Detection of Human Herpesvirus-8 DNA in Bone Marrow Biopsies From Patients With Multiple Myeloma and Waldenström’s Macroglobulinemia

To the Editor:

Said et al recently showed that human herpesvirus-8 (HHV-8) DNA could be amplified from bone marrow biopsies of patients with multiple myeloma (MM). These data reinforce their initial findings in cultured bone marrow cells and rule out the possibility that detection of HHV-8 in cultured dendritic cells may be artifactual. However, the biology of HHV-8 in MM remains controversial because serologic studies are negative, although antibodies are usually detectable in other HHV-8–associated disease’s such as Kaposi’s sarcoma or cavity-based lymphomas. We obtained data in 10 patients with myeloma that support the findings of Berenson’s group. In addition, we studied 10 patients with Waldenström’s macroglobulinemia (WM).

Polymerase chain reaction (PCR) amplification was made with KS330233-specific primers on DNA extracted from paraffin-embedded bone marrow sections. We obtained fragments of the expected size that hybridized with an internal probe in 5 out of 10 bone marrow biopsies from patients with MM (Fig 1). Furthermore, there were different point mutations in the two PCR products that were sequenced as compared with the original sequence. These data make PCR artifacts unlikely.

No amplification was noted with DNA from 10 normal bone marrow samples and 9 out of 10 bone marrow biopsies from patients with non-Hodgkin’s lymphomas (the one positive case presented with follicular lymphoma). In vitro long-term bone marrow cultures from 3 MM patients were also studied; 2 of 3 were positive for HHV-8 sequences. HHV-8 PCR performed on bone marrow biopsy from the negative sample was also negative. Interestingly, no antibodies to lytic HHV-8 antigens were detectable by immunofluorescence in the sera of MM patients or controls.

Detection of HHV-8 DNA on bone marrow biopsies may be less sensitive than other techniques; nevertheless, it shows that HHV-8 infection exists in vivo and offers the opportunity to determine the onset and fate of HHV-8 infection in MM patients.

These results prompted us to similarly study bone marrow biopsies from patients with WM. Amplification of HHV-8 sequences was obtained in 6 out of 10 samples studied (fig 1). Again no antibodies to HHV-8 were detected in WM patients’ sera. Interestingly, the pathogenesis of WM involves interleukin-6, a cytokine with a viral HHV-8 homolog that may play a key role in the development of MM as postulated by Said et al.

Félix Agbalika
Xavier Mariette
Jean-Pierre Morleau
Jean-Paul Fernand
Jean-Claude Brouet
Department of Microbiology
Blood Bank and Department of Clinical Immuno-Hematology
Hôpital Saint-Louis
Paris, France

References


Pancytopenia Secondary to Oxalosis in a 23-Year-Old Woman

To the Editor:

A 23-year-old woman described left-sided abdominal discomfort and stomach bloating for 4 months. Her past medical history was significant for recurrent kidney stones, which began at the age of 9 years. She developed progressive renal failure secondary to nephrolithiasis and for the past 3 years had required hemodialysis. Five months ago she developed a painless hard mass on the distal phalanx of her left fifth finger; the mass was biopsied. The biopsy specimen was consistent with granulomatous dermatitis with birefringent crystals in the dermis. The finger mass continued to enlarge, and a repeat biopsy was taken. On physical examination there was massive hepatosplenomegaly with no lymphadenopathy or peripheral edema. There was a nontender, firm, flesh-colored nodule on her left fifth distal phalanx. Laboratory studies showed pancytopenia with a hemoglobin level of 6.3/dL, a white blood cell count of 2,600/µL, and a platelet count of 106,000/µL. Values for serum aspartate transaminase, alanine transaminase, and bilirubin were normal. Her peripheral-blood film had numerous teardrop forms compatible with myelophthisis. A bone marrow biopsy revealed extensive crystal deposition with almost complete obliteration of hematopoietic cells (Fig 1). Infrared spectroscopy performed on the bone marrow biopsy and finger mass identified calcium oxalate monohydrate crystals.

Conditions associated with calcium oxalate crystal deposition include primary and familial hyperoxaluria, a diet rich in oxalate, increased absorption or production of oxalate, and decreased excretion of oxalate as seen in renal failure. The most likely cause of calcium oxalate deposition in this patient was primary hyperoxaluria. To confirm the diagnosis a liver biopsy was obtained and showed markedly reduced alanine:glyoxylate aminotransferase (AGT) activity consistent with primary hyperoxaluria type 1 (PH1). PH1 is inherited as an autosomal recessive disorder characterized by hyperoxaluria, calcium oxalate urinary lithiasis in childhood, nephrocalcinosis, and renal failure. Once renal failure occurs, blood oxalate concentrations rise and precipitation occurs throughout the body. This stage is termed “oxalosis.” Extrarenal manifestations of oxalosis are becoming more apparent as hemodialysis is being used to treat end-stage renal failure in PH1. We corroborate that pancytopenia is a complication of oxalosis, as manifested by this patient, and believe it indicates the need for aggressive therapeutic intervention.

Therapy for oxalosis should be pursued early in disease because oxalate deposited in tissues can be resorbed once normal production and urinary excretion are maintained. Exogenous oxalate ingestion should be avoided in PH1, although only 10% of excreted oxalate is from dietary origin. The remainder of excreted oxalate comes from endogenous production. Definitive treatment of PH1 requires AGT enzyme replacement, which can be achieved with liver transplantation. This ultimately reduces endogenous production of oxalate and in combination with renal transplantation has been successful in treating PH1 patients with irreversible kidney failure. The patient was referred for evaluation of a kidney-liver transplant and remains on hemodialysis.

Matthew J. Walter
Chi V. Dang
Johns Hopkins University
School of Medicine
Baltimore, MD

REFERENCES

Detection of Human Herpesvirus-8 DNA in Bone Marrow Biopsies From Patients With Multiple Myeloma and Waldenström’s Macroglobulinemia

Félix Agbalika, Xavier Mariette, Jean-Pierre Marolleau, Jean-Paul Fermand and Jean-Claude Brouet