Recognition, Diagnosis and Therapeutic Approach to KSHV Inflammatory Cytokine Syndrome (KICS) and KSHV associated sequelae

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Background/Purpose: Kaposi sarcoma-associated herpesvirus (KSHV/HHV8) encodes genes that can mimic human oncogenes. Thus, KSHV is the primary aetiologic agent in three malignancies [KS, PEL and Multi-centric Castleman's disease (MCD)]. An additional association exists with the little-known clinical entity of KICS, which is characterized by multi-system involvement and features of systemic inflammation without biopsy features of MCD

Approach: A 46yo male was admitted with exertional dyspnoea and left lower-limb swelling. Relevant background included virally suppressed HIV on Biktarvy®, diagnosed seven months prior with delayed immune recovery [CD4+ 64 cells/µL (5%)] and extensive cutaneous Kaposi sarcoma (KS) in remission following six cycles of liposomal-doxorubicin. Initial evaluation revealed a recurrence of KS lesions, critical hyponatraemia, significant anasarca, pleural effusions and inguinal lymphadenopathy. Whilst a diagnostic workup was being conducted, he experienced a precipitous decline with progressive respiratory failure, diuresis resistant pleural effusions, anuric renal impairment, profound vasoplegia and bi-cytopaenia. A microbiological evaluation was unrevealing, and steroids were commenced empirically for possible immune reconstitution inflammatory syndrome (KS-IRIS).

Outcomes/Impact: Subsequent imaging and immune-histopathological assessments performed on pleural fluid and lymph nodes revealed concurrent diagnoses of relapsed KS and Primary Effusion Lymphoma (PEL) whilst also fulfilling the diagnostic criteria for KSHV Inflammatory Cytokine Syndrome (KICS). He was commenced on R-CHOP and Daratumumab and displayed a significant metabolic response to chemotherapy. Despite this, his clinical state failed to improve with persistent multi-organ dysfunction, leading to his death forty-seven days into admission.

Innovation and Significance: The recognition and workup of patients with suspected PEL or KICS can be challenging. In addition, these entities have poor median overall survival rates, with KICS carrying the worst prognosis. Whilst treatment options continue to evolve for KS; there remains variable guidance in the management of PEL and KICS. We discuss the clinical manifestations, time course, diagnostics and therapeutic options for KSHV associated sequelae with a focus on KICS.

Disclosure of Interest Statement: None