pandemic. Despite advances in antiretroviral therapy we continue to see cases of KS even in PLWH who are fully adherent to their medications and virally suppressed. Further research including observational studies and case series are important in understanding this new entity. It is important to still consider KS in stable PLWH so that early histological diagnosis can be made and adjuvant treatment be considered.

References

1. Palich R, Makinson A, Veyri M, Guihot A, Valantin M, Brégigeon-Ronot S et al. Kaposi's Sarcoma in Virally Suppressed People Living with HIV: An Emerging Condition. Cancers. 2021;13(22):5702.

2. Royston L, Isnard S, Calmy A, Routy J. Kaposi sarcoma in ART-treated people living with HIV. AIDS. 2021;Publish Ahead of Print

3. Lajaunie R, Cuzin L, Palich R, Makinson A,, Bani- Sadr F,Duvivier C, Arvieux C et al. No increased risk of Kaposi sarcoma relapse in patients with controlled HIV-1 infection after switching protease inhibitor-based antiretroviral therapy. HIV Medicine. 2022; 23 (3):301-306.

4. Martinez V, Caumes E, Gambotti L, Ittah H, Morini J, Deleuze J et al. Remission from Kaposi's sarcoma on HAART is associated with suppression of HIV replication and is independent of protease inhibitor therapy. British Journal of Cancer. 2006;94(7):1000-1006.

5. Colafigli M, Ciccullo A, Borghetti A, Fanti I, Melis F, Modica S et al. Impact of Antiretroviral Therapy on the Risk of Recurrence in HIV-1 Infected Patients with Kaposi Sarcoma: A Multicenter Cohort Experience. Journal of Clinical Medicine. 2019;8(12):2062.

6. Simonetti F, Ricaboni D, Cattaneo D, Micheli V, Rusconi S, Gervasoni C. Relapse of Kaposi's Sarcoma and HHV-8 viremia in an HIV-infected patient switching from protease inhibitor to integrase inhibitor-based antiretroviral therapy. Journal of Clinical Virology. 2016;74:75-77.

7. 8. Philibert P, Chiche L, Caillères S, Allemand J, Rebaudet S, Delord M et al. HHV8 and Kaposi's sarcoma. AIDS. 2017;31(15):2167-2169.

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