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CASE 2008 - 7

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Clinical History: The patient was a 56-year-old man with a history of polycythemia vera, diagnosed in 1986. He underwent splenectomy in 1993. His last bone marrow biopsy, in 01/2007, showed hypercellular bone marrow with multilineage dysplasia, megakaryocytic hyperplasia and mild fibrosis. He also had a history of coronary artery disease, hypertension, dyslipidemia, depression, oral herpes, and squamous cell carcinoma removed from his upper extremities.

In 02/2007, he experienced several weeks of right sided headaches, nausea and vomiting. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) studies of the head were interpreted as normal. A temporal artery biopsy showed no active arteritis. He was treated empirically with prednisone.

After discharge from the hospital in 02/07, his nausea and vomiting continued. He additionally developed progressive numbness that began in the right side of his face and his right arm, then spread to involve his left leg, right leg, and right body. He lost the ability to ambulate, requiring the use of a walker and then a wheelchair. Upon admission on 3/22/07, MRI of the spine showed ring enhancing spinal lesions at C2 and T11-T12. He was treated empirically with broad spectrum antibiotics (ceftriaxone and vancomycin), antiviral medication (valcyclovir and acyclovir), and antifungal agents (voriconazole and posizonazole). Cytological examination of a cerebrospinal fluid (CSF) sample taken on 3/22/07 showed a mixture of atypical lymphoid cells, small lymphocytes and monocytes. PCR (polymerase chain reaction) testing of the CSF detected the presence of Epstein-Barr virus; all CSF cultures were negative. Flow cytometry performed on CSF taken on 3/26/07 showed no evidence of malignancy. CT of the body performed on 3/28/07 showed a 1.3 x 1.5 cm soft tissue mass within the superior segment of the left lower lobe. Positron emission tomography (PET) showed avid FDG uptake within the lung mass. A CT guided fine needle aspiration biopsy of the lung lesion was performed on 3/30/07; cytological examination of the aspirate yielded the diagnosis 'suspicious for malignant neoplasm,' based on identification of scattered cells with markedly enlarged nuclei and prominent nucleoli.

The patient experienced respiratory decompensation and was treated with heparin for a suspected pulmonary embolus. Although a lower extremity Doppler study performed on 4/02/07 identified a deep venous thrombus, a CT study of the chest did not identify a pulmonary embolus. Echocardiography showed no evidence of cardiac dysfunction. Treatment with high dose steroids did not produce a clinical response.

He received radiation therapy to the spine for presumed malignancy beginning on 4/05/07. He deteriorated further and on 04/10/07 an MRI study of the brain and spinal cord showed multiple new, vaguely enhancing, T2 intense lesions in the brain. The largest lesion (1.1 x 2.6 x 1 cm) was located in the right frontal lobe; smaller lesions were identified in the right frontal lobe, right medial occipital lobe, left temporal lobe, left frontal periventricular white matter, right medulla, and left cerebellum. The cerebellar lesion showed evidence of leptomeningeal involvement. The previously identified thoracic spine lesion had increased in craniocaudal extent, and demonstrated associated edema. The patient died on 4/12/07.

Necropsy Findings: General autopsy revealed a 2.5 cm ulcer on the dorsum of the right hand, two ill-defined white nodules in the left lower lobe of the lung, and a pulmonary embolus in the right lower lobe. The brain weighed 1440 g. Coronal sections of the hemispheres showed several lesions: a 1 x 2 x 1.5 cm lesion in the right frontal lobe, with a soft, gray-tan cortical component and a dusky white matter component with petechial hemorrhages; a smaller lesion in the right frontal cortex, with mildly soft and pink superficial white matter; and a focus of mild reddish mottling in the right temporal pole. Axial sections of the brainstem showed subtle duskiness and sparse, mild petechial hemorrhages in the right dorsal quadrant, extending from the right superior colliculus, through the right dorsal pons, and through the rostral medulla. Axial sections of the spinal cord were unremarkable.

Material Submitted: 1 H&E slide

Points for discussion: 1) Diagnosis 2) Pathogenesis