CASE 8

Submitted by: Adekunle M. Adesina, M.D. and William W. Pendlebury, M.D.
Department of Pathology (Neuropathology)
University of Vermont
Burlington, Vermont 05405

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Clinical Abstract:

The patient is a two year, eight month old girl who was normal until two months of age when she developed a persistant fever associated with hepatosplenomegaly, anemia and elevated liver function tests. Blood, CSF and urine cultures were negative for bacteria, virus and fungus. Nasopharyngeal viral cultures were also negative. There was no serologic or culture evidence for hepatitis A or B, cytomegalovirus or toxoplasmosis. Epstein-Barr virus (EBV) IGG was elevated at 40 dilutions, and a presumptive diagnosis of mononucleosis was made.

Because of persistant hepatosplenomegaly and a repeat, negative evaluation for EBV, the patient underwent liver biopsy at five months of age. Light microscopy disclosed lymphoproliferative infiltrates that by immunostaining consisted of T helper lymphocytes. A bone marrow aspirate showed dysplastic erythropoiesis and erythrophagocytosis. Evaluation (Western Blot and EIA) for HIV infection was negative. The patient was begun on chemotherapy with a response indicated by decreased liver and spleen size.

Despite continued chemotherapy, the patient developed recurrent hepatosplenomegaly and hypersplenism. At thirteen months of age, splenectomy, mesenteric lymph node biopsy and repeat liver biopsy were performed. Examination of the spleen disclosed patchy infiltrates of large lymphocytes with morphology identical to those seen previously in the liver. Probing of DNA extracted from the spleen showed evidence of T_{Beta} cell receptor gene rearrangement.

Subsequently, chemotherapy (Vincristine, Cytoxan, Adriamycin and Prednisone) was continued and the child remained well until twenty-one months of age when she developed anorexia, somnolence, irritability and left sided facial weakness. CSF examination disclosed no cells, normal protein and glucose, and negative viral, bacterial and fungal cultures. CT scan showed bilateral cerebellar calcifications and a large area of low density in the left cerebellar hemisphere. With contrast, there were areas of enhancement in both cerebellar hemispheres. The patient underwent left cerebellar biopsy and since surgery has remained lethargic and asocial. There has been no change in the size of the cerebellar lesions and recent repeat CSF analysis was completely negative. She has shown no evidence of systemic viral infection, including on repeat serum testing for HIV and EBV. A consultant at a second institution has suggested the possibility of virus-associated hemophagocytic syndrome to explain the systemic disease.

Material submitted: One H & E slide from the left cerebellar lesion

Points for discussion: 1. Diagnosis
2. Relationship of CNS lesion to systemic process