The Bing-Neel Syndrome: Clinical observations on nine new cases and the literature

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Waldenström's macroglobulinemia can involve the dura, leptomeninges, brain, and CSF. We attempt to provide diagnostic criteria for this involvement which has been termed Bing-Neel Syndrome [BNS]. We review 31 examples of BNS including those with (Group A) evidence of lymphoplasmacytoid (LMP) cells within the CNS or CSF and (Group B) those without apparent LMP cells . A Median of 36 months separated WM diagnosis from BNS diagnosis but 26% of patients had coincident occurrence of WM and BNS. Fifty-five percent of BNS cases had received WM therapy to stabilize IgM levels in two-thirds of these patients. At the time of BNS nine patients had stable WM at and sixty one percent revealed BNS symptoms in the setting of progressive WM. Cortical dysfunction (42%) was manifest as memory deficits and behavioral changes and correlated with MRI white matter changes (54%). MRI FLAIR changes without cortical dysfunction appeared in five BNS patients (16%) . A total of sixty-five percent of BNS had some abnormality on brain MRI: including Flair changes, enhancing lesions (7 of 31), or both. Five patients harbored white matter changes which were read as "non-specific" changes. Isolated brain lesions were observed in 10 patients. A smaller group of BNS patients (26%) developed visual field deficits, optic nerve lesions, cranial nerve sensory changes. Spinal cord syndromes appeared in 67% of BNS patients and included cauda equina difficulties, and disorders of the meninges, dura, and intrinsic spinal cord. Thirty-five percent of BNS patients had a diagnostic biopsy of brain or dura or meninges with LMP cells staining for IgM. But there is an under-appreciation of BNS as few patients (16%) had CSF studies performed. When studied, the CSF contained over 3 leukocytes/mm^3 but few examples exist of appropriate molecular and immunohistochemical analyses including evaluation of CD19 and/or CD20 bearing cells (n = 6 BNS patients). CSF contained no LMP cells in eight patients of whom four had diagnostic brain or dural biopsies with demonstrated WM cells. Four patients with acellular CSF did not undergo biopsy.

Treatment responses provided improvement in forty-two percent of patients wth sustained response from 6 months to 4 years. Three non-responders succumbed within 8 months. Nine patients died four months after PR or PD.

Since the epinomonic reports of Bing and Neel and collaborators (Bing and Neel, 1936), the diagnosis "BNS" has been applied without discretion to many central neurologic conditions in WM patients. We provide criteria for the diagnosis of BNS with LMP infiltrates as well as for those lacking CSF LMP cells for whom brain IgM deposits may be responsible for white matter lesions. The diagnostic criteria, in the setting of a relevant clinical history and staging of WM, depend upon CSF flow cytometry and/or immunohistochemistry and light chain quantification, and contrast-enhanced MRI.