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Clinical History:

The patient was a 58 year old woman, previously healthy, who developed weakness and persistent sinusitis two weeks prior to hospital admission. She was treated with antibiotics, but developed nausea, vomiting, posterior cervical lymphadenopathy, and diarrhea. Changes in mental status prompted an emergency room evaluation (3/24/05). CT scan of the brain was negative, as was examination of CSF, including PCR for viruses. A CBC showed lymphocytosis (absolute lymphocyte count 6580/ul). She was discharged with a diagnosis of “viral illness”, but admitted to the hospital one day later (3/25/05) with confusion, fatigue, declining mental status, and urinary and fecal incontinence. Initial evaluation included an abdominal CT scan that revealed splenomegaly, and a brain MRI scan that revealed multiple, ovoid, non-enhancing abnormalities in cerebral and cerebellar white matter. A lupus inhibitor was positive. Two days later (3/27/05), a right frontal brain biopsy was performed revealing proteinaceous deposition. On 3/29/05, serum protein electrophoresis with immunofixation showed free monoclonal kappa light chains, and a systemic analysis for cryoglobulin was negative. All studies for infectious etiologies were negative. A subsequent bone marrow specimen with flow cytometric analysis showed malignant non-Hodgkin’s lymphoma, B-cell type with a non-specific immunophenotype. Cytogenetic analysis of the marrow specimen was performed. The patient was treated with Rituximab, high-dose steroids, and plasmapheresis. On 3/30/05, a repeat brain MRI showed progression of the intracranial lesions prompting the patient to be started on Cyclophosphamide. Ultimately there was no response to chemotherapy, and the patient became comatose. Repeat analysis of CSF was negative for malignant cells or infection. She died on 4/10/05, approximately 30 days after the onset of her illness.

Necropsy Findings:

The general autopsy showed pulmonary congestion; hilar, mediastinal and abdominal lymphadenopathy; and splenomegaly. Microscopic examination revealed a non-Hodgkin’s lymphoma involving spleen, lymph nodes, bone marrow, and lungs.
Additional information about the lymphoma, and gross and microscopic features of the brain, will be presented at the slide session.

Material submitted: One H&E section of cerebral hemisphere with lesion; one unstained slide.

Points for discussion: 1. Diagnosis
                      2. Pathogenesis