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**Kaposi's sarcoma-associated herpesvirus gene sequences are detectable at low copy number in primary amyloidosis.**

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Primary amyloidosis (AL), like multiple myeloma (MM), results from a clonal proliferation of plasma cells. Recent detection of Kaposi's sarcoma-associated herpesvirus (KSHV) gene sequences in MM patients, although controversial, suggested that KSHV may also be present in AL. In the present study, we assayed for KSHV gene sequences in patients with primary AL independently in 2 laboratories. Nested polymerase chain reaction (PCR) was performed on DNA isolated from 21 bone marrow (BM) core biopsy samples to amplify orf26 and orf72, 2 regions of the KSHV genome. Eighteen of 21 (86%) BM core biopsy samples were KSHV PCR positive. BM aspirates from 16 of these 21 AL patients were cultured for 4-6 weeks to generate long term bone marrow stromal cells (LT-BMSCs), and 13 of 16 (81%) LT-BMSCs were also KSHV PCR positive. Results in all but 1 sample were consistent in the 2 laboratories. Sequencing of the PCR products in the 2 laboratories confirmed 94-98% and 95-98% homology to the published orf 26 and orf 72 KSHV gene sequences respectively, with interpatient base pair differences. Despite the presence of KSHV gene sequences, only 4/18 (22%) KSHV PCR positive patients demonstrated KSHV lytic antibodies by immunoblot assay. A sensitive assay performed on the BCBL-1 cell line confirmed the presence of KSHV at a very low copy number in AL. PCR using patient specific light chain gene primers also amplified DNA isolated from 2 AL BM core biopsies and 3 AL LT-BMSCs which were KSHV PCR positive, suggesting the presence of clonotypic cells. Our results therefore demonstrate KSHV gene sequences albeit at a very low copy number in the majority of BM core biopsies and LT-BMSCs from AL patients, and serological responses in only a minority of cases. Ongoing studies to identify viral transcripts and gene products will determine the biological relevance of KSHV in AL disease pathogenesis.