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Chemotherapy-induced seizures: A rare case of paclitaxel-induced neurotoxicity at Chris Hani Baragwanath Oncology Centre

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Paclitaxel is widely used for advanced Kaposi sarcoma (KS) in resource-limited settings because of cost-effectiveness and proven efficacy. Neurotoxicity is recognised, but infusion-related seizures are exceedingly rare, particularly in human immunodeficiency virus (HIV)-positive patients. A 32-year-old HIV-positive male, virologically suppressed (CD4 450 cells/mm^3), presented with T1-stage nodular KS. Paclitaxel (120 mg/m^2) infusion induced a self-limiting generalised tonic-clonic seizure within 10 min. Despite a 20% dose reduction during the second cycle, a similar seizure recurred. Neuroimaging, cerebrospinal fluid analysis, and laboratory investigations were unremarkable. Electroencephalography was unavailable. Paclitaxel was discontinued; doxorubicin-based chemotherapy was initiated, with no further seizures and partial regression of lesions after two cycles.

Contribution: This case identifies paclitaxel-induced seizures as a rare adverse event in an HIV-positive patient, underscoring the need for vigilant infusion monitoring, prompt diagnostic exclusion of opportunistic causes, and individualised chemotherapy selection.

Keywords: South Africa; Chris Hani Baragwanath Hospital; Gauteng; Kaposi sarcoma; paclitaxel; neurotoxicity

Case summary

This is a case of a 32-year-old male from Soweto who was referred to our oncology unit for further management of his condition. He is known to be human immunodeficiency virus (HIV)-positive, virologically suppressed on first-line antiretroviral therapy, with a cluster of differentiation 4 (CD4) count of 450 cells/mm^3. The patient reported a 2-year history of right lower limb swelling, accompanied by violaceous plaques and areas of hyperpigmentation. A 2 mm punch biopsy confirmed nodular stage Kaposi sarcoma (KS), with a clinical staging of T1 according to the acquired immunodeficiency syndrome (AIDS) Clinical Trials Group (ACTG) criteria. Doppler ultrasound excluded the presence of a deep vein thrombosis. In accordance with local treatment protocols, he was initiated on single agent paclitaxel at 120 mg/m^2, with appropriate premedication administered prior to chemotherapy.

During the first infusion of paclitaxel, the patient experienced a generalised tonic-clonic seizure approximately 10 min into the infusion. At the time of the event, he was normoglycaemic and other vitals remained within normal limits. The seizure self-aborted and lasted less than 3 min. The patient made full recovery within an hour. He was subsequently admitted for observation and monitored for 24 h, during which no further seizure activity was witnessed.

Given the unclear aetiology of the initial seizure and need for ongoing treatment, the decision was made to cautiously rechallenge the patient during the second cycle with a 20% reduction of paclitaxel. Unfortunately, he developed a second seizure, similar to the first episode. He was evaluated with a contrast-enhanced computed tomography (CT) scan of the brain (Figure 1), and it revealed no intracranial abnormalities. Cerebrospinal fluid analysis and blood workup were all within normal limits. An electroencephalogram could not be obtained because of resource constraints.

Because of these recurrent infusion-associated seizures and absence of other identifiable triggers, paclitaxel was discontinued. For the third cycle, the patient was transitioned to doxorubicin-based chemotherapy following a normal baseline echocardiogram. He has since completed two cycles of this regimen without any further seizure activity and is tolerating treatment well.



CT, computed tomography.

FIGURE 1: CT – Brain imaging demonstrating no pathology.

Discussion

The management of AIDS-related KS is based on clinical staging.[1] However, in all patients, the aim is ameliorating the state of immunosuppression with combined antiretroviral therapy (cART) usage for 6–12 months with the lesions expected to reduce in size by at least 50%. Liposomal doxorubicin is the recommended first-line agent systemic chemotherapy agent; however, in the South African context, paclitaxel's cost-effectiveness and demonstrated efficacy make it an ideal option for first-line systemic treatment because of the high disease burden, provided patients are virally suppressed and compliant to their cART.[1] The mechanism of action of paclitaxel involves binding to microtubules, resulting in arrest of cell division and induction of apoptosis.[2] Another pro-apoptotic mechanism involves the generation of reactive oxygen species.[2] Because of the lipophilic nature of paclitaxel, it has a greater affinity for neural tissue, thus contributing to its known neurotoxic adverse effects. With reference to neural cells, it results in axonal degeneration, which manifests as peripheral neuropathy.[3,4] It has also been found to accumulate in the dorsal columns resulting in length-dependent sensory neuropathy because of symmetrical axonal death.[3,4] To our knowledge, no cases within the last 5 years reporting seizures in response to paclitaxel single agent therapy have been reported, especially in HIV-positive patients.

While HIV itself can cause seizures by causing direct damage to the brain,[5] the prognosis for people with seizures related to HIV has improved significantly with modern therapies. It largely depends on the underlying cause and the individual's response to treatment. There are various aetiologies related to seizures in the HIV population such as tuberculosis (TB) meningitis, other space occupying lesions such tuberculomas, toxoplasmosis, Cryptococcal Meningitis (CCM) and Herpes Viruses can lead to encephalitis and vasculitis.[6,7] Human immunodeficiency virus-Associated Neurocognitive Disorder (HAND) could be a consideration in advanced cases; however, motor and cognitive symptoms would be more pre-dominant.[5] Neoplasms in this population should always be considered as part of the differential diagnosis such as primary central nervous system lymphoma (PCNSL), which is often associated with the Epstein–Barr virus and can present as single or multiple brain lesions. Considering the hypercoagulable state seen in HIV, higher risk of cerebrovascular disease, including strokes, can be a direct cause of seizures.[5] In view of this, a thorough diagnostic workup was crucial in identifying the underlying cause. This included a detailed medical history, physical examination, and neuroimaging (contrasted CT brain) and a lumbar puncture, which all proved negative. A magnetic resonance imaging (MRI) and electroencephalogram were not performed because of cost restraints. Thus, the likely pathogenesis of the seizures in this patient was attributed to the paclitaxel infusion.

Alternative treatments to systemic chemotherapy include local treatment options such as intralesional chemotherapy with vinblastine, radiotherapy for symptomatic treatment, topical alitretinoin, topical imiquimod and cryotherapy. While these options offer effective indications, their use and patient response vary, requiring decisions to be based on expert experience and the individual patient's clinical profile.

Therefore, in the South African context, at Chris Hani Baragwanath Hospital, paclitaxel cost-effectiveness and demonstrated efficacy make it an ideal option for reaching more patients in populations facing a high disease burden as a first-line systemic treatment provided patients are virally suppressed and compliant with their cART.

Conclusion

We present a case of an HIV-positive patient with KS that developed recurrent seizures secondary to paclitaxel despite being rechallenged at a reduced dose at a slower infusion rate. While paclitaxel is an excellent systemic chemotherapy for stage T1 KS with superior outcomes, especially in resource-limited settings, paclitaxel has known neurotoxic side effects, emphasising the importance of patient monitoring during infusions. This case highlights the differential diagnosis of seizures in an immunocompromised patient, which is a common presentation in our patient population. These patients are at risk of concurrent opportunistic infection; thus, a guided workup is pivotal in avoiding misdiagnoses, and the importance of viral suppression is emphasised. The limitations in our case were limited access to MRI and an electroencephalogram at the time of seizures. However, with the change of therapy, the outcome of our patient was favourable, and the lesions are regressing on the new chemotherapy regimen.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

CRediT authorship contribution

Asma Adam: Methodology, Formal analysis, Investigation, Writing – original draft, Project administration, Resources, Writing – review & editing. Tivanya Pillay: Methodology, Formal analysis, Investigation, Writing – original draft, Project administration, Resources, Writing – review & editing. Rofhiwa T. Mathiba: Writing – review & editing, Supervision. All authors reviewed the article, contributed to the discussion of results, approved the final version for submission and publication, and take responsibility for the integrity of its findings.

Ethical considerations

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Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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